Risk Factors Comparison 2024-02-27 to 2023-02-27 Form: 10-K

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An investment in our stock involves risks. You should carefully read this entire report and consider the following uncertainties and risks, which may adversely affect our business, financial condition or results of operations, along with all of the other information included in our other filings with the SEC, before making an investment decision regarding our common stock.
Risks Relating to Our Business ~~Risks Relating to COVID- 19 Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by the effects of the ongoing COVID- 19 pandemic on us or on third parties with whom we conduct business, including without limitation our development partners, manufacturers, CROs, and others, as well as on the regulatory and government agencies with whom we work. The global COVID- 19 pandemic continues to affect the United States and global economies, and could cause disruptions to our business, operations, and clinical development or commercialization plans and timelines, as well as the business and operations of third parties with whom we conduct business. For example, government orders and evolving business policies and procedures have impacted and may continue to impact, among other things: (1) our personnel and those of third parties on whom we rely, including our development partners (such as Torii), manufacturers, CROs, and others; (2) the conduct of our current and future clinical trials and commercial interactions; and (3) the operations of the FDA, EMA, PMDA, and other health and governmental authorities, which could result in delays of reviews and approvals, including as we continue to expand internationally and bring ORLADEYO to additional global markets. If our operations or those of third parties with whom we conduct business are impaired or curtailed as a result of these events, the development and commercialization of our products and product candidates could be stopped or delayed, or the costs of such development and commercialization activities could increase, any of which could have a material adverse impact on our business. For example, our suppliers or other vendors may be unable to meet their obligations to us or perform their services as expected as a result of the COVID- 19 pandemic or other health epidemics. In such circumstances, we may not be able to enter into arrangements with alternative suppliers or vendors or do so on commercially reasonable terms or in a timely manner. Such delays could adversely impact our ability to meet our desired clinical development and any commercialization timelines. Although we carefully manage our relationships with our suppliers and vendors, there can be no assurance that we will not encounter challenges or delays in the future or that these challenges or delays will not have an adverse impact on our business, financial condition and prospects. In addition, our clinical trials have been and may continue to be affected by the COVID- 19 pandemic. For example, the acceleration of COVID- 19 slowed the startup of the inadequate C5 responder cohorts in our complement oral Factor D program and, as a result, delayed the reporting of related data in 2020. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID- 19 pandemic or concerns among patients about participating in clinical trials during a pandemic. Some patients may have difficulty following certain aspects of clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our inability to successfully recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID- 19 or experience additional restrictions by their institutions, city, or state could adversely impact our clinical trial operations. If global health concerns prevent the FDA, EMA, PMDA or other regulatory authorities from conducting their inspections, reviews, or other regulatory activities, it could significantly impact the ability of such authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business and clinical development and commercialization plans and timelines. Where possible and practical, we continue to provide work- from- home flexibility for our employees, which could negatively impact productivity, disrupt our business and delay our clinical programs and timelines. In addition, we are a government contractor, and as such, we are subject to the federal COVID- 19 safety protocols. We cannot accurately predict the impact on operations of any return- to- the- office plan, nor of the federal COVID- 19 safety protocols on our business or on third parties with whom we conduct business. Our business may be negatively impacted in the event that large numbers of employees or key employees do not comply with these protocols. These and similar, and perhaps more severe, disruptions to our operations could negatively impact our business, operating results and financial condition. The spread of COVID- 19, which has caused a broad impact globally, could also materially affect our access to capital. While the future economic impact brought by, and the duration of, COVID- 19 may be difficult to assess or predict, the pandemic could result in further significant disruption of global financial markets, reducing our ability to access the equity or debt capital markets or obtain other sources of capital, which could negatively affect our liquidity. In addition, a recession or market correction could materially affect our business and the value of our common stock. The global pandemic continues to evolve, with the ultimate impact of the COVID- 19 pandemic or a similar health epidemic being uncertain and subject to change. These effects could be material, and we will continue to monitor the COVID- 19 situation closely. We do not yet know the full extent and magnitude of the impacts that COVID- 19 has had or will have on our business, the healthcare system, the pharmaceutical industry, or the global economy. In addition, the COVID- 19 pandemic could have the effect of heightening many of the other risks described below.~~
Financial and Liquidity Risks We have incurred losses since our inception ~~, expect to continue to incur such losses,~~ and may never be profitable. Since our inception, we have not achieved sustained profitability. **Our expectations** ~~We expect to incur additional losses for the foreseeable future, and our losses could increase~~ as **to when we may achieve profitability may change based upon our ability to execute our commercialization goals and operational initiatives and whether** ~~our~~ **or** ~~research~~ **not the assumptions underlying our projected revenues** and **expenses are correct** ~~development efforts and commercial activities progress~~ . ~~We expect that such losses will fluctuate~~ **Our beliefs and projections regarding the attainment of our financial goals may differ** from ~~quarter to quarter~~ **actual results**

based on market factors like competition, patient and ~~that losses~~ **physician acceptance of our products, reimbursement levels, or on our ability to execute our operational** and ~~fluctuations may be substantial~~ **budget plans, including management' s ability to properly forecast our capital allocation needs** . To ~~become~~ **achieve and maintain** ~~profitable~~ **profitability** , we, or our collaborative partners, must successfully manufacture and develop products and product candidates, receive regulatory approvals, and successfully commercialize our products and / or enter into profitable commercialization arrangements with other parties. ~~It could take longer than expected before we receive, or we may never receive, significant revenue from any current or future license agreements or significant revenues directly from product sales.~~ Even if we are able to successfully commercialize our existing products, or to develop or otherwise acquire new commercially viable products, certain obligations we have to third parties, including, without limitation, our obligation to pay RPI and OMERS, as applicable, royalties on certain revenues from ORLADEYO and BCX10013 under the Royalty Purchase Agreements, may reduce the profitability of such products. Because of the numerous risks and uncertainties associated with developing our product candidates, launching new products, and their potential for commercialization, we are unable to predict the extent of any future losses. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we are unable to achieve and sustain profitability **on our anticipated timeline, or at all** , the market value of our common stock will likely decline. We may need to raise additional capital in the future. If we are unable to raise capital ~~as~~ **if** and when needed, we may need to adjust our operations. We have sustained operating losses for the majority of our corporate history and expect that our **total** ~~2023~~ **2024** expenses will exceed our **total** ~~2023~~ **2024** revenues. We expect to continue to incur operating losses and negative cash flows unless and until revenues reach a level sufficient to support ongoing operations. ~~In~~ **Even if we are able to achieve profitability, in** order to continue future operations, progress our drug discovery and development programs, and commercialize our current products and product candidates, we may be required to raise additional capital **in the future** . In addition to seeking strategic partnerships and transactions, we may access the equity or debt markets, incur additional borrowings, pursue royalty or other monetization transactions, or seek other sources of funding to meet liquidity needs at any time, including to take advantage of attractive opportunities in the capital markets. Additional funding, whether through additional sales of securities, additional borrowings, royalty or other monetization transactions, collaborative arrangements with partners, ~~including corporate partners such as Torii,~~ or from other sources, may not be available **if or** when needed or in a form or on terms acceptable to us. The issuance of preferred or common stock or convertible securities, with terms and prices significantly more favorable than those of our currently outstanding common stock, could have the effect of diluting or adversely affecting the holdings or rights of our existing stockholders. Additional borrowings may subject us to more restrictive covenants than are currently applicable to us under ~~our Credit~~ **the Pharmakon Loan** Agreement ~~with Athyrium Opportunities III Co- Invest 1 LP~~ (~~" Athyrium " and such agreement,~~ as **defined below** ~~amended, the " Credit Agreement "~~). In addition, collaborative arrangements may require us to transfer certain material rights to our corporate partners. Insufficient funds or lack of an acceptable partnership may require us to delay, scale- back or eliminate certain of our research and development programs. See " Risks Relating to Our Business — Risks Relating to Drug Development and Commercialization — If we fail to obtain additional financing or acceptable partnership arrangements ~~as~~ **if** and when needed, we may be unable to complete the development and commercialization of our products and product candidates or continue operations " in this section for further discussion of the capital requirements for our development and commercialization efforts. Our liquidity needs will largely be determined by the success of operations in regard to the commercialization of our products, particularly ORLADEYO, ~~and~~ the progression of our product candidates in the future **, and our ability to execute our budget plans** . Our **current** plans for managing our liquidity needs primarily include controlling the timing and spending on our research and development programs ~~,~~ ~~raising additional funds as discussed herein,~~ and commercializing our approved products. See " Management' s Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources " in Part II, Item 7 of this report for additional information about our liquidity needs, capital requirements, potential funding alternatives, and adequacy of available funds. There can be no assurance that any of our plans will be successful or that additional capital will be available to us on reasonable terms, or at all, ~~when~~ **if** needed. If we are unable to obtain sufficient additional capital ~~as~~ **if** and when needed, we may be forced to adjust or curtail our operations; delay, reduce, or stop ongoing clinical trials or commercialization efforts; cease operations altogether; or file for bankruptcy. Our success depends upon our ability to manage our product candidate pipeline, advance our product candidates through the various stages of development, especially through the clinical trial process, and to receive regulatory approvals for the commercial sale of our product candidates. The success of our business depends upon our ability to manage our product candidate pipeline, including through expanding the pipeline, as appropriate, through our internal identification and discovery of product candidates or otherwise in- licensing or acquiring products or product candidates and integrating them into our business effectively and efficiently; advancing our product candidates through the various stages of development; and receiving regulatory approvals for the commercial sale of our product candidates. Identifying, selecting, and in- licensing or acquiring products or product candidates requires substantial expense and technical and financial expertise, and if we are unable to effectively manage our pipeline ~~and~~ **or** integrate viable products or product candidates into our business on acceptable terms, or at all, our business and drug development efforts ~~would~~ **could** suffer. To receive the regulatory approvals necessary for the commercial sale of our product candidates, we or our partners must demonstrate through preclinical studies and clinical trials that each product candidate is safe and effective. The development process and related regulatory process are complex and uncertain. The preclinical and clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy and safety, failure to demonstrate adequate benefit- risk balance, failure to achieve a commercially attractive and competitive product label, failure to achieve approval in commercially attractive indications, the occurrence of adverse events that are severe or medically or commercially unacceptable, our or our partners' failure to comply with trial protocols, applicable regulatory requirements, or industry standards, or a determination by the FDA or any comparable foreign regulatory authority that a product candidate may not

continue development or be approved in accordance with our development plans or at all. We cannot guarantee that any preclinical studies and clinical trials will be conducted as planned or completed on schedule, if at all, or that the results of such trials will be sufficient to support regulatory approval for our product candidates. Progression of our product candidates through the clinical development process is dependent upon our trials indicating that our product candidates have adequate safety and efficacy in the patients being treated by achieving pre- determined safety and efficacy endpoints according to the clinical trial protocols, **as well as** ~~and~~ **an** adequate benefit- risk profile. Failure to achieve any of these endpoints or to show adequate benefit- risk profile in any of our programs, including our complement program (inclusive of BCX10013) and our other rare disease product candidates **(including the additional therapies in our pipeline described in " Management' s Discussion and Analysis of Financial Condition and Results of Operations — Overview — Recent Developments " in Part II, Item 7 of this report)** , could result in delays in or modifications to our trials or require the performance of additional unplanned trials. For example, ~~recent~~ dose- related observations in an ongoing BCX10013 nonclinical study ~~will~~ **reported in 2023** ~~delay~~ **delayed** the clinical program. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a benefit- risk perspective. Product candidates that initially show promise in clinical or preclinical testing could later be found to be associated with or to cause undesirable or unexpected side effects that could result in substantial modifications or delays in the development plans for our product candidates, significant unexpected costs, or the termination of programs, such as we experienced with BCX9930 in 2022 prior to discontinuing its development later that year. In addition, the development plans for our product candidates, including our clinical trials (~~including for~~ **inclusive of** BCX10013), may not be adequately designed or executed, which could negatively affect the outcome and analysis of study results. Because of the cost and duration of clinical trials, we have decided in the past, and may in the future decide, to discontinue development of product candidates for various reasons, including, but not limited to, that they are unlikely to show favorable results in clinical trials, unlikely to help advance a product to the point of a meaningful collaboration, or unlikely to have reasonable commercial potential. Undesirable or inconclusive data in our preclinical studies and clinical trials or side effects in humans could result in the FDA or foreign regulatory authorities (including, e. g., the EMA, the MHLW or the **United Kingdom' s Medicines and Healthcare products Regulatory Agency ("** MHRA **")**) refusing to approve a product candidate for any targeted indications or imposing restrictions or warnings that could impact development or the ultimate commercial viability of a product candidate. In addition, the FDA or foreign regulatory authorities may determine that study data from our product candidates necessitates additional studies or study designs which differ from our planned development strategy, and such regulatory authorities may also require patient monitoring and testing or may implement restrictions or other conditions on our development activities, any of which could materially impact the cost and timing of our planned development strategy. We, our partners, the FDA, or foreign regulatory authorities have previously, and may again in the future, pause enrollment in, suspend **,** or terminate clinical trials at any time if we or they believe the trial participants face unacceptable health risks. Our ability to complete the clinical development process successfully is dependent upon many factors, including, but not limited to: • our or our partners' ability to secure suitable clinical sites and investigators and to enroll and maintain an adequate number of patients on a timely basis or at all; • patients that enroll in a clinical trial may not comply with the clinical trial ~~protocol~~ **protocols** or maintain contact with investigators to provide complete data during and after treatment; • our product candidates may not prove to be either safe or effective **for our targeted indications, or at all,** or may produce unfavorable or inconclusive results; • we or our partners may decide, or be required by regulatory authorities, to pause enrollment in, suspend **,** or terminate clinical research for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate, noncompliance with regulatory requirements or their standards of conduct, or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate; • regulatory authorities may disagree with our or our partners' clinical trial protocols or our or their interpretation of data from preclinical studies and clinical trials; • clinical protocols or study procedures may not be adequately designed or followed by the investigators; • formulation improvements may not work as expected, which could negatively impact commercial demand for our product candidates; • regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third- party manufacturers with which we or our partners enter into agreements for clinical and commercial supplies; • the supply or quantity of raw materials or manufactured product candidates or other materials necessary to conduct development activities may be insufficient, inadequate, or unavailable at an acceptable cost, and we or our partners may experience interruptions in supply; • our or our partners' development plans may be delayed or changed as a result of changes in development strategy, the impact of new or different regulations, requirements, and guidelines, or other unexpected events or conditions; • the cost of preclinical studies and clinical trials may be greater than we anticipate; • we or our third- party contractors, including those manufacturing our product candidates or components or ingredients thereof, or conducting clinical trials or laboratory testing on our or our partners' behalf, may fail to comply with regulatory requirements and industry standards or meet contractual obligations in a timely manner or at all; and • the impact of ~~the ongoing~~ **any global health pandemic, such as** COVID- 19 ~~pandemic~~ **,** on one or more of the foregoing factors. Clinical trials are lengthy and expensive. Many of the factors listed above could result in increased clinical development costs or longer clinical development times for any of our programs. We and our partners incur substantial expense for, and devote significant time to, preclinical testing and clinical trials, yet we cannot be certain that the tests and trials will ever result in the commercial sale of a product. Even if we or our partners successfully complete clinical trials for our product candidates, we or our partners might not file the required regulatory submissions in a timely manner or may not receive regulatory approval for the product candidates, which in either case would adversely impact or preclude our ability to generate any revenues from product sales or licensing arrangements. In addition, any product candidate, if approved, may be subject to restrictions on labeling, marketing, distribution, prescribing, and use, which

