Risk Factors Comparison 2024-02-15 to 2023-02-10 Form: 10-K

Legend: **New Text** ~~Removed Text~~ Unchanged Text Moved Text Section

Investing in our common stock involves a high degree of risk, and you should carefully consider the risks and uncertainties described below in addition to the other information included or incorporated by reference in this Annual Report on Form 10- K. If any of the following risks or uncertainties actually occurs, our business, financial condition or results of operations would likely suffer, possibly materially. In that case, the trading price of our common stock could decline. SUMMARY OF RISK FACTORS Our business is subject to numerous risks and uncertainties, discussed in more detail in the following section. These risks include, among others, the following key risks: Risks Related to Our Business • We invest significant resources in the research, development, manufacturing and supply of therapies for serious diseases ~~other than CF~~ , and if we are unable to successfully **develop and** commercialize **additional products** ~~one or more of these therapies~~ , our business could be materially harmed. • ~~All~~ **Over the last several years all** of our product revenues **were** ~~and the vast majority of our total revenues are~~ derived from sales of **our CF** medicines ~~for the treatment of CF~~ . If we are unable to continue to increase revenues from sales of our CF medicines ~~or to eventually derive revenues from the sales of our pipeline products~~ , our business would be materially harmed and the market price of our common stock would likely decline. • ~~We have~~ **If we are not successful in commercializing CASGEVY, our revenue growth could be** limited ~~experience developing~~ and **our business** ~~commercializing cell and genetic therapies and~~ could ~~experience challenges with these programs~~ **be materially harmed. • If we are unable to successfully develop** , ~~which~~ **obtain approval, and commercialize treatments for acute and neuropathic pain, our business** could **be materially harmed** ~~result in delays or prevent the development, manufacturing and commercialization of our cell and genetic therapies~~ . • If our competitors bring products with superior product profiles to market, our products may not be competitive **,** and our revenues could decline. • If we discover safety issues with any of our products or if we fail to comply with continuing U. S. and applicable foreign regulations, commercialization efforts for the product could be negatively affected, the approved product could lose its approval or sales could be suspended, and our business could be materially harmed. • If physicians and patients do not accept our products, or if patients do not remain on treatment or comply with their prescribed dosing regimen, our product revenues would be materially harmed in future periods. **• Cell and genetic therapies face increased scrutiny from the public and medical communities and commercial success will depend, in part, upon the acceptance of those communities.** Risks Related to Pricing of Our Products • Government and other third- party payors seek to contain costs of health care through legislative and other means. If they fail to provide coverage and adequate reimbursement rates for our products, our revenues will be harmed. • We may experience ~~incremental~~ pricing pressure on our products, which could reduce our revenues and future profitability. • Current health care laws and regulations in the U. S. and future legislative or regulatory reforms to the U. S. health care system may affect our ability to commercialize our marketed products profitably. • We have experienced challenges commercializing products outside of the U. S., and our future revenues will be dependent on our ability to obtain adequate reimbursement for our products **in ex- U. S. markets. • Insurance coverage and reimbursement of our cell or genetic therapies is uncertain** . Risks Related to Development and Clinical Testing of Our Products and Product Candidates • Our product candidates remain subject to clinical testing and regulatory approval, and our future success is dependent on our ability to successfully develop additional product candidates for both CF and non- CF indications. • If we are unable to obtain or are delayed in obtaining regulatory approval, we may incur additional costs, experience delays in commercialization, or be unable to commercialize our product candidates. • If clinical trials are prolonged or delayed, our development timelines for the affected development program could be extended, our costs to develop the product candidate could increase and the competitive position of the product candidate could be adversely affected. • Difficulty in enrolling patients could delay or prevent clinical trials of our product candidates, and ultimately delay or prevent regulatory approval. **• Enrollment for clinical trials for our cell and gene therapies may face additional and unique challenges and adverse developments associated with these clinical trials could result in action by regulatory bodies, including revised requirements for approval.** Risks Related to Government Regulation • If regulatory authorities interpret any of our conduct, including our marketing practices, as being in violation of applicable health care laws, including fraud and abuse laws, laws prohibiting off- label promotion, disclosure laws or other similar laws, we may be subject to civil or criminal penalties. • If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the U. S., we could be subject to additional reimbursement requirements, penalties, sanctions **,** and fines that could have a material adverse effect on our business, financial condition, results of operations and growth prospects. • If our processes and systems are not compliant with regulatory requirements, we could be subject to restrictions on marketing our products or could be delayed in submitting regulatory filings seeking approvals for our product candidates. • **The** ~~We are subject to various and evolving laws and regulations~~ - **regulatory approval process** ~~governing the privacy and security of personal data, and our failure to comply could adversely affect our business, result in fines and / or~~ **for** ~~criminal penalties, and damage~~ our **cell** ~~reputation. Risks Related to Business Development Activities • Our ability to execute on our long- term strategy depends in part on our ability to engage in transactions~~ and ~~collaborations~~ **genetic therapies involves additional consultations** with ~~other entities that add~~ **regulatory agencies, costs, and potentially longer timelines as compared** to **those** ~~our pipeline or~~ **for small molecules** ~~provide us with new commercial opportunities. • We may not realize the anticipated benefits of acquisitions of businesses or technologies, and the integration following any such acquisition may disrupt our business and management. • We face risks in connection with existing and future collaborations with respect to the development, manufacture and commercialization of our products and product candidates. • We may not be able to attract collaborators or external funding for~~

~~the development and commercialization of certain of our product candidates~~ . Risks Related to Supply, Manufacturing and Reliance on Third Parties • We depend on third- party manufacturers and our internal capabilities to manufacture our products and the materials we require for our clinical trials. We **rely on third party logistics providers to manage our shipments globally. We** may not be able to maintain our third- party relationships and could experience supply disruptions outside of our control. • We rely on third parties to conduct pre- clinical work, clinical trials and other activities, and those third parties may not perform satisfactorily, including failing to meet established deadlines for the completion of such studies and / or trials or failing to satisfy regulatory requirements. Risks Related to **Business Development Activities • Our ability to execute on our long- term strategy depends in part on our ability to engage in transactions and collaborations with other entities that add to our pipeline or provide us with new commercial opportunities. • We face risks in connection with existing and future collaborations with respect to the development, manufacture and commercialization of our products and product candidates. • We may not realize the anticipated benefits of existing or future acquisitions of businesses or technologies, and the integration following any such acquisition may disrupt our business and management. Risks Related to** Intellectual Property • If our patents do not protect our products ~~or~~ **and** our products infringe third- party patents, we could be subject to litigation which could result in injunctions preventing us from selling ~~our~~ **out** products ~~or~~ **,** substantial ~~liabilities~~ **damages, or circumvention of our patents by third parties** . • Uncertainty over intellectual property in the pharmaceutical and biotechnology industry has been the source of litigation and other disputes ~~,~~ that are inherently costly and unpredictable. • We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property. Risks Related to Our Operations **• If we fail to scale our operations to accommodate growth, our business may suffer.** • A variety of risks associated with operating in foreign countries could materially adversely affect our business. • If we fail to attract and retain skilled employees, our business could be materially harmed. • A breakdown or breach of our information technology systems could subject us to liability or interrupt the operation of our business. Risks Related to Financial Results and Holding Our Common Stock • Our effective tax rate fluctuates, and changes in tax laws, regulations and treaties, unfavorable resolution to the tax positions we have taken or exposure to additional income tax liabilities could have a material impact on our future taxable income. We invest significant resources in the research and development of ~~medicines~~ **therapies** for serious diseases **,** including **CF,** SCD, **TDT** ~~beta