could adversely impact the sales of such product. If our development collaborations with third parties, such as our development partners, contractors and contract research organizations, fail, the development of our product candidates will be delayed or stopped. We rely heavily upon third parties for many important stages of our product candidate development, including, but not limited to: • discovery of natural proteins that cause or enable biological reactions necessary for the progression of the disease or disorder ~~, called enzyme targets~~ ; • execution of certain pharmacology preclinical studies and late- stage development for our compounds and product candidates; • management of our phase 1, 2 and 3 clinical trials, including medical monitoring, laboratory testing, and data management; • execution of toxicology studies that may be required to obtain approval for our product candidates; • formulation improvement strategies and methods; • manufacturing the starting materials and drug substance required to formulate our products and the product candidates to be used in our clinical trials, toxicology studies and any potential commercial product; and • management of certain regulatory interactions outside of the United States. Our failure to engage in successful collaborations at any one of these stages would greatly impact our business. If we do not license ~~enzyme~~ **protein** targets or inhibitors from academic institutions or from other biotechnology companies on acceptable terms, or at all, our drug development efforts ~~would~~ **could** suffer. Similarly, if the contract research organizations or third- party contractors that conduct our initial or late- stage clinical trials, conduct our toxicology or other studies, manufacture our starting materials, drug substance and product candidates, provide laboratory testing or other services **(including clinical operation services)** in connection with our clinical trials **, provide medical writing services** , or assist with our regulatory function breach their obligations to us, perform their services inconsistent with industry standards, or fail to comply with regulatory requirements, this would delay or prevent both the development of our product candidates and the availability of any potential commercial product. If we lose our relationship with any one or more of these parties, we could experience a significant delay in both identifying another comparable provider and then contracting for its services. We may be unable to retain an alternative provider on reasonable terms, if at all. Even if we locate an alternative provider, it is likely that this provider may need additional time to respond to our needs and may not provide the same type or level of service as the original provider. In addition, any provider that we retain will be subject to applicable FDA current Good Laboratory Practices, cGMP, and current Good Clinical Practices, and comparable foreign standards. We do not have control over compliance with these regulations by these providers. Consequently, if these practices and standards are not adhered to by these providers, the development and commercialization of our product candidates could be delayed. If any of the foregoing risks is realized, our business, financial condition and results of operations could be materially adversely affected. If we fail to obtain additional financing or acceptable partnership arrangements ~~as~~ **if** and when needed, we may be unable to complete the development and commercialization of our products and product candidates or continue operations. As our programs advance, our costs **could** ~~are likely to~~ increase. Our current and planned discovery, development, approval, and commercialization efforts ~~will~~ **may** require significant capital. Our expenses, revenues and cash utilization rate could vary significantly depending on many factors, including: our ability to effectively manage our product candidate pipeline; our ability to obtain regulatory approvals for our product candidates ~~, including BCX10013~~ ; our ability to maintain regulatory approvals for, successfully commercialize, and achieve market acceptance of our products, including ORLADEYO; our ability to raise additional capital **if needed; our ability to secure partnerships with third parties for our product candidates when deemed advisable (such as for the potential out- licensing of the late- stage development and commercialization of BCX10013)** ; the amount of funding we receive from partnerships with third parties for the development and commercialization of our products and product candidates ~~(including our collaboration with Torii)~~ ; the commercial success of our products achieved by our partners; the progress and results of our current and proposed clinical trials for our product candidates; and the progress made in the manufacture of our lead products and the progression of our other programs. In order to continue future operations, progress our drug discovery and development programs, and commercialize our current products and product candidates, we may be required to raise additional capital. Our ability to raise additional capital as and when needed, or at all, may be limited and may greatly depend upon our success in commercializing and achieving market acceptance of ORLADEYO and the success of our current drug development programs, including the progress, timeline and ultimate outcome of the development programs (including, but not limited to, formulation progress, long- term human safety studies, clinical trial investigations, and carcinogenicity, drug- drug interaction, toxicity, or other required studies) for our complement program ~~(including BCX10013)~~ for diseases of the complement system and other rare disease product candidates **(including the additional therapies in our pipeline described in " Management' s Discussion and Analysis of Financial Condition and Results of Operations — Overview — Recent Developments " in Part II, Item 7 of this report)** , as well as any post- approval studies for our products. In addition, constriction and volatility in the equity and debt markets, including as a result of the impacts of **inflation, increased interest rates, disruption or instability in the banking industry, geopolitical instability, or public health emergencies such as the** COVID- 19 **pandemic** ~~, rising inflation or increased interest rates~~ , may restrict our future flexibility to raise capital **if and** when such needs arise. See " Risks Relating to Our Business — Financial and Liquidity Risks — We may need to raise additional capital in the future. If we are unable to raise capital ~~as~~ **if** and when needed, we may need to adjust our operations " in this section and " Management' s Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources " in Part II, Item 7 of this report for additional information about our liquidity risks and capital requirements. Furthermore, we have exposure to many different industries, financing partners and counterparties, including commercial banks, investment banks and partners (which include investors, licensing partners, distribution partners, and others), which may be unstable or may become unstable in the current economic and political environment, including as a result of the impacts of **inflation, increased interest rates, disruption or instability in the banking industry, a potential U. S. Government shutdown, the upcoming presidential election in the United States, geopolitical instability (including the Ukraine- Russia and Israel- Hamas conflicts or rising tensions between China and Taiwan), or public health emergencies such as the** COVID- 19 **pandemic** ~~, rising inflation, increased interest rates, or the conflict in Ukraine~~ . Any such instability may impact these parties' ability to fulfill contractual obligations to us, or it might

limit or place burdensome conditions upon future transactions with us. Also, it is possible that suppliers may be negatively impacted. Any such unfavorable outcomes in our current programs or unfavorable economic conditions have in the past and could again place severe downward pressure on the price of our common stock and may decrease opportunities to raise capital in the capital or credit markets, and further could reduce the return available on invested corporate cash, which, if severe and sustained, could have a material and adverse impact on our results of operations and cash flows and limit our ability to continue development and commercialization of our products and product candidates. If we or our partners do not obtain regulatory approvals for our product candidates or maintain regulatory approvals for our products, we or our partners will not be able to commercialize and sell these products and potential products, which would significantly harm our business because we will receive no revenue. We or our partners must obtain regulatory approvals before marketing or selling our products. If the FDA or a comparable foreign regulatory authority delays or denies regulatory approval of one of our product candidates, or revokes approval of a previously approved product, we would be unable to market or sell the product in the applicable jurisdiction and would not receive revenue from sales or licensing arrangements related thereto, which could have a material and adverse impact on our business. The process of preparing for and obtaining regulatory approval in any jurisdiction may be lengthy and expensive, and approval is never certain. Because of the risks and uncertainties inherent to the development process ~~, including risks and uncertainties related to the impact of COVID- 19~~, our product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. As discussed under " Risk Factors — Risks Relating to Our Business — Risks Relating to Drug Development and Commercialization — Our success depends upon our ability to manage our product candidate pipeline, advance our product candidates through the various stages of development, especially through the clinical trial process, and to receive regulatory approvals for the commercial sale of our product candidates, " we ~~or~~ **and** our partners have experienced, and may again in the future experience, any number of unfavorable outcomes during or as a result of preclinical studies and clinical trials that could delay or prevent regulatory approval of our product candidates, or negatively impact our management' s credibility, our value and our operating results. Even if the FDA or foreign regulatory authorities approve a product candidate, the approval may limit the indicated uses for a product candidate, impose other restrictions on the product candidate, and / or may require post- approval studies that could impair the commercial viability of a product candidate. Even upon any approval to market our potential products, whether in the United States or internationally, we will continue to be subject to extensive regulatory requirements **, as discussed under " Risk Factors — Risks Relating to Our Business — Legal and Regulatory Risks — We are subject to various laws and regulations related to our products and product candidates, and if we or our partners do not comply with these laws and regulations, we could face substantial penalties** . **"** Our failure to comply with existing or future regulatory requirements for regulatory approval, or our loss of, or changes to, previously obtained approvals, could impair our ability to generate any revenues from product sales or licensing arrangements, which could have a material adverse effect on our business, financial condition, and results of operations. We focus on rare diseases, which may create additional risks and challenges **, including that the target patient populations of our products and product candidates may be small** . Because we focus on developing drugs as treatments for rare diseases, we may seek orphan drug, breakthrough therapy or fast track designations for our product candidates in the United States or the equivalent designations elsewhere in the world. Often, regulatory authorities have broad discretion in determining whether or not to grant such designations. We cannot guarantee that our product candidates will receive orphan drug status from the FDA or equivalent designations from other regulatory authorities **. Even with an orphan drug designation for our current and potential future product candidates, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for an existing or future product candidate, that exclusivity may not effectively protect the product from competition. See " Business — Government Regulation — FDA Regulation — Orphan Drugs " in Part I, Item 1 of this report** . We also cannot guarantee that we will receive breakthrough therapy, fast track, or equivalent designations, which provide certain potential benefits such as more frequent meetings with the applicable regulatory authorities to discuss development plans, intensive guidance on efficient drug development programs, and potential eligibility for rolling review or priority review. Even if we are successful in obtaining any such designations for our product candidates, such designations may not lead to faster development or regulatory review or approval and do not increase the likelihood that our product candidates will receive marketing approval. We may not be able to obtain or maintain these designations for our product candidates that receive them, and our competitors may obtain these designations for their product candidates, which could impact our ability to develop and commercialize our products and product candidates or compete with such competitors, which may adversely impact our business, financial condition or results of operations. **Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our products and product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for each of our products and product candidates may be limited or may not be amenable to treatment with our products and product candidates, and new patients may become increasingly difficult to identify or access. Further, even if we obtain significant market share for our products and product candidates, because the potential target populations are small, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business. If the FDA or comparable foreign regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of data or market exclusivity before approving generic**