thalassemia~~ , **acute and neuropathic** pain, AMKD, T1D, **DM1, and** AATD ~~, DMD and DM1. Some of these programs have progressed into clinical trials, while others are still in pre- clinical development~~ . Product development is highly uncertain and expensive, and we may experience unforeseen delays, including regulatory and commercialization delays. Product candidates that may appear promising in the early phases of research and development may fail to reach commercial success for many reasons, including the failure to demonstrate acceptable clinical trial results or obtain marketing approval, the inability to manufacture or commercialize the product candidate on economically feasible terms, or the appearance of safety issues. **When** ~~For example, in October 2020,~~ we **receive** ~~decided not to progress VX- 814, a drug candidate for the treatment of AATD, into further development based on safety and pharmacokinetic data observed in a Phase 2 clinical trial. Even if we gain~~ marketing approval for **a** ~~one or more~~ pipeline ~~products~~ **product** , we cannot be sure that we will obtain market acceptance or adequate reimbursement levels from third- party payors or foreign governments for such ~~products~~ **product** . Additionally, many of the therapies that we are developing in our pipeline target rare diseases that affect a limited number of patients. There can be no guarantee that we will effectively identify patients that are eligible for enrollment in our clinical trials or treatment with our product candidates. Even if we do successfully identify eligible patients, the number of patients that our product candidates are able to treat may turn out to be lower than we expect or new patients may become increasingly difficult to identify, each of which may adversely affect our revenues and materially harm our business. **If** ~~For these and other reasons,~~ we ~~may never~~ **are not able to successfully develop and commercialize additional products our business could** be **materially harmed** ~~successful in expanding our pipeline and future revenue may continue to depend on sales of our CF medicines~~ . ~~Our~~ **Substantially all of our** net product revenues **have been** ~~and the vast majority of our total revenues are~~ derived from the sale of our CF medicines **over the last several years** . As a result, our **business** ~~future success~~ is ~~largely~~ dependent upon our ability to **sustain and** increase revenues from sales of our CF medicines. **We seek** ~~This will require us~~ to continue to ~~gain~~ **increase our CF product revenue through serial innovation, including the potential** approval **of our vanzacaftor** ~~and reimbursement for TRIKAFTA~~ / **tezacaftor** ~~KAFTRIO in ex- U. S. markets, successfully develop and commercialize TRIKAFTA~~ / ~~KAFTRIO for~~ **deutivacaftor triple combination, development and commercialization CF medicines in** younger children with CF **and through securing additional approvals and reimbursements** ~~or for successfully develop and commercialize products from~~ our ~~pipeline~~ **CF medicines in ex- U. S. markets** . Our concentrated source of revenues presents a number of risks to our business, including: • that one or more competing therapies may be developed successfully as a treatment for people with CF; • that reimbursement policies of payors and other third parties may make it difficult to obtain reimbursement or reduce the net price we receive for our products; • that we may experience manufacturing or supply disruptions for our CF medicines; and • that we may experience adverse developments with respect to development or commercialization of our CF medicines ~~and / or pipeline product candidates~~ . If any of the above risks were to materialize, if we are otherwise unable to increase revenues from sales of our CF medicines, or if we do not meet the expectations of investors or public equity market analysts, our business would be materially harmed and our ability to fund our operations could be adversely affected. We ~~are investing~~ **recently obtained approval for CASGEVY for the treatment of people 12 years and older with SCD and TDT in the U. S., the E. U., the U. K., Saudi Arabia, and Bahrain. We invested** significant resources in the research ~~,~~ **and** development ~~, manufacturing, and commercialization~~ of **CASGEVY** ~~cell and genetic therapies, including exa- cel~~ . While we have previously successfully ~~developed, manufactured, and~~ commercialized several small molecule drugs, we have limited experience with the ~~development, manufacture, and~~ commercialization of cell and genetic therapies. ~~Development, manufacturing~~ **Manufacturing** , and commercialization of **CASGEVY is** ~~cell and genetic therapies are~~ subject to similar risks and uncertainties as small