versions of our products, the sales of our products could be adversely affected. Once an NDA is approved, the drug covered thereby becomes a " reference- listed drug " in the FDA' s publication, " Approved Drug Products with Therapeutic Equivalence Evaluations. " Manufacturers may seek marketing approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States, as described in " Business — Government Regulation — FDA Regulation — Abbreviated New Drug Applications for Generic Drugs " in Part I, Item 1 of this report. Generic drugs may be significantly less costly to bring to market than the reference- listed drug and companies that produce generic drugs are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference- listed drug is typically lost to the generic drug. The FDA may not approve an ANDA for a generic drug until any applicable period of non- patent exclusivity for the reference- listed drug has expired, as described in " Business — Government Regulation — FDA Regulation — Abbreviated New Drug Applications for Generic Drugs " in Part I, Item 1 of this report, but such exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well- controlled clinical trials necessary to demonstrate safety and effectiveness. Manufacturers may seek to launch generic drugs following the expiration of the marketing exclusivity period, even if we still have patent protection for such drugs. Competition that our products or product candidates may face from generic drugs could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates. Our future revenues, profitability and cash flows could also be materially and adversely affected and our ability to obtain a return on the investments we have made in those product candidates may be substantially limited if our products or, if and when approved, product candidates, are not afforded the appropriate periods of non- patent exclusivity. The commercial viability of any approved product could be compromised if the product is less effective than expected, causes undesirable side effects that either were not previously identified or **were** worse than expected, or fails to achieve market acceptance within the medical community. If, after obtaining regulatory approval of a product, we or others discover that the product is less effective than previously believed or causes undesirable side effects that either were not previously identified or **were** worse than expected, any of the following adverse events could occur: • regulatory authorities may withdraw their approval of, or impose marketing or manufacturing restrictions on, the product, or require us or our partners to create a medication guide outlining the risks of unidentified side effects for distribution to patients; • we or our partners may be required to recall the product, change the way the product is administered, conduct additional clinical trials, or be subject to civil or criminal penalties; and • the product may become less competitive and our reputation may suffer. Even after receiving regulatory approval, any product could fail to gain sufficient, or any, market acceptance by physicians, patients, third- party payors, health authorities and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies. If an approved product does not achieve an adequate level of market acceptance, it may not generate significant revenues. The occurrence of any of the foregoing could have a material and adverse impact on our business. If we fail to successfully commercialize or establish collaborative relationships to commercialize certain of our products and product candidates, or if any partner terminates or fails to perform its obligations under agreements with us, potential revenues from commercialization of our products and product candidates could be reduced, delayed or eliminated. Our business strategy includes increasing the asset value of our product and product candidate portfolio. We believe this is best achieved by retaining full product rights or through collaborative arrangements with third parties as appropriate. As needed, potential third- party relationships could relate to preclinical development, clinical development, regulatory approval, marketing, sales, and distribution of our products and product candidates. Currently, we have established collaborative relationships, including with Torii for the commercialization of ORLADEYO in Japan, with third- party distributors for ORLADEYO in certain other markets, and with each of Shionogi and Green Cross for the development and commercialization of peramivir. The process of establishing and implementing collaborative relationships is difficult, time- consuming and involves significant uncertainty, including: • we or our partners may seek to renegotiate or terminate our relationships due to unsatisfactory commercial, regulatory or clinical results, including post- approval clinical commitments, a change in business strategy, a change of control or other reasons; • our contracts for collaborative arrangements may expire; • the possibility that expiration or termination of collaborative relationships, such as those with certain of our distribution partners, may trigger repurchase obligations of the Company for unsold product held by our partners; • our partners may choose to pursue alternative technologies, including those of our competitors; • we have had in the past, and in the future may have, disputes with a partner that could lead to litigation or arbitration, which could result in substantial costs and divert the attention of our management; • we do not have day- to- day control over the activities of our partners and have limited control over their decisions; • our ability to generate future event payments and royalties from our partners depends upon their abilities to establish the safety and efficacy of our product candidates, obtain regulatory approvals and achieve market acceptance of products developed from our product candidates; • we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may utilize our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability; • we or our partners may not devote sufficient capital or resources toward our products and product candidates; and • we or our partners may not comply with applicable government regulatory requirements. If we or our partners fail to fulfill our responsibilities in a timely manner, or at all, our development and commercialization efforts related to that collaboration could be reduced, delayed or terminated, or it may be necessary for us to assume responsibility for activities that would otherwise have been the responsibility of our partner.

If we are unable to establish and maintain collaborative relationships on acceptable terms, we may have to delay or discontinue further development or commercialization of one or more of our products or product candidates, undertake commercialization activities at our own expense or find alternative sources of funding. Any delay in the development or commercialization of our products and product candidates would severely affect our business, because if our product candidates do not progress through the development process or reach the market in a timely manner, or at all, or if our products do not achieve market success, we may not receive any revenues from product sales or licensing arrangements. The results of our partnership with Torii may not meet our current expectations. We have ~~an~~ **a partnership** agreement with Torii for ~~the development and commercialization of~~ ORLADEYO in Japan. **Under** ~~Our ability to realize~~ the **Torii Agreement** ~~expected benefits of this collaboration~~ , ~~including~~ **we are responsible for all field promotional activities** with respect to ~~the receipt or amounts of royalty payments, is subject to a number of risks, including that the commercial potential of~~ ORLADEYO **in Japan** ~~may not meet our current expectations~~ , ~~we or Torii may fail to comply with our respective obligations under the Torii Agreement, and third parties may fail to perform their obligations to us on a timely basis or at all. The Torii Agreement provides that we are entitled to receive tiered royalty payments, the amounts of~~ which **we conduct through our Japanese subsidiary, BioCryst** ~~will depend upon the amount of annual net sales of ORLADEYO in~~ Japan **K** ~~during each calendar year and other factors~~ . ~~We currently~~ **K. Furthermore, we** remain responsible for regulatory activities with respect to ORLADEYO in Japan, and we ~~continue to~~ use third parties to satisfy ~~many of our~~ **those regulatory responsibilities and certain other** obligations ~~under the Torii Agreement, including, but not limited to, our regulatory and other responsibilities~~ in Japan. If **any** ~~our interactions, or those of our third-~~ party ~~agents, are unsuccessful, we could fail~~ **fails** to meet ~~our~~ **its** obligations ~~under the Torii Agreement~~ , ~~which could negatively impact~~ the commercial success **of ORLADEYO in Japan** and ~~the partnership, impact~~ the economic benefit expected ~~or require additional development of ORLADEYO. Torii may terminate the Torii Agreement under certain limited circumstances, including upon one year's written notice after the sixth anniversary of the first commercial sale of ORLADEYO in Japan. If the Torii Agreement is terminated in connection with these provisions, or at all, we will no longer be entitled to receive any milestone or royalty payments thereunder, which could have a material adverse impact on our business and results of operations. Torii has sole control over, and decision- making authority with respect to, commercialization activities for ORLADEYO for the prevention of HAE attacks in Japan, subject to oversight from a joint steering committee. Therefore, our receipt, and the amounts, of any royalty payments under the Torii Agreement are dependent upon Torii's successful performance of such commercialization activities. In addition, competitive products and variations in patient demand, prescription levels, reimbursement determinations or other factors may limit the commercial potential of ORLADEYO in Japan, which could materially reduce the amount of any royalties we are entitled to receive under the Torii Agreement. Under the Torii Agreement, we are responsible for supplying Torii with its required amounts of ORLADEYO for commercial sale. If, due to the failure of our third- party contract manufacturers to produce sufficient drug product, we fail to supply to Torii the required amounts of ORLADEYO, then Torii's ability to successfully commercialize ORLADEYO in Japan~~ could be **negatively** ~~materially impaired, and we may receive less royalty income under the Torii Agreement, or none at all. Any of the foregoing risks could materially adversely impact~~ **impacted** ~~our ability to perform our obligations under the Torii Agreement, which could materially reduce the economic benefits of the Torii Agreement to us and impair or result in the termination of our collaboration with Torii~~ . There can be no assurance that our or our partners' commercialization efforts, methods, and strategies for our products or technologies will succeed, and our future revenue generation is uncertain. There can be no assurance that our or our partners' commercialization efforts, methods and strategies will succeed. We may be unable to establish or sufficiently increase our sales, marketing and distribution capabilities for products we currently, or plan to, commercialize. Our ability to receive revenue from products we or our partners commercialize is subject to several risks, including: • we or our partners may fail to complete clinical trials successfully, or satisfy post- marketing commitments, sufficient to obtain and maintain regulatory agency marketing approval; • many competitors are more experienced and have significantly more resources, and their products could reach the market faster, be more cost effective or have a better efficacy or tolerability profile than our products and product candidates; • we may fail to employ a comprehensive and effective intellectual property strategy, which could result in decreased commercial value of our Company, our products and product candidates, or royalties associated with such products (e. g., the loss of the peramivir patent in Korea, which may result in a reduced royalty from Green Cross); • we may fail to employ a comprehensive and effective regulatory strategy, which could result in a delay or failure in commercialization of our products; • our and our partners' ability to successfully commercialize our products is affected by the competitive landscape, which cannot be fully known at this time; • revenue from product sales depends on our ability to obtain and maintain favorable pricing; • reimbursement is constantly changing, which could greatly affect usage of our products; • future revenue from product sales will depend on our ability to successfully complete clinical studies, obtain regulatory approvals, and manufacture, market, distribute and commercialize our approved drugs; and • the impact of **public health emergencies or the outbreak of disease, such as** the COVID- 19 pandemic **,** on us or our partners. In addition, future revenue from sales of ORLADEYO is subject to uncertainties and will depend on several factors, including the success of our and our partners' commercialization efforts in the United States and elsewhere, the number of new patients switching to ORLADEYO, patient retention and demand, the number of physicians prescribing ORLADEYO, the rate of monthly prescriptions, reimbursement from third- party and government payors **, the number of patients receiving free product** , the conversion of patients from our clinical trials and early access programs to commercial customers, our pricing strategy, and market trends. Even if we are able to successfully commercialize our existing products, or to develop new commercially viable products, certain obligations we have to third parties, including, without limitation, our obligations to pay royalties on certain revenues from ORLADEYO and BCX10013 under the Royalty Purchase Agreements, may reduce the profitability of such products. We have expanded, and may continue expanding, our development and regulatory capabilities and **are** implementing sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. We have experienced, and may continue to experience, significant

growth in the number of our employees and the scope of our operations in the United States and internationally, particularly in the areas of drug development, regulatory affairs, sales, marketing, and distribution. To manage our growth, we must continue to implement and improve our managerial, operational and financial systems and processes, expand our facilities and continue to recruit and train qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, we may not be able to effectively manage the expansion of our operations, implement appropriate systems and processes in a timely manner or at all, or recruit, train, and retain qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. In addition, if a commercial launch for any product or product candidate for which we recruit a commercial team and establish marketing capabilities in any region is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. We depend on third- party vendors in the manufacture and distribution of our products, product candidates and the materials for our products and product candidates. If we cannot rely on existing third- party vendors, we will be required to incur significant costs and potential delays in finding new third- party vendors, which could adversely impact the development and commercialization timeframes for our products and product candidates. We depend on third- party vendors, including third-party manufacturers, distributors, and specialty pharmacies, in the manufacture and distribution of our products, product candidates, and the materials for our products and product candidates. Often, especially in the early development and commercialization process, we have only one or limited sources for a particular product or service, such as manufacturing and / or distribution. We depend on these third- party vendors to perform their obligations in a timely manner and in accordance with applicable governmental regulations. Our third- party vendors, particularly our third- party manufacturers and distributors, each of which may be the only vendor we have engaged for a particular product, product candidate, or service or in a particular region, may encounter difficulties with meeting our requirements, including, but not limited to, problems involving, as applicable: • insufficient resources being devoted in the manner necessary to satisfy our requirements within expected timeframes; • inconsistent production yields; • product liability claims or recalls of commercial product; • difficulties in scaling production to commercial and validation sizes; • interruption of the delivery of materials required for the manufacturing process; • failure to distribute commercial supplies of our products to commercial vendors or end users in a timely manner; • scheduling of plant time with other vendors or unexpected equipment failure; • potential catastrophes that could strike their facilities or have an effect on infrastructure; • potential impurities in our drug substance or products that could affect availability of product for our clinical trials or future commercialization; • poor quality control and assurance or inadequate process controls; • failure to provide us with accurate or timely information regarding inventories, the number of patients who are using our products, or serious adverse events and / or product complaints regarding our products; • inability of third parties to satisfy their financial obligations to us or to others; • potential breach of the manufacturing or distribution agreement by the third party; • possible termination or nonrenewal of a critical agreement by the third party at a time that is costly or inconvenient to us; and • lack of compliance or cooperation with regulations and specifications or requests set forth by the FDA or other foreign regulatory agencies or local customs, particularly associated with ORLADEYO, BCX10013, peramivir and our early- stage compounds. Many additional factors could cause production or distribution interruptions with the manufacture and distribution of any of our products and product candidates, including human error, natural disasters, pandemics, labor disputes or shortages, acts of terrorism or war, equipment malfunctions, raw material shortages or supply chain issues. If our commercial distribution partners are not able to satisfy our requirements within the expected timeframe, or are unable to provide us with accurate or timely information and data, including with respect to inventories and sales, serious adverse events, and / or product complaints, our business, including our commercialization efforts for and sales of ORLADEYO, may be at risk. In addition, if specialty pharmacy services, including our third- party call center services, which provide patient support and financial services, prescription intake and distribution, reimbursement adjudication, and ongoing compliance support, are not effectively managed, the continuance of our commercialization efforts for and sales of ORLADEYO ~~,~~ may be delayed or compromised. In addition, our contract manufacturers may not be able to manufacture the materials required for our products or product candidates at a cost or in quantities necessary to make them commercially viable. Our raw materials, drug substances, products, and product candidates are manufactured by a limited group of suppliers, including some at a single facility. If any of these suppliers were unable to produce these items, this could significantly impact our supply of products and product candidate material for further preclinical testing and clinical trials. Our third- party manufacturers also may not meet our manufacturing requirements. Furthermore, changes in the manufacturing process or ~~procedure~~ **procedures** , including a change in the location where the drug is manufactured or a change of a third- party manufacturer, may require prior review and approval in accordance with the FDA' s cGMP and comparable foreign requirements. This review may be costly and time- consuming and could delay or prevent the launch of a product. The FDA or foreign regulatory authorities may at any time implement new standards, or change their interpretation and enforcement of existing standards, for manufacture, packaging or testing of products. If we or our contract manufacturers are unable to comply, we or they may be subject to regulatory action, civil actions or penalties, any of which could be costly to us and could result in a delay or shortage of product. If we are unable to maintain current third- party relationships, or enter into new agreements with additional third parties on commercially reasonable terms **, or at all** , or if there is poor manufacturing or distribution performance or failure to comply with any regulatory agency on the part of any of our third- party vendors, we may not be able to complete development of, obtain timely approval of, or commercialize our products and product candidates. Commercialization of our products by us and our partners is subject to the potential commercialization risks described herein and numerous additional risks. Any potential revenue benefits to us, including in the form of milestone payments, royalties or other consideration are highly speculative. Commercial success of our products is uncertain and is subject to all the risks and uncertainties disclosed in our other risk factors relating to drug development and commercialization. In addition, commercialization of our products is subject to further risks and may be negatively impacted by a number of factors,

including, but not limited to, the following: • our products may not prove to be adequately safe and effective for market approval in markets other than the markets in which they are currently approved; • necessary funding for post- marketing commitments and further development of our products may not be available timely, at all, or in sufficient amounts; • advances in competing products could substantially replace potential demand for our products; • government and third- party payors may not provide sufficient coverage or reimbursement, which would negatively impact the demand for our products; • we may not be able to supply commercial material to our partners and our partners may not be able to maintain or establish sufficient and acceptable commercial manufacturing, either directly or through third- party manufacturers; • the commercial demand and acceptance for our products by healthcare providers and by patients may not be sufficient to result in substantial product revenues to us or to our partners and may result in little to no revenue, milestone payments, or royalties to us; • effectiveness of marketing and commercialization efforts for our products by us or our partners; • market satisfaction with existing alternative therapies; • perceived efficacy relative to other available therapies; • disease prevalence; • cost of treatment; • our pricing and reimbursement strategy may not be effective; • **new legislative or regulatory proposals may influence our pricing and reimbursement strategy, which could impact product revenues; •** pricing and availability of imports or alternative products; • marketing and sales activities of competitors; • shifts in the medical community to new treatment paradigms or standards of care; and • relative convenience and ease of administration. Risks Relating to Competing in Our Industry We face intense competition, and if we are unable to compete effectively, the demand for our products may be reduced. The biotechnology and pharmaceutical industries are highly competitive and subject to rapid and substantial technological change. There are many companies seeking to develop products for the same indications that we currently target. Our competitors in the United States and elsewhere are numerous and include, among others, major multinational pharmaceutical and chemical companies and specialized biotechnology firms. Most of these competitors have greater resources than we do, including greater financial resources, larger research and development staffs and more experienced manufacturing, marketing, and sales organizations. In addition, most of our competitors have greater experience than we do in conducting clinical trials and obtaining FDA and other regulatory approvals. Accordingly, our competitors may succeed in obtaining FDA or other regulatory approvals of product candidates more rapidly than we do for products that compete with our products. Companies that complete clinical trials, obtain required regulatory approvals, and commence commercial sale of their drugs before we do may achieve a significant competitive advantage, including patent and FDA exclusivity rights that would delay our ability to market products. We face, and will continue to face, competition in the commercialization of our products, licensing of potential product candidates for desirable disease targets, licensing of desirable product candidates, and development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may also arise from, among other things: • other drug development technologies; • methods of preventing or reducing the incidence of disease, including vaccines; and • new small molecule or other classes of therapeutic agents. Developments by others may render our products, product candidates, or technologies obsolete or noncompetitive. We received FDA approval of ORLADEYO, an oral, once- daily therapy for the prevention of HAE attacks in adults and pediatric patients aged 12 years and older, in December 2020. We subsequently received regulatory approvals for ORLADEYO in multiple markets. In addition, we are performing research on or developing products for the treatment of several other rare diseases, including diseases of the complement system. We expect to encounter significant competition for our pharmaceutical products and product candidates. Companies that complete clinical trials, obtain required funding or government support, obtain required regulatory approvals and commence commercial sales or stockpiling orders of their products before their competitors may achieve a significant competitive advantage. In addition, various government entities throughout the world may offer incentives, grants and contracts to encourage additional investment into certain preventative and therapeutic agents, which may have the effect of further increasing the number of our competitors and / or providing advantages to certain competitors. See " Business — Competition " in Part I, Item 1 of this report for further discussion of our competitors, competitive products or programs, and the competitive conditions in these and other therapeutic areas. If one or more of our competitors' products or programs, including potential competitors not currently identified, are successful, the market for our products may be reduced or eliminated. Compared to us, many of our competitors and potential competitors have substantially greater: • capital resources; • research and development resources, including personnel and technology; • regulatory experience; • preclinical study and clinical testing experience; • manufacturing, marketing, and sales experience; and • production facilities. Any of these competitive factors could impede our funding efforts, render our products, product candidates, or technologies noncompetitive or eliminate or reduce demand for our products and product candidates. ~~Legal and Regulatory Risks~~ We are subject to various laws and regulations related to our products and product candidates, and if we or our partners do not comply with these laws and regulations, we could face substantial penalties. Our and our partners' activities related to approved products or, following their regulatory approval (if applicable), any of our product candidates under development, such as BCX10013, are subject to regulatory and law enforcement authorities in the United States (including the FDA, the Federal Trade Commission, the Department of Justice (" DOJ "), and state and local governments) and their foreign equivalents (including the EMA, MHLW, MHRA, and others). We are responsible for reporting adverse drug experiences, have responsibility for certain post- approval studies, and may have responsibilities and costs related to a recall or withdrawal of our products from sale in the jurisdictions in which they are approved. We may also incur liability associated with product manufacturing contracted by us or in support of any of our partners. We are required to maintain records and provide data and reports to regulatory agencies related to our products (e. g. risk evaluation and mitigation strategies, track and trace requirements, and adverse events), and we may incur certain promotional regulatory and government pricing risks, all of which could have a material adverse impact on our operations and financial condition. Similar responsibilities would apply upon regulatory approval of any of our other product candidates currently under development. In addition, we are subject to the federal physician sunshine act and certain similar physician payment and drug pricing transparency legislation in various states. We are also subject to various federal and state

laws pertaining to healthcare " fraud and abuse, " including both federal and state anti- kickback and false claims laws. Outside of the United States, we may be subject to analogous foreign laws and regulations in the various jurisdictions in which we operate. These laws and regulations apply to our and our partners' operations, sales and marketing practices, price reporting, and relationships with physicians and other customers and third- party payors. Although we seek to comply with these statutes, it is possible that our practices, or those of our partners, might be challenged under healthcare fraud and abuse, anti- kickback, false claims or similar laws. Violations of the physician sunshine act and similar legislation or the fraud and abuse laws may be punishable by civil or criminal sanctions, including fines and civil monetary penalties, and future exclusion from participation in government healthcare programs. The principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to certain regulatory authorities, including the FDA and comparable foreign regulatory authorities. Consequently, the FDA or other regulatory authority may conclude that a financial relationship between us and a principal investigator creates a conflict of interest or otherwise affects interpretation of the study. In the event of a conflict of interest with respect to a study, the integrity of the data generated at the applicable clinical trial site may be questioned or the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates. The FDA and foreign regulatory authorities may also impose post- approval commitments on us for approved products, which we may not complete successfully or on time for any number of reasons, including **,** but not limited to **,** lack of funds to complete the studies and insufficient interest by appropriate sites, investigators or study subjects. We are currently subject to certain post- approval commitments. If we fail to comply with post- approval legal and regulatory requirements, we could be subject to penalties, and our products could be subject to continual recordkeeping and reporting requirements, review and periodic inspections by the FDA and other regulatory bodies. Regulatory approval of a product may be subject to limitations on the indicated uses for which the product may be marketed or to the other restrictive conditions of approval that limit our ability to promote, sell or distribute a product. Furthermore, the approval of our products and any other future product candidates may be subject to requirements for costly post- approval testing and surveillance to monitor their safety or efficacy **or certain post- approval labeling, packaging and storage requirements** . Advertising and promotion are subject to stringent **oversight from the** FDA ~~rules~~ and ~~oversight~~ **foreign regulators** , and as an NDA holder, we may be held responsible for any advertising and promotion that is not in compliance with ~~the~~ **applicable** rules and regulations. Applicable regulatory authorities, competitors, and other third parties may take the position that we are not in compliance with such regulations. In addition to medical education efforts, we may offer patient support services to assist patients receiving treatment with our commercially approved products which have increasingly become the focus of government investigation. Adverse event information concerning approved products must be reviewed, and as an NDA holder, we are required to make expedited and periodic adverse event reports to the FDA and other regulatory authorities. In addition, the research, manufacturing, distribution, sale and promotion of products are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services **(" CMS ")** , other divisions of ~~the~~ HHS, the DOJ and individual U. S. Attorney offices within the DOJ, state and local governments, and foreign equivalents of the foregoing. All of these activities are also potentially subject to healthcare false claims and fraud and abuse laws, as well as consumer protection and unfair competition laws. If our operations with respect to our products that are subject to healthcare laws and regulations are found to be in violation of any of the healthcare fraud and abuse laws described above or in " Business — Government Regulation " in Part I, Item 1 of this report or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines **, debarment or exclusion from participating in government- funded healthcare programs such as Medicare or Medicaid,** and the curtailment or restructuring of our operations. Any penalties, damages, fines **, debarment, exclusion** , curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management' s attention from the operation of our business. Moreover, achieving and sustaining compliance with all applicable fraud and abuse laws may be costly. Our employees, consultants and partners may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation. We are subject to the risk of fraud or other misconduct by our employees, consultants and partners, including intentional or unintentional failures to comply with FDA regulations or similar regulations of comparable other regulatory authorities, provide accurate information to the FDA or comparable other regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable other regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee and consultant misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee and consultant misconduct, whether intentional, reckless, negligent, or unintentional, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions. We and our partners may be subject to new legislation, regulatory proposals and healthcare payor initiatives that may increase our costs of compliance and adversely affect our or our partners' ability to market our products ~~,~~ **or** develop our product candidates ~~,~~

~~obtain collaborators and raise capital~~ . We are subject to new legislation, regulatory, and healthcare payor initiatives, including the PPACA, which made extensive changes to the delivery of healthcare in the United States, as discussed in " Business — Government Regulation " in Part I, Item 1 of this report. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare could result in decreased net revenues from our pharmaceutical products and decrease potential returns from our development efforts. In addition, pharmaceutical and device manufacturers are also required to report and disclose certain payments and transfers of value to, and investment interests held by, physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in civil monetary penalties for payments, transfers of value, or ownership or investment interests not reported in an annual submission. Compliance with the PPACA and state laws with similar provisions is difficult and time consuming, and companies that do not comply with these state laws face civil penalties. Because of the breadth of these laws and the narrowness of the applicable safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Such a challenge could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In addition, there have been a number of other legislative and regulatory proposals aimed at changing the pharmaceutical industry. For example, legislation has been enacted in certain states and at a federal level that requires development of an electronic pedigree to track and trace each prescription drug at the saleable unit level through the distribution system. Compliance with these electronic pedigree requirements may increase our operational expenses and impose significant administrative burdens. In addition, our compliance may be deemed insufficient and we could face a material adverse effect on our business, financial condition, results of operations and growth prospects. As a result of these and other new proposals, we may determine to change our current manner of operation, provide additional benefits or change our contract arrangements, any of which could have a material adverse effect on our business, financial condition and results of operations. Adequate coverage and reimbursement in the United States and other markets is critical to the commercial success of our approved products. Recently in the United States, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. For example, the ~~Inflation Reduction Act of 2022 (" IRA ")~~ implements a number of drug pricing measures intended to lower the cost of prescription drugs and related healthcare reforms, including limits on price increases and subjecting an escalating number of drugs to annual price negotiations with **CMS. The IRA includes several provisions that will impact our business to varying degrees, including provisions that reduce** the ~~Centers~~ **out- of- pocket spending cap** for Medicare ~~and~~ **Part D beneficiaries to $ 2, 000 starting in 2025; impose new manufacturer financial liability on all drugs in** ~~Medicaid~~ **Medicare** ~~Services~~ **Part D; allow the U. S. Government to negotiate Medicare Part B and Part D pricing for certain high- cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for drug prices that increase faster than inflation; and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication or indications are for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications for more than one disease or condition, it may not qualify for the orphan drug exemption** . We cannot be sure whether additional legislation or rulemaking related to the IRA will be issued or enacted, **how insurance pharmacy benefit managers and other insurance providers that manage benefits for Medicare recipients will react to the IRA,** or what impact, if any, such changes will have on the **insurance coverage and** profitability of our products or any of our product candidates, if approved for commercial use, in the future. The effect of the IRA on our business and the healthcare industry in general is not yet known **. The IRA or other government efforts to reduce the price of prescription drugs or to limit the amount that governments pay for healthcare products and services could result in additional pricing pressure and have a significant impact on our business** . In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Third- party payors are increasingly challenging the prices charged for medical products and services and, in some cases, imposing restrictions on the coverage of particular drugs. Many third- party payors negotiate the price of medical services and products and develop formularies which establish pricing and reimbursement levels. Exclusion of a product from a formulary can lead to its sharply reduced usage in the third- party payor' s patient population. The process for obtaining coverage can be lengthy and costly, and we expect that it could take several months before a particular payor initially reviews a product and makes a decision with respect to coverage. For example, third- party payors may require cost- benefit analysis data from us in order to demonstrate the cost- effectiveness of our products or any other product we might bring to market. For any individual third- party payor, we may not be able to provide data sufficient to gain reimbursement on a similar or preferred basis to competitive products, or at all, which may have a material adverse effect on our business, financial condition and results of operations. We ~~are~~ **may be** subject to data **privacy and** security ~~and privacy~~ risks, and our actual or perceived failure to comply with regulations and other legal obligations related to privacy and data protection could harm our business. We ~~are~~ **may be** subject to legal obligations **at the federal, state, and local level** related to privacy and data protection **, as described in " Business — Government Regulation — Data Privacy and Security Laws " in Part I, Item 1 of this report** . Compliance with **stringent and evolving** U. S. ~~and international~~ data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use, and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. For example, we may be subject to the **CCPA** ~~California Consumer Privacy Act~~ , which gives California residents expanded rights to access and require deletion of their personal ~~information~~ **data** , opt out of certain personal ~~information~~ **data** sharing, and receive detailed information about how their personal ~~information~~ **data** is used **. The CCPA provides for civil penalties of up to $ 7, 500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data processed in the context of clinical trials, the**

CCPA may increase compliance costs and potential liability with respect to other personal data we may maintain about California residents . We also may be subject to the GDPR in the EEA and similar legislation in the United Kingdom and Switzerland. See " Business — Government Regulation — Data Privacy and Security Laws " in Part I, Item 1 of this report and " Risks Relating to Our Business — Risks Relating to International Operations — Our actual or perceived failure to comply with European governmental laws and regulations and other legal obligations related to privacy, data protection and information security could harm our business " in this section for additional discussion of privacy laws and regulations. Failure to comply with these laws and regulations could result in government enforcement actions, private litigation, or harm to our reputation and our business. **Despite our efforts, our personnel or third parties on whom we rely may fail to comply with such data privacy and security obligations, which could negatively impact our business operations. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including, but not limited to, regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.** If, because of our use of hazardous materials, we violate any environmental controls or regulations that apply to such materials, we may incur substantial costs and expenses in our remediation efforts. Our research and development involves the controlled use of hazardous materials, chemicals and various radioactive compounds. We are subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and some waste products. Accidental contamination or injury from these materials could occur. In the event of an accident, we could be liable for any damages that result, and any liabilities could exceed our resources. Compliance with environmental laws and regulations or a violation of such environmental laws and regulations could require us to incur substantial unexpected costs, which would materially and adversely affect our results of operations. Intellectual Property Risks If we fail to adequately protect or enforce our intellectual property rights, the value of those rights would diminish, and if we fail to secure the rights to patents of others, it could adversely affect our business. Our success will depend in part on our ability and the abilities of our partners to obtain, protect and enforce viable intellectual property rights including, but not limited to, trade name, trademark and patent protection for our Company and its products, methods, processes and other technologies we may license or develop, to preserve our trade secrets, and to operate without infringing the proprietary rights of third parties both domestically and abroad. The patent position of biotechnology and pharmaceutical companies is generally highly uncertain, involves complex legal and factual questions and has recently been the subject of much litigation. Neither the United States Patent and Trademark Office (" USPTO "), the Patent Cooperation Treaty offices, nor the courts of the United States and other jurisdictions have consistent policies nor predictable rulings regarding the breadth of claims allowed or the degree of protection afforded under many biotechnology and pharmaceutical patents. Further, we may not have worldwide patent protection for all of our product candidates and our intellectual property rights may not be legally protected or enforceable in all countries throughout the world. In some jurisdictions, some of our product candidates in certain programs, including our HAE program, may have short or no composition of matter patent life and we may therefore rely on orphan drug exclusivity or data exclusivity. There can be no assurance that we will obtain orphan drug exclusivity or data exclusivity in every jurisdiction. Further, in some jurisdictions, we may rely on formulation patents or method of use patents. Both the ability to achieve issuance and the enforcement of formulation and method of use patents can be highly uncertain and can vary from jurisdiction to jurisdiction, and such patents may therefore not adequately prevent competitors and potential infringers in some jurisdictions. The validity, scope, enforceability and commercial value of the rights protected by such patents, therefore, is highly uncertain. We also rely on trade secrets to protect technology in cases when we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborators and advisors, our ability to receive patent protection or protect our proprietary information may be imperiled. We may be involved in legal proceedings to protect or enforce our patents, the patents of our partners or our other intellectual property rights, which could be expensive, time consuming and unsuccessful. Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive, time- consuming , and unsuccessful. An adverse result in any legal proceeding could put one or more of our patents at risk. Our success depends in part on avoiding the infringement of other parties' patents and other intellectual property rights as well as avoiding the breach of any licenses relating to our technologies and products. In the United States, patent applications filed in recent years are confidential for 18 months, while older applications are not published until the patent issues. As a result, avoiding patent infringement may be difficult and we may inadvertently infringe third- party patents or proprietary rights. These third parties could bring claims against us, our partners or our licensors that even if resolved in our favor, could cause us to incur substantial expenses and, if resolved against us, could additionally cause us to pay substantial damages. Further, if a patent infringement suit were brought against us, our partners or our licensors, we or they could be forced to stop or delay research, development, manufacturing or sales of any infringing product in the country or countries covered by the patent we infringe, unless we can obtain a license from the patent holder. Such a license may not be available on acceptable terms, or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we, our partners or our licensors were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. If we or our partners are unable or fail to adequately initiate, protect, defend or enforce our intellectual property rights in any area of commercial interest or in any part of the world where we wish to seek regulatory approval for our products, methods, processes and other technologies, the value of our products and product candidates to produce revenue would diminish. Additionally, if our products, methods, processes, and other technologies or our commercial use of such products, processes, and other technologies, including, but not limited to, any trade name, trademark or commercial strategy infringe the proprietary rights of other parties, we could incur substantial costs. The USPTO and the patent offices of other jurisdictions have issued to us a

number of patents for our various inventions, and we have in- licensed several patents from various institutions. We have filed additional patent applications and provisional patent applications with the USPTO. We have filed a number of corresponding foreign patent applications and intend to file additional foreign and U. S. patent applications, as appropriate. We have also filed certain trademark and trade name applications worldwide. We cannot assure you as to: • the degree and range of protection any patents will afford against competitors with similar products; • if and when patents will issue; • if patents do issue, we cannot be sure that we will be able to adequately defend such patents and whether or not we will be able to adequately enforce such patents; or • whether or not others will obtain patents claiming aspects similar to those covered by our patent applications. If the USPTO or other foreign patent office upholds patents issued to others or if the USPTO grants patent applications filed by others, we may have to: • obtain licenses or redesign our products or processes to avoid infringement; • stop using the subject matter claimed in those patents; or • pay damages. We may initiate, or others may bring against us, litigation or administrative proceedings related to intellectual property rights, including proceedings before the USPTO or other foreign patent office. Any judgment adverse to us in any litigation or other proceeding arising in connection with a patent or patent application could materially and adversely affect our business, financial condition and results of operations. In addition, the costs of any litigation or administrative proceeding may be substantial whether or not we are successful. Our success is also dependent upon the skills, knowledge and experience, none of which is patentable, of our scientific and technical personnel. To help protect our rights, we require all employees, consultants, advisors and partners to enter into confidentiality agreements that prohibit the disclosure of confidential information to anyone outside of our Company and require disclosure and assignment to us of their ideas, developments, discoveries and inventions. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information, and if any of our proprietary information is disclosed, our business will suffer because our revenues depend upon our ability to license or commercialize our products and product candidates and any such events would significantly impair the value of such products and product candidates. **We have diversified our pipeline to include the development of protein therapeutics, which may create additional risks and challenges. We have diversified our pipeline beyond small- molecule medicines to develop protein therapeutics. The development of protein therapeutics may create additional risks and challenges, including, among others: • patent protection for protein therapeutics may be narrower in scope than for our small- molecule medicines, and our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our protein therapeutic candidates or prevent others from designing around our claims; • formulation issues with our protein therapeutic candidates may require redevelopment of the formulation, which may be time- consuming or unsuccessful; • the patent applications that we own or in- license may fail to result in issued patents with claims that cover our protein therapeutic candidates in the United States or in other countries; • our competitors may be able to more easily develop and seek patent protection on similar protein therapeutic candidates; and • orally-administered drugs are often less expensive and present a reduced treatment burden as compared to protein therapeutics and therefore would have competitive advantages if they were developed and shown to be safe and effective for the indication that our protein therapeutics product candidates are targeting. Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involves both technological and legal complexity. Therefore, obtaining and enforcing such patents is costly, time consuming, and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide- ranging patent reform legislation. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U. S. Congress, the U. S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. We employ certain individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Our efforts to vet our employees, consultants, and independent contractors and prevent their use of the proprietary information or know- how of others in their work for us may not be successful, and we may in the future be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distract management and other employees.** Product Liability Risks We face an inherent risk of liability in the event that the use or misuse of our products or product candidates results in personal injury or death **,** and our product liability insurance coverage may be insufficient. If the use or misuse of any products we sell, or a partner sells, harms people, we may be subject to costly and damaging product liability claims brought against us by consumers, healthcare providers, pharmaceutical companies, third- party payors or others. The use of our product candidates in clinical trials, including post- marketing clinical studies, could also expose us to product liability claims. We cannot predict all of the possible harms or side effects that may result from the use of our products or the testing of product candidates, and therefore, the amount of insurance coverage we currently have may not be adequate to cover

all liabilities or defense costs we might incur. A product liability claim or series of claims brought against us could give rise to a substantial liability that could exceed our resources. Even if claims are not successful, the costs of defending such claims and potential adverse publicity could be harmful to our business. We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and face even greater risks upon commercialization by us of our products or product candidates. We have product liability insurance covering our clinical trials. Clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance or increase our existing coverage at a reasonable cost to protect us against losses that could have a material adverse effect on our business. An individual may bring a product liability claim against us if one of our products or product candidates causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in: • liabilities that substantially exceed our product liability insurance, which we would then be required to pay from other sources, if available; • an increase of our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, or at all; • withdrawal of clinical trial volunteers or patients; • damage to our reputation and the reputation of our products, resulting in lower sales; • regulatory investigations that could require costly recalls or product modifications; • litigation costs; and • the diversion of management' s attention from managing our business. Risks Relating to Contractual Arrangements We face risks related to our government- funded programs and are subject to various U. S. Government contract requirements, which may create a disadvantage and additional risks to us. We ~~have~~ **had** contracts with BARDA / HHS and NIAID / HHS for the development of galidesivir as a treatment for diseases caused by RNA pathogens, including Marburg virus disease, Yellow Fever and Ebola virus disease. In contracting with these government agencies, we ~~are~~ **became** subject to various U. S. Government contract requirements, including general clauses for a cost-reimbursement research and development contract, which may limit our reimbursement. While all government funding for galidesivir expired in 2022, we still face risks related to our U. S. Government contracts. U. S. Government contracts typically contain a number of extraordinary provisions that would not typically be found in commercial contracts and which may create a disadvantage and additional risks to us as compared to competitors that do not rely on U. S. Government contracts. These risks include the ability of the U. S. Government to unilaterally: • terminate or reduce the scope of our contract with or without cause; • interpret relevant regulations (federal acquisition regulation clauses); • require performance under circumstances which may not be favorable to us; • require an in- process review where the U. S. Government will review the project and its options under the contract; • control the timing and amount of funding, which impacts the development progress of our programs; and • audit and object to our contract- related costs and fees, including allocated indirect costs. Upon termination or expiration of a contract, the U. S. Government may dispute wind- down and termination costs and may question prior expenses under the contract and deny payment of those expenses. Should we choose to challenge the U. S. Government for denying certain payments under a contract, such a challenge could subject us to substantial additional expenses which we may or may not recover. In addition, as a U. S. Government contractor, we are required to comply with applicable laws, regulations and standards relating to our accounting practices and are subject to periodic audits and reviews, including a final financial audit. As part of any such audit or review, the U. S. Government may review the adequacy of, and our compliance with, our internal control systems and policies, including those relating to our purchasing, property, estimating, compensation and management information systems. Audits under the BARDA / HHS and NIAID / HHS galidesivir contracts may occur at the election of the U. S. Government and have been concluded through fiscal 2019; all subsequent fiscal years are still open and auditable. Based on the results of its audits, the U. S. Government may adjust our contract- related costs and fees, including allocated indirect costs. This adjustment could impact the amount of revenues reported on a historic basis. In addition, in the event BARDA / HHS or NIAID / HHS determines that certain costs and fees were unallowable or determines that the allocated indirect cost rate was higher than the actual indirect cost rate, BARDA / HHS or NIAID / HHS would be entitled to recoup any overpayment from us as a result. In addition, if an audit or review uncovers any improper or illegal activity, we may be subject to civil and criminal penalties and administrative sanctions, including forfeiture of profits, suspension of payments, fines and suspension or prohibition from doing business with the U. S. Government. We could also suffer serious harm to our reputation if allegations of impropriety were made against us. In addition, under U. S. Government purchasing regulations, some of our costs may not be reimbursable or allowed under our contracts. Further, as a U. S. Government contractor, we are subject to an increased risk of investigations, criminal prosecution, civil fraud, whistleblower lawsuits and other legal actions and liabilities as compared to private sector commercial companies. ~~There are risks related to the potential government use or sale of our antivirals. Government use or sale, in emergency situations or otherwise, of our antivirals (including peramivir for the treatment of influenza) may result in risks to us or our collaborative partners. There can be no assurance that government use of our antivirals (whether as indicated or outside of their current indications) will prove to be generally safe, well- tolerated and effective. Any government sale or use (on an emergency basis or otherwise) of our antivirals in any country may create liabilities for us or our partners. There can be no assurance that we or our manufacturers will be able to fully meet the demand for our antivirals with respect to any future arrangements. Further, we may not receive a favorable purchase price for future orders, if any, of our antivirals by governmental entities. Our competitors may develop products that could compete with or replace any antivirals selected for government sale or use. We may face competition in markets where we have no existing intellectual property protection or are unable to successfully enforce our intellectual property rights. There can be no assurance that the non- U. S. partnerships that we have entered into for peramivir will result in any order for peramivir in those countries or that peramivir will be approved for any use or will achieve market approval in additional countries. In the event that any emergency use or market approval is granted in any country, there can be no assurance that any government order or commercialization of the applicable product or product candidate in such countries will be substantial or will be profitable to us.~~ If we fail to reach milestones or to make annual minimum payments or otherwise breach our obligations under our license agreements, our licensors may terminate our agreements with them and / or seek additional remedies. If we are unable or fail to meet payment obligations, performance milestones relating to the timing of

regulatory filings, product supply obligations, post- approval commitments, or development and commercial diligence obligations; are unable or fail to make milestone payments or material data use payments in accordance with applicable provisions; or fail to pay the minimum annual payments under any of our in- licenses relating to our products or product candidates, our licensors may terminate the applicable license and / or seek other available remedies. As a result, our development of the respective product candidate or commercialization of the product would cease. Because continuing events of default exist under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub. As a result, we may not realize the benefit of future royalty payments, if any, that might otherwise accrue to us following repayment of the PhaRMA Notes and we could otherwise be adversely affected. In March 2011, **JPR Royalty Sub LLC,** our wholly- owned subsidiary ~~,~~ **(“** Royalty Sub **”)** , issued $ 30. 0 million in aggregate principal amount of PhaRMA **Senior Secured 14 %** Notes **due on December 1, 2020 (the “ PhaRMA Notes ”)** . The PhaRMA Notes are secured principally by (i) certain royalty and milestone payments under **our agreement with Shionogi (** the **“** Shionogi Agreement **”)** , pursuant to which Shionogi licensed from us the rights to market peramivir in Japan and Taiwan and (ii) the pledge by us of our equity interest in Royalty Sub ~~. Payments, if any, from Shionogi to us on non- governmental sales under the Shionogi Agreement will generally not be available to us for other purposes unless and until Royalty Sub has repaid in full its obligations under the PhaRMA Notes. Accordingly, these funds have been and will continue to be required to be dedicated to Royalty Sub' s debt service and not available to us for product development or other purposes~~ . Since September 1, 2014, payments from Shionogi have been insufficient for Royalty Sub to service its obligations under the PhaRMA Notes, resulting in a continuing event of default with respect to the PhaRMA Notes since that time. In addition, the PhaRMA Notes had a final legal maturity date of December 1, 2020, at which time the outstanding principal amount of the PhaRMA Notes of $ 30. 0 million, together with accrued and unpaid interest of $ 20. 6 million, was due in full. The failure by Royalty Sub to repay these amounts at the maturity date constituted an additional event of default under the PhaRMA Notes. As Royalty Sub has been unable to service its obligations under the PhaRMA Notes and continuing events of default exist under the PhaRMA Notes, the holders of the PhaRMA Notes may be able to foreclose on the collateral securing the PhaRMA Notes and our equity interest in Royalty Sub and may exercise other remedies available to them under the indenture or other documents related to the PhaRMA Notes. In such event, we may not realize the benefit of future royalty payments, if any, that might otherwise accrue to us following repayment of the PhaRMA Notes, we may incur legal costs, and we might otherwise be adversely affected. We cannot predict whether holders of PhaRMA Notes will seek to pursue any remedies as a result of the continuing events of default with respect to the PhaRMA Notes. The PhaRMA Notes are the obligation of Royalty Sub. Due to the non- recourse nature of the PhaRMA Notes, in the event of any potential foreclosure, we believe the primary impact to us would be the loss of future royalty payments, if any, from Shionogi and the legal costs associated with retiring the PhaRMA Notes. As a result, we do not currently expect the continuing events of default on the PhaRMA Notes to have a significant impact on our future results of operations or cash flows. However, we cannot assure you that this will be the case or that we will not otherwise be adversely affected as a result **of** the continuing events of default under the PhaRMA Notes or the failure by Royalty Sub to repay the PhaRMA Notes at maturity. We wrote off the balance due under the PhaRMA Notes to other income as a debt extinguishment as of December 31, 2021. See “ Note 8 — Royalty ~~Monetizations~~ **Financing Obligations** — RAPIACTA — Non- Recourse Notes Payable — Debt Extinguishment ” in the Notes to Consolidated Financial Statements in Part II, Item 8 of this report for additional information about the write- off. We have incurred significant indebtedness, which could adversely affect our business. Additionally, ~~our Credit~~ **the Pharmakon Loan** Agreement contains conditions and restrictions that limit our flexibility in operating our business. We may be required to make a prepayment or repay our outstanding indebtedness earlier than we expect if a prepayment event or an event of default occurs, including a material adverse change with respect to us, which could have a material adverse effect on our business. **On April 17, 2023, we entered into the $ 450. 0 million Pharmakon Loan Agreement (the “ Pharmakon Loan Agreement ”) with BioPharma Credit Investments V (Master) LP and BPCR Limited Partnership, as lenders, and BioPharma Credit PLC, as collateral agent for the lenders, and closed on an initial term loan thereunder in the principal amount of $ 300. 0 million.** As of December 31, ~~2022~~ **2023** , we had an outstanding principal balance under ~~our Credit~~ **the Pharmakon Loan** Agreement of $ ~~240~~ **313** . ~~5~~ **7** million, inclusive of the ~~quarterly~~ **Pharmakon** PIK Interest Payments **(as defined in “ Note 9 — Debt — Pharmakon Loan Agreement ” in the Notes to the Consolidated Financial Statements included in Part II, Item 8 of this report)** . ~~We~~ **Under the Pharmakon Loan Agreement, we** will be required to pay to ~~Athyrium~~ **Pharmakon** , for the account of the lenders, **a prepayment premium or** a make- whole premium **, as applicable,** plus certain fees **or expenses** set forth in the ~~Credit~~ **Pharmakon Loan** Agreement in the event that we prepay ~~or repay~~ , or are required to prepay ~~or repay~~ , voluntarily or pursuant to a mandatory prepayment obligation under the ~~Credit~~ **Pharmakon Loan** Agreement (e. g., ~~with the proceeds of certain asset sales, certain ORLADEYO out- licensing or royalty monetization transactions (excluding the Royalty Sales), extraordinary receipts, debt issuances, or~~ upon a change of control of the Company and specified other events, subject to certain exceptions), all **or part** of the then- outstanding ~~Term~~ **term** ~~Loans~~ **loans** under the ~~Credit~~ **Pharmakon Loan** Agreement, in each case, subject to certain exceptions set forth in the ~~Credit~~ **Pharmakon Loan** Agreement. Our indebtedness could have important consequences to our stockholders. For example, it: • increases our vulnerability to adverse general economic or industry conditions; • limits our flexibility in planning for, or reacting to, changes in our business or the industry in which we operate; • makes us more vulnerable to increases in interest rates, as borrowings under ~~our Credit~~ **the Pharmakon Loan** Agreement ~~are~~ **accrue interest** at variable **, uncapped** rates **, such that increases in interest rates will increase the associated interest payments that we are required to make on outstanding borrowings** ; • requires us to dedicate a portion of our cash flow from operations to interest payments, limiting the availability of cash for other purposes; • limits our ability to obtain additional financing or refinancing in the future for working capital or other purposes; and • places us at a competitive disadvantage compared to our competitors that have less indebtedness. Furthermore, ~~our Credit~~ **the Pharmakon Loan** Agreement contains various covenants that limit our ability to engage in

specified types of transactions. Subject to certain exceptions, these covenants limit our ability to, among other things, **dispose** ~~grant certain types~~ of ~~liens on our~~ assets ~~; make certain investments; incur or assume certain debt~~ ; engage in certain mergers, acquisitions, and similar transactions; ~~dispose of assets~~ **incur additional indebtedness** ; **grant** ~~license~~ -- **liens** ~~certain property; distribute dividends~~ ; make **investments; pay dividends or make distributions or** certain **other** restricted payments ~~; change the nature of our business; engage~~ in **respect of equity** ~~transactions with affiliates and insiders~~ ; prepay other indebtedness; **enter into restrictive** ~~or engage in sale and leaseback transactions. The Credit Agreement~~ **agreements** ~~also contains~~ **; undertake fundamental changes; or amend** certain **material contracts** ~~financial covenants, including a minimum liquidity covenant that requires us to maintain at all times at least $ 15. 0 million (or, in certain circumstances, $ 20. 0 million) of unrestricted cash and cash equivalents, subject to certain exceptions. In addition, we are required to achieve certain minimum targets for consolidated net revenues from ORLADEYO sales in the United States~~ . The covenants contained in the ~~Credit~~ **Pharmakon Loan** Agreement could cause us to be unable to pursue business opportunities that we or our stockholders may consider beneficial without the lenders' permission or without repaying all outstanding obligations under the ~~Credit~~ **Pharmakon Loan** Agreement. A breach of any of these covenants could result in an event of default under the ~~Credit~~ **Pharmakon Loan** Agreement. An event of default will also occur if, among other things, we fail to pay amounts due under the ~~Credit~~ **Pharmakon Loan** Agreement, we fail to repay certain other indebtedness having an aggregate principal amount in excess of **a threshold amount, an insolvency event occurs with respect to us, judgments for the payment of** ~~one~~ **money** ~~percent~~ **in excess** of ~~our borrowings under the Credit Agreement~~ **a threshold amount are entered into against us** , a material adverse change in our business, assets, properties, liabilities, or condition occurs, or a material impairment of our ability to perform our obligations under the ~~Credit~~ **Pharmakon Loan** Agreement occurs ~~, we experience a change of control~~ , certain negative regulatory events occur, including without limitation **certain withdrawal events with respect to ORLADEYO** ~~the loss of a required permit or a recall of a product~~ , or we fail to make required payments under our Royalty Purchase Agreements. In the case of a continuing event of default under the ~~Credit~~ **Pharmakon Loan** Agreement, the lenders under the ~~Credit~~ **Pharmakon Loan** Agreement could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted to the lenders a security interest, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the ~~Credit~~ **Pharmakon Loan** Agreement are secured by a security interest in, subject to certain exceptions, substantially all of our assets. Because substantially all of our assets are pledged to secure the ~~Credit~~ **Pharmakon Loan** Agreement obligations, our ability to incur additional secured indebtedness or to sell or dispose of assets to raise capital may be impaired, which could have an adverse effect on our financial flexibility. International expansion of our business exposes us to business, legal, regulatory, political, operational, financial, and economic risks. Our business strategy includes international expansion, including the commercialization of products outside of the United States. In addition, we currently conduct clinical studies and regulatory activities and have hired, and expect to continue hiring, employees outside of the United States. Doing business internationally involves a number of risks, including, but not limited to: • multiple, conflicting, and changing laws and regulations such as privacy and data regulations, transparency regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses; • introduction of new health authority requirements and / or changes in health authority expectations; • failure by us or our partners to obtain and maintain regulatory approvals for the use of our products in various countries; • complexities and difficulties in obtaining and maintaining protection for, and enforcing, our intellectual property; • difficulties in staffing and managing foreign operations; • complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems; • limits on our ability to penetrate international markets; • financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products, and exposure to foreign currency exchange rate fluctuations, which have been increasingly prevalent alongside a fluctuating U. S. dollar; • natural disasters and political and economic instability, including wars (e. g., the ~~conflict in~~ Ukraine **- Russia and Israel- Hamas conflicts**), terrorism, political unrest, results of certain elections and votes, actual or threatened public health emergencies and outbreak of disease (e. g., the ~~ongoing~~ COVID- 19 pandemic), boycotts, adoption or expansion of government trade restrictions, and other business restrictions; • certain expenses including, among others, expenses for travel, translation, and insurance; • regulatory and compliance risks that relate to maintaining accurate information and control over commercial operations and activities that may fall within the purview of the **FCPA** ~~U. S. Foreign Corrupt Practices Act~~ , including its books and records provisions or anti- bribery provisions, or the U. K. Bribery Act and similar foreign laws and regulations; and • regulatory and compliance risks relating to doing business with any entity that is subject to sanctions administered by the Office of Foreign Assets Control of the U. S. Department of the Treasury. Any of these factors could significantly harm our international expansion of operations and adversely affect our business and results of operations. Additionally, in some countries, such as Japan and the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our partners may be required to conduct a clinical trial that compares the cost- effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed. Foreign currency exchange rate fluctuations could have an adverse impact on our results of operations, financial position, and cash flows. We conduct operations in many countries outside of the United States involving transactions in a variety of currencies other than the U. S. dollar. These transactions include, without limitation, commercial sales, contract manufacturing, and clinical trial activities. Although most of our revenues and expenses are denominated in U. S. dollars, our commercial sales in Europe are primarily denominated in Euros and British Pounds. ~~In addition, our royalties from Torii are derived from Torii' s sales of ORLADEYO in Japan, which sales are denominated in Japanese yen and converted into U. S. dollars for purposes of determining the royalty owed to us.~~ We also have foreign currency

exposure to fluctuations in other foreign currencies, such as the Swiss Franc, Danish Krone, Swedish Krona, **Norwegian Krone, Japanese Yen** and ~~the~~ Canadian Dollar. Changes in the value of these currencies relative to the U. S. dollar may impact our consolidated operating results, including our revenues and expenses, causing fluctuations in our operating results from period to period and / or resulting in foreign currency transaction losses that adversely impact our results of operations, financial position, and cash flows. As we continue to expand our operations internationally, our exposure to foreign currency transaction gains or losses may become more significant. See " Quantitative and Qualitative Disclosures about Market Risk — Foreign Currency Risk " in Part II, Item 7A of this report for additional information about our foreign currency risk. Our actual or perceived failure to comply with European governmental laws and regulations and other legal obligations related to privacy, data protection and information security could harm our business. **Outside the United States, an increasing number of laws and regulations may govern data privacy and security.** EU member states, the United Kingdom, Switzerland and other countries have adopted data protection laws and regulations, which impose significant compliance obligations. These laws include the GDPR and similar national legislation **within the EEA, the United Kingdom GDPR, Switzerland' s Federal Data Protection Act** , the EU Clinical Trials Regulation, and the e- Privacy Directive (2002 / 58 / EC), and are discussed in more detail in " Business — Government Regulation — Data Privacy and Security Laws " in Part I, Item 1 of this report. Failure to comply with the requirements of **these laws may result in significant fines. For example,** the GDPR or related national data protection laws, which may deviate from the GDPR, may result in significant fines of up to 4 % of global revenues, or € 20. 0 million, whichever is greater **. In** ~~, and in~~ addition to such fines, ~~our~~ failure to comply with the requirements of **the** GDPR or similar national legislation may **result in temporary or definitive bans on data processing and other corrective actions and** subject us to litigation and / or adverse publicity, which could have material adverse effects on our reputation and business. As a result of the implementation of the GDPR, we are required to put in place additional mechanisms to ensure compliance with the data protection rules. For example, the GDPR requires us to make more detailed disclosures to data subjects, requires disclosure of the legal basis on which we can process personal data, makes it harder for us to obtain valid consent for processing, requires the appointment of a data protection officer where sensitive personal data (i. e., health data) is processed on a large scale, introduces mandatory data breach notification throughout the European Union, imposes additional obligations on us when we are contracting with service providers and requires us to adopt appropriate privacy governance including policies, procedures, training and data ~~audit~~ **audits** . We depend on a number of third parties in relation to the provision of our services, a number of which process personal data of EU individuals on our behalf. With each such provider, we are required to enter into contractual arrangements under which they are contractually obligated to only process personal data according to our instructions, and conduct diligence to ensure that they have sufficient technical and organizational security measures in place. Compliance with **evolving laws regarding** the ~~requirements imposed by~~ **transfer of personal data to** the ~~GDPR~~ **United States** and other **countries also requires** ~~such laws can be time- consuming, expensive and difficult, and may increase~~ **increased resources and may result in increased exposure to regulatory actions, fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing** ~~our~~ **or** ~~cost~~ **transferring** of ~~doing~~ **personal data necessary to operate our** business ~~or require us to change our business practices, and despite our efforts we may not be successful in achieving compliance if our personnel, collaborators, partners or vendors do not comply with applicable data protection obligations~~ . We are also subject to evolving European privacy laws on electronic marketing and cookies. The European Union is in the process of replacing the e- Privacy Directive (2002 / 58 / EC) with a new set of rules taking the form of a regulation that will be directly implemented in the laws of each EU member state. While this e- Privacy Regulation was originally intended to be adopted on May 25, 2018, it is still going through the European legislative process and the timing of its adoption remains unclear. **Compliance with the requirements imposed by the GDPR and other such laws can be time-consuming, expensive and difficult, and may increase our cost of doing business or require us to change our business practices, and despite our efforts we may not be successful in achieving compliance if our personnel, collaborators, partners or vendors do not comply with applicable data protection obligations. Despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; and other adverse business consequences.** The United Kingdom' s decision to withdraw from the European Union could result in increased regulatory and legal complexity, which may make it more difficult for us to do business in Europe and impose additional challenges in securing regulatory approval of our product candidates in Europe. The United Kingdom' s exit from the European Union, or Brexit, has caused political and economic uncertainty, including in the regulatory framework applicable to our operations and product candidates, and this uncertainty may persist for years. Brexit could, among other outcomes, disrupt the free movement of goods, services and people between the United Kingdom and the European Union, and result in increased legal and regulatory complexities, as well as potential higher costs of conducting business in Europe. The long- term effects of Brexit will depend in part on how the current and future trade agreements between the United Kingdom and the European Union take effect in practice. Changes in U. K. or EU regulations may cause disruption or delays in granting clinical trial authorization or opinions for marketing authorization, disruption of importation and export of active substance and other components of new drug formulations, and disruption of the supply chain for clinical trial product and final authorized formulations. The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the European Union and / or the United Kingdom. It is possible that there will be increased regulatory complexities, which can disrupt the timing of our clinical trials and regulatory approvals. In addition, changes in, and legal uncertainty with regard to, national and international laws and regulations may present difficulties for our clinical and regulatory strategy. Any delay in obtaining, or an inability to obtain, any

marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and / or the European Union and restrict our ability to generate revenues and achieve and sustain profitability. In addition, as a result of Brexit, other European countries may seek to conduct referenda with respect to their continuing membership with the European Union. Given these possibilities and others we may not anticipate, as well as the absence of comparable precedent, it is unclear what financial, regulatory and legal implications the withdrawal of the United Kingdom from the European Union will have and how such withdrawal will affect us, and the full extent to which our business could be adversely affected. Risks Relating to Technology If our facilities, or the facilities of our third- party vendors, incur damage or power is lost for a significant length of time, our business will suffer. We and our third- party vendors store commercial product, clinical and stability samples **, and manufacturing data** at our facilities that could be damaged if the facilities incur physical damage or in the event of an extended power failure. We have backup power systems in addition to backup generators to maintain power to all critical functions, but any loss of these products or samples could result in significant delays in our commercialization or drug development process. In addition, we store most of our preclinical and clinical data at our facilities. **While** ~~Duplicate~~ **duplicate** copies of most ~~critical~~ **clinical** data are secured off- site **, and a significant portion of our data is included in regular backups of our systems, we could lose important data if our facilities incur damage, or if our vendor data systems fail, suffer damage or are destroyed** . Any significant degradation or failure of our computer systems could cause us to inaccurately calculate or lose our data. Loss of data could result in significant delays in our drug development process, and any system failure could harm our business and operations. ~~A significant~~ **Cyber incidents and related** ~~disruption~~ **disruptions** in our or our third- party **vendors'** information technology systems ~~or a cybersecurity breach~~ could adversely affect our business. We are increasingly dependent on information technology systems to operate our business. In addition, the FDA and comparable foreign regulatory authorities regulate, among other things, the record keeping and storage of data pertaining to potential pharmaceutical products. **Like other** ~~We currently store most of our preclinical research data, our clinical data and our manufacturing data at our facilities. While we do store duplicate copies~~ **companies** ~~of most of our clinical data offsite and a significant portion of our data is included~~ in ~~regular backups of our systems, we could lose important data if our facilities incur damage, or~~ **our industry** ~~if our vendor data systems fail~~ , ~~suffer damage or are destroyed. In addition, we have outsourced significant parts of~~ our information technology **systems** and ~~business~~ infrastructure ~~to~~ **(as well as those of our** third- party providers ~~,~~ **)** and **our lab equipment and operations** ~~we currently use these providers to perform business critical information~~ technology ~~and business services for us. We are therefore vulnerable to cybersecurity attacks and incidents on the associated networks and systems, whether they are managed by us directly or by the third parties with whom we contract, and we have experienced and may in the future experience such cybersecurity threats and attacks. Like other companies in our industry, our networks and infrastructure~~ may be vulnerable to cyber **incidents,** ~~- attacks or~~ intrusions **, and other similar activities that threaten the confidentiality, integrity, and availability of our information. These threats come from a variety of sources** , including by computer hackers, foreign governments, foreign companies, or competitors, or may be breached by employee error, malfeasance or other disruption **. These threats are prevalent, continue to rise, and are becoming increasingly difficult to detect. Recently, there have been reports of disruptions in billing and data systems in healthcare (e. g., the cybersecurity incident affecting Change Healthcare). Such cybersecurity events which materially disrupt the healthcare system upon which our business relies could adversely affect our business if such disruption is widespread and continues for an extended period of time. Cyber incidents could also include the use of artificial intelligence (" AI ") and machine learning to launch more automated, targeted and coordinated attacks on targets. Cyber incidents may lead to operational outages, loss of intellectual property due to industrial espionage, malware, and financial or data attacks via social engineering** . These risks have increased as we have experienced significant growth in the number of our employees and the scope of our operations and as virtual and remote working have become more widely used, and sensitive data is accessed by employees working in less secure, home- based environments. A breakdown, invasion, corruption, destruction, or interruption of ~~critical~~ information technology systems could negatively impact operations. If our systems are damaged, fail to function properly or otherwise become unavailable, we may incur substantial costs to repair or replace them, and we may experience loss of critical data and interruptions or delays in our ability to perform critical functions, which could adversely affect our business, financial condition or results of operations. **Similarly, the increasing use of AI and machine learning technology in the biopharmaceutical industry presents new risks and challenges. The use of AI- based software may lead to the inadvertent release of confidential or proprietary information, which may adversely impact our ability to realize the benefit of our intellectual property, cause us to incur liabilities as the result of any breaches of confidentiality or impact our ability to comply with data security and privacy laws. Further, as the regulatory framework for these technologies evolves, it is possible that new laws and regulations will be adopted, or that existing laws and regulations may be interpreted in ways that would affect our business, including as a result of the cost to comply with such laws or regulations. In addition, we rely on third- party service providers and technologies to operate significant information technology systems and business infrastructure, and we currently use these providers to perform business critical information technology and business services. Supply- chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third- party partners' supply chains have not been compromised. We have experienced cybersecurity threats and incidents, which to date have not had a material impact on our reputation, business, financial condition, or operations; however; there is no assurance that such impacts will not be material in the future.** Any compromise of our data security could also result in a violation of applicable privacy and other laws, significant legal **, regulatory,** and financial exposure, damage to our reputation, loss or misuse of the information and a loss of confidence in our data security measures, which could harm our business. **Loss or misuse of our intellectual property, clinical trial data, or commercially sensitive data could adversely impact our business. While we have implemented security measures designed to protect against security incidents and a significant portion of our data**

is included in regular backups of our systems, ~~There~~ **there** can be no assurance that our efforts to protect our data and information technology systems will prevent breakdowns or breaches in our systems, or those of third parties with which we do business, and any such events could adversely affect our business **Our** business,operations,clinical development or commercialization plans and timelines,and access to capital could be adversely affected by unpredictable and unstable market and economic conditions,including as a result of **rising** inflation,increased interest rates, ~~disruption or instability in~~ the ~~banking industry~~ **effects of the ongoing COVID- 19 pandemic** ,foreign exchange rate fluctuations, **and** ~~a potential U.S.Government shutdown,instability in connection with~~ the **conflict** ~~upcoming presidential election~~ in ~~the United States,geopolitical instability (such as the~~ Ukraine ~~- Russia and Israel- Hamas conflicts or rising tensions between China and Taiwan),or public health emergencies,such as the COVID- 19 pandemic~~ .The magnitude,duration and long- term effect of each of these factors,as well as the effects of actions taken by governments to address them,are unknown at this time,but they could result in further significant disruption of the global economy and financial markets.Our business may be adversely affected by any related economic downturn,volatile geopolitical and business environment,or continued market instability.Unstable market and economic conditions could materially affect our ability to access the equity or debt capital markets or obtain other sources of capital ~~if needed in the future~~ ,which could negatively affect our liquidity.In addition,a recession or market correction could materially affect our business and the value of our common stock.Market and economic conditions continue to evolve,with the ultimate impacts being uncertain and subject to change.These effects could be material,and we will continue to monitor the economic climate **,COVID- 19 pandemic,and the conflict in Ukraine** closely.We do not yet know the full extent and magnitude of the impacts that these developments will **have on our business,on the healthcare system,or on the global economy.In addition,unstable market conditions could have the effect of heightening many of the other risks described in this " Risk Factors " section.** . Risks Relating to Investing in Our Common Stock Our existing principal stockholders hold a substantial amount of our common stock and may be able to influence significant corporate decisions, which may conflict with the interest of other stockholders. Some of our stockholders own greater than 5 % of our outstanding common stock. Our top ten stockholders own approximately ~~50~~ **45** % of our common stock and can individually, and as a group, influence our operations based upon their concentrated ownership and may also be able to influence the outcome of matters requiring approval of the stockholders, including the election of our directors and other corporate actions. Our stock price has been, and is likely to continue to be, highly volatile, which could cause the value of an investment in our common stock to decline significantly. The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be highly volatile in the future. Moreover, our stock price has fluctuated frequently, and these fluctuations are often not related to our financial results. For the twelve months ended December 31, ~~2022~~ **2023** , the 52- week range of the market price of our stock was from $ ~~7~~ **4** . ~~61~~ **83** to $ ~~19~~ **12** . ~~99~~ **08** per share. The following factors, in addition to other risk factors described in this section, may have, and in some cases have had, a significant impact on the market price of our common stock: • announcements of technological innovations or new products by us or our competitors; • developments or disputes concerning patents or proprietary rights; • additional dilution through sales of our common stock or other derivative securities; • status of new or existing licensing or collaborative agreements and government contracts; • announcements relating to the status of our programs; • us or our partners achieving or failing to achieve development milestones; • publicity regarding actual or potential medical results relating to products under development by us or our competitors; • publicity regarding certain public health concerns for which we are or may be developing treatments; • regulatory developments in both the United States and foreign countries; • public concern as to the safety of pharmaceutical products; • actual or anticipated fluctuations in our operating results; • changes in financial estimates or recommendations by securities analysts and the comparison of such estimates to our actual results; • changes in our public guidance; • changes in the structure of healthcare payment systems, including developments in price control legislation; • announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, capital commitments or other monetization transactions; • additions or departures of key personnel or members of our ~~board~~ **Board** of ~~directors~~ **Directors** ; • purchases or sales of substantial amounts of our stock by existing stockholders, including officers or directors; • economic and other external factors or other disasters or crises; and • period- to- period fluctuations in our financial results. This volatility could cause the value of an investment in our common stock to decline significantly. In addition, companies that have experienced volatility in the market price of their stock in the past have been subject to securities class action litigation. Securities litigation, and any other type of litigation, brought against us could result in substantial costs and divert our management' s attention from other business concerns, which could seriously harm our business and adversely affect our results of operations. **We have identified a material weakness in our internal control over financial reporting. This material weakness could divert management' s attention and adversely affect our ability to produce accurate and timely financial statements, which may adversely affect investor confidence in us and our financial reporting, adversely affect our business and operating results and may negatively impact the trading price of our common stock. Our management has identified a material weakness in our internal control over financial reporting, as described in " Controls and Procedures " in Part II, Item 9A of this report. As further described in that section, we are implementing measures, and will continue to implement measures, to remediate the material weakness identified by management and to improve our internal control over financial reporting such that these controls are designed, implemented, and operating effectively. This material weakness will not be considered remediated until the applicable remediated controls are operating for a sufficient period of time and management has concluded, through testing, that these controls are operating effectively. Remediating the material weakness could take longer than expected and divert management' s attention away from other areas of the business. A material weakness, as defined in Rule 12b- 2 under the Exchange Act, is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Although we believe the financial statements included in this report fairly present, in all material respects, our financial**

condition, results of operations and cash flows for the periods presented in conformity with U. S. GAAP, any failure to maintain effective internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If our internal control over financial reporting is not effective, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Future sales and issuances of securities may dilute the ownership interests of our current stockholders and cause our stock price to decline. Future sales of our common stock by us or our current stockholders into the public market could cause the market price of our stock to fall. As of ~~January~~ **December** 31, 2023, there were ~~188~~ **205** , ~~451~~ **770** , ~~137~~ **667** shares of our common stock outstanding. We may from time to time issue securities in relation to a license arrangement, collaboration, merger or acquisition. We may also sell, for our own account, shares of common stock or other equity securities, from time to time at prices and on terms to be determined at the time of sale. As of ~~January~~ **December** 31, 2023, there were ~~34~~ **41** , ~~992~~ **096** , ~~042~~ **637** stock options and restricted stock units outstanding and ~~4~~ **3** , ~~254~~ **375** , ~~957~~ **511** shares available for issuance under our Amended and Restated Stock Incentive Plan, 6, ~~150~~ **442** , ~~129~~ **678** stock options and restricted stock units outstanding and ~~607~~ **1** , ~~208~~ **650, 708** shares available for issuance under our Amended and Restated Inducement Equity Incentive Plan, and 5, ~~616~~ **454** , ~~817~~ **386** shares available for issuance under our Amended and Restated Employee Stock Purchase Plan. In addition, we could also make equity grants outside of our Amended and Restated Stock Incentive Plan or Amended and Restated Inducement Equity Incentive Plan. The shares underlying existing stock options, restricted stock units and possible future stock options, stock appreciation rights **, restricted stock units** and stock awards have been **, or will be,** registered pursuant to registration statements on Form S- 8. If some or all of such shares are sold or otherwise issued into the public market over a short period of time, our current stockholders' ownership interests may be diluted and the value of all publicly traded shares is likely to decline, as the market may not be able to absorb those shares at then- current market prices. Additionally, such sales and issuances may make it more difficult for us to sell equity securities or equity- related securities in the future at a time and price that our management deems acceptable, or at all. ~~In March 2017, we entered into a Registration Rights Agreement with entities affiliated with Baker Bros. Advisors LP (the " Baker Entities ") to provide that, if requested, we will register the shares of our common stock beneficially owned by the Baker Entities for resale under the Securities Act of 1933, as amended (the " Securities Act "). Our registration obligations pursuant to the Registration Rights Agreement cover all shares then held or thereafter acquired by the Baker Entities, for up to ten years, and include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. On May 10, 2017, we filed a registration statement on Form S- 3 with respect to 11, 710, 951 shares of common stock held by the Baker Entities. Subsequently, on November 21, 2019, certain of the Baker Entities acquired pre- funded warrants to purchase 11, 764, 706 shares of our common stock at a price of $ 1. 69 per warrant, of which warrants to purchase 11, 511, 472 shares of our common stock remain outstanding. In addition, on June 1, 2020, we issued to certain of the Baker Entities pre- funded warrants to purchase 3, 511, 111 shares of our common stock at a price of $ 4. 49 per warrant. Each warrant has an exercise price of $ 0. 01 per share. If the Baker Entities, by exercising their registration rights or otherwise, sell a large number of our shares, or the market perceives that the Baker Entities intend to sell a large number of our shares, this could adversely affect the market price of our common stock.~~ We have anti- takeover provisions in our corporate charter documents that may result in outcomes with which you do not agree. Our ~~board~~ **Board** of ~~directors~~ **Directors** has the authority to issue up to 5, 000, 000 shares of undesignated preferred stock and to determine the rights, preferences, privileges and restrictions of those shares without further vote or action by our stockholders. The rights of the holders of any preferred stock that may be issued in the future may adversely affect the rights of the holders of common stock. The issuance of preferred stock could make it more difficult for third parties to acquire a majority of our outstanding voting stock. In addition, our Certificate of Incorporation provides for staggered terms for the members of the ~~board~~ **Board** of ~~directors~~ **Directors** and supermajority approval of the removal of any member of the ~~board~~ **Board** of ~~directors~~ **Directors** and prevents our stockholders from acting by written consent. Our Certificate of Incorporation also requires supermajority approval of any amendment of these provisions. These provisions and other provisions of our Amended and Restated ~~Bylaws~~ **By- Laws** and of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us. We have never paid dividends on our common stock and do not anticipate doing so in the foreseeable future. We have never paid cash dividends on our stock. We currently intend to retain all future earnings, if any, for use in the operation of our business. Accordingly, we do not anticipate paying cash dividends on our common stock in the foreseeable future. Our Amended and Restated ~~Bylaws~~ **By- Laws** provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for certain litigation that may be initiated by our stockholders, which may limit a stockholder' s ability to obtain a favorable judicial forum for such disputes with us or our directors, officers or employees. Our Amended and Restated ~~Bylaws~~ **By- Laws** provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, stockholders, employees or agents to us or our stockholders, (iii) any action asserting a claim against us or any of our directors, officers, stockholders, employees or agents arising out of or relating to any provision of the General Corporation Law of Delaware or our Certificate of Incorporation or Amended and Restated ~~Bylaws~~ **By- Laws** , or (iv) any action against us or any of our directors, officers, stockholders, employees or agents governed by the internal affairs doctrine of the State of Delaware. This exclusive forum provision does not apply to establish the Delaware Court of Chancery as the forum for actions or proceedings brought to enforce a duty or liability created by the Securities Act or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction. This exclusive forum provision may limit a stockholder' s ability to choose its preferred judicial forum for disputes with us or our directors, officers, employees or agents, which may discourage the filing of lawsuits with respect to such claims. If a court were to find this exclusive forum provision to be inapplicable or unenforceable in an

action, we may incur additional costs associated with resolving such action in another jurisdiction, which could adversely affect our business and financial condition. General Risk Factors Natural disasters, epidemic or pandemic disease outbreaks, trade wars, armed conflicts, political unrest or other events could disrupt our business or operations or those of our development partners, manufacturers, regulators or other third parties with whom we conduct business now or in the future. A wide variety of events beyond our control, such as natural disasters (including as a result of climate change), epidemic or pandemic disease outbreaks (such as the ~~ongoing~~ COVID- 19 pandemic), trade wars, armed conflict, political unrest **, government shutdowns, instability in connection with the upcoming presidential election in the United States,** or other events could disrupt our business or operations or those of our development partners ~~(such as Torii)~~, manufacturers, regulatory authorities, or other third parties with whom we conduct business. These events may cause businesses and government agencies to be shut down, supply chains **or trade** to be interrupted, slowed, or rendered inoperable, and individuals to become ill, quarantined, or otherwise unable to work and / or travel due to health reasons or governmental restrictions. If our operations or those of third parties with whom we conduct business are impaired or curtailed as a result of these events, the development and commercialization of our products and product candidates could be impaired or halted, which could have a material adverse impact on our business. See, for example, " Risk Factors — ~~General Risk~~ **Risks** ~~Factors~~ **Relating to Our Business — Other Operational Risks** — Our business, operations, clinical development or commercialization plans and timelines, and access to capital could be adversely affected by unpredictable and unstable market and economic conditions. " In addition, other events, such as the ~~armed~~ **Ukraine- Russia and Israel- Hamas** ~~conflict~~ **conflicts , or rising tensions** between ~~Russia~~ **China** and ~~Ukraine~~ **Taiwan** , could adversely impact our business. For example, the ~~conflict~~ **conflicts** could lead to sanctions, embargoes, supply shortages, regional instability, geopolitical shifts, cyber- attacks, other retaliatory actions, and adverse effects on macroeconomic conditions, currency exchange rates, and financial markets, which could adversely impact our operations and financial results, as well as those of third parties with whom we conduct business. Our business, operations, clinical development..... this " Risk Factors " section. We are subject to legal proceedings, which could harm our reputation or result in other losses or unexpected expenditure of time and resources. From time to time, we may be involved in disputes, including, without limitation, disputes with our employees, collaborative partners, and third- party vendors. We may be called upon to initiate legal proceedings or to defend ourselves in such legal proceedings relating to our relationships with these parties, our decisions and actions or omissions with respect thereto, and our business. In addition, if our stock price is volatile, we may become involved in securities class action lawsuits in the future. Due to the inherent uncertainties in legal proceedings, we cannot accurately predict the ultimate outcome of any such ~~proceedings~~ **proceeding** . An unfavorable outcome in any such ~~proceedings~~ **proceeding** could have an adverse impact on our business, financial condition and results of operations. Any current or future dispute resolution or legal proceeding, regardless of the merits of any such proceeding, could harm our reputation and result in substantial costs and a diversion of management' s attention and resources that are needed to successfully run our business. ~~Insurance coverage is increasingly more costly and difficult to obtain or maintain. While we currently have insurance for our business, property, directors and officers, and our products, insurance is increasingly more costly and narrower in scope, and we may be required to assume more risk in the future. If we are subject to claims or suffer a loss or damage in excess of our insurance coverage, we will be required to bear any loss in excess of our insurance limits. If we are subject to claims or suffer a loss or damage that is outside of our insurance coverage, we may incur significant uninsured costs associated with loss or damage that could have an adverse effect on our operations and financial position. Furthermore, any claims made on our insurance policies may impact our ability to obtain or maintain insurance coverage at reasonable costs or at all. If we fail to retain our existing key personnel or fail to attract and retain additional key personnel, the development of our product candidates, the commercialization of our products, and the related expansion of our business will be delayed or stopped. We are highly dependent upon our senior management and scientific team, the unexpected loss of whose services might impede the achievement of our development and commercial objectives. Competition for key personnel with the experience that we require is intense and is expected to continue to increase. Our inability to attract and retain the required number of skilled and experienced management, commercial, operational and scientific personnel would harm our business because we rely upon these personnel for many critical functions of our business.~~