molecules. In addition: • the manufacturing ~~processes~~ -- **process** for **CASGEVY is** ~~cell and genetic therapies are different, less mature and~~ more complex than the manufacturing processes ~~required~~ for ~~small molecule drugs~~ **our CF medicines** and ~~require investments in systems, equipment, facilities, and expertise to develop and maintain; •~~ we may encounter difficulties in the production of **CASGEVY** ~~our cell and genetic therapies~~ and ensuring that the product meets required specifications; • there ~~have been~~ **are multiple steps along the CASGEVY patient treatment journey, many of which involve significant clinical complexities performed by third parties, including the collection of blood cells from patients, transfer of those cells to and from** a ~~limited number of regulatory approvals~~ **manufacturing facility, and other procedures either before** ~~for~~ **or after delivery of CASGEVY** ~~genetic therapies to date, the regulatory requirements governing genetic therapies continue to evolve, and regulatory positions and interpretations can change or lead to delays or significant unexpected costs with respect to our genetic therapy programs~~ ; • the commercial success of **CASGEVY** ~~cell or genetic therapies, including exa- cel and VX- 880, if approved,~~ will depend in part on the medical community, patients, governments, and third- party or governmental payors accepting and providing adequate reimbursement **of CASGEVY** ~~for cell or genetic therapy~~ products ~~in general~~ , and recognizing the applicable medicine as medically useful, cost- effective, ethical, and safe; and • market acceptance will be dependent in part on the prevalence and severity of side effects associated with the procedure by which **CASGEVY** ~~the cell or genetic therapy~~ is administered ~~, including, with respect to exa- cel and VX- 880, if approved~~ , the prevalence and severity of any side effects resulting from the myeloablative preconditioning regime **. If we are unable to successfully develop, obtain approval and commercialize treatments** ~~or~~ **for** ~~immunosuppression~~ **acute and neuropathic pain** , ~~respectively~~ **our business could be materially harmed** . ~~For~~ **We believe that a portion of the value attributed to our company by investors is based on our potential treatments for acute and neuropathic pain, including VX- 548. We have completed the Phase 3 development** ~~programs~~ **program** ~~addressing~~ **for VX- 548 in acute pain and we** ~~rare~~ **are** ~~genetic diseases with small patient populations,~~ **planning to submit an NDA to the FDA by mid- 2024. We are planning to initiate a Phase 3 development program for VX- 548 in neuropathic pain based on positive Phase 2 clinical results we received in the fourth quarter of 2023. Obtaining approval for VX- 548 is uncertain process and** we may not be **successful. If we do not obtain approval** ~~able to identify, recruit and enroll a sufficient number~~ of ~~patients~~ **VX- 548** , ~~or~~ **our business** ~~those with required or desired characteristics, to complete our clinical studies in an adequate and timely manner. Additionally, patients~~ may be ~~unwilling to participate in~~ **materially harmed. VX- 548, if approved, may not gain** ~~our~~ **or** ~~clinical trials because~~ **maintain market acceptance among physicians and patients or other members** of ~~concerns~~ **the medical community. In addition to the risks normally associated with launching a new branded product, VX- 548 will need to compete in an acute pain market** that ~~cell and~~ **largely consists of low- cost** ~~genetic~~ **generic drugs** ~~therapies are unsafe or unethical, negative publicity from adverse events in the biotechnology or gene therapy industries, or for other reasons~~ , including ~~competitive clinical studies for~~ **opioids, non- steroidal anti- inflammatory drugs, acetaminophen and local anesthetics.** ~~similar~~ **Similarly** ~~patient populations. Moreover~~ , adverse developments in clinical trials conducted by..... we otherwise would have expected. Even if we **are successful in** ~~comply with applicable laws, rules, and regulations, and even if we maintain close coordination with the applicable regulatory authorities with oversight over our cell and genetic therapy product candidates, our development~~ **developing and** ~~programs may experience delays or fail to succeed. Delay or failure to obtain, or unexpected costs in~~ obtaining ~~,~~ ~~the regulatory~~ approval ~~necessary to bring a potential cell or~~ **for VX** genetic therapy product to market would materially..... treatment candidates or lead to significant post - **548 in neuropathic pain** ~~approval limitations or restrictions. To develop and commercialize cell or genetic therapies~~ , **VX** ~~including exa-~~ **548** ~~cel, we are incurring substantial expenditures to develop, contract for, or otherwise arrange for the necessary supplies and manufacturing capabilities. Additionally, the manufacture of cell and genetic therapies requires significant expertise. Even with the relevant experience and expertise, manufacturers of cell and genetic therapy products often encounter difficulties in production, including difficulties with production costs and yields, quality control, and compliance with federal, state and foreign regulations. We cannot make any assurances that these problems~~ will **face competition** ~~not occur, or that we will be able to resolve or address problems that occur in a timely manner, or at all. To the extent we develop manufacturing capabilities internally, there are many risks that could result in delays and additional costs, including the need to hire and train qualified employees and obtain access to necessary equipment and third- party technology. To the extent we partner with third parties to manufacture our cell or genetic therapies, the complexity in the manufacture of our products and product candidates may require lengthy technology transfers. In addition, the third parties on which we rely to manufacture our cell or genetic therapies may experience their own compliance challenges or delays. We are also devoting substantial resources to expand our commercial organization to prepare for the anticipated future product launches~~ from ~~our pipeline programs. For example, with respect to exa- cel, we are creating and developing the internal and external support systems to reach and support potential future patients, in addition to establishing and ensuring the necessary supply and manufacturing infrastructure. We cannot make any assurances that we will obtain approval for products from our pipeline programs, or that, if approved, a future product will generate substantial revenues and cash flows. We also face uncertainty as to whether cell and gene therapy treatments will gain the acceptance of the public or the medical community. If we obtain regulatory approval, the commercial success of cell and gene therapy treatments will depend, in part, on the acceptance of physicians, patients, and third- party payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost- effective, and safe. In particular, our success will depend upon physicians prescribing our product candidates in lieu of existing treatments they are already familiar with and for which greater clinical data may be available. Moreover, physicians and patients may delay acceptance of cell and gene therapy product candidates until the product candidates have been on the market for a certain amount of time. In addition, medical centers that administer procedures accompanying treatment could experience capacity constraints, and these centers are subject to competing priorities that could delay patient access to procedures associated with cell and gene therapy products. Negative public opinion or more restrictive government regulations may delay or impair the successful commercialization of, and demand for, cell and gene therapies.~~

~~There also is significant uncertainty related to the insurance coverage and reimbursement of cell or genetic~~ **generic anticonvulsant** ~~therapy products, including gene therapies that are potential one- time treatments. It is difficult to predict what third party payors, including U. S. or ex- U. S. governments or private insurance companies, will decide with respect to reimbursement for novel cell and genetic therapies like the ones in our pipeline. Additionally, reimbursement rates for cell and genetic therapies approved before ours could create an~~ **and antidepressant drugs** adverse environment for reimbursement of any therapies..... which are subject to additional regulatory requirements . If we are **not** ~~unable~~ -- **able** to successfully develop, ~~manufacture,~~ **obtain approval** ~~or~~ **for and** commercialize **treatments** ~~such therapies on a timely or~~ **for** ~~profitable basis~~ **acute and neuropathic pain** , ~~or~~ **our future net product revenues and** ~~at all, we may not realize benefits or generate~~ cash flows **will** ~~based on our investments in these programs and our business, financial condition, results of operations and our stock price would likely~~ be adversely affected **and our business could be materially harmed** . A number of companies are seeking to identify and develop product candidates for the treatment of CF **, SCD, TDT, pain,** and other therapeutic areas we are targeting with our research and development activities. Our success in rapidly developing and commercializing our CF medicines may increase the resources that our competitors allocate to the development of potential competitive treatments. If one or more competing therapies are successfully developed as a treatment for people with CF **, SCD, TDT, pain** or any of the other ~~diseases~~ **disease areas** we are currently targeting in our pipeline, our products and our net product revenues could face competitive pressures. If one or more competing therapies prove to be superior to our then **-** existing products and / or product candidates, our business could be materially adversely affected. In addition, our business faces competition from major pharmaceutical companies possessing substantially greater financial resources than we possess **, as well as** ~~. We also face competition~~ from numerous smaller public and private companies, academic institutions, government agencies, public and private research organizations, and charitable venture philanthropy organizations that conduct research, seek patent protection, and / or establish collaborative arrangements for research, development, manufacturing, and commercialization. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early- stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our products and any products that we develop in the future may not be able to compete effectively with marketed ~~drugs~~ **therapies** or new ~~drugs~~ **therapies** that may be developed by competitors. The risk of competition is particularly important to our company because substantially all of our revenues are related to the treatment of people with CF. There are many other companies developing products for the same patient populations that we are pursuing. To compete successfully in these areas, we must demonstrate improved safety, efficacy and / or tolerability, ease of manufacturing, and gain and maintain market acceptance over competing products. Our products are subject to continuing regulatory oversight, including the review of additional safety information. Products are more widely used by patients once approval has been obtained and therefore side effects and other problems may be observed after approval that were not seen or anticipated, or were not as prevalent or severe, during pre- approval clinical trials or nonclinical studies. The subsequent discovery of previously unknown or underestimated problems with a product could negatively affect commercial sales of the product, result in restrictions on the product or lead to the withdrawal of the product from the market. Each of our CF products shares at least one active pharmaceutical ingredient with another of our products. As a result, if any of our CF products were to experience safety issues, our other CF products may be adversely affected. **In SCD and TDT, as part of the FDA approval for CASGEVY, we are required to conduct two post- marketing requirement safety studies to assess the long- term risk of hematologic malignancies and off- target genome editing effects by CRISPR / Cas9. Negative or ambiguous results from these studies could also have a significant impact on our ability to commercialize CASGEVY.** The reporting of adverse safety events involving our products or public speculation about such events could cause our stock price to decline or experience periods of volatility. Our business also may be materially harmed by impaired sales of our products, denial or withdrawal of regulatory approvals, **non- renewal of conditional regulatory approvals,** required label changes or additional clinical trials, reputational harm, or government investigations or lawsuits brought against us. Our products are subject to ongoing regulatory requirements governing the testing, manufacturing, labeling, packaging, storage, advertising, promotion, sale, distribution, import, export, recordkeeping, and submission of safety and other post- market information. We and our third- party manufacturers must comply with cGMP and other applicable regulations governing the manufacturing and distribution of our products. Regulatory authorities periodically inspect our drug manufacturing facilities, and those of our third- party manufacturers, to evaluate compliance with cGMP and other regulatory requirements. If we or our collaborators, or third- parties acting on our behalf, fail to comply with applicable continuing regulatory requirements, we or our collaborators may be subject to fines, suspension or withdrawal of regulatory approvals for specific products, product recalls and seizures, operating restrictions and / or criminal prosecutions, any of which could have a material adverse effect on our business, reputation, financial condition, and results of operations. ~~In addition, treatment with some of our cell and genetic therapy product candidates, including exa- cel and VX- 880, involve myeloablative preconditioning regimens or immunosuppression, and the patients in our clinical trials receiving these treatments may experience side effects (ranging from mild to severe) or adverse events. Such events could have a significant negative impact on our ability to develop or commercialize our product candidates.~~ Our ~~medicines~~ **approved products** may not gain or maintain market acceptance among physicians and patients or other members of the medical community. Effectively marketing our products and any of our product candidates or investigational therapies, if approved, requires substantial efforts, both prior to launch and after approval. Physicians may elect not to prescribe our products or recommend our cell or genetic therapies, and patients may elect not to take them or receive them or they may discontinue use of our products after initiation of treatment, for a variety of reasons including: • prevalence and severity of adverse side effects; • lack of reimbursement availability from third- party payors, including governmental entities; • lower

demonstrated efficacy, safety and / or tolerability compared to alternative treatment methods; • lack of cost- effectiveness; • a decision to wait for the approval of other therapies in development that have significant perceived advantages over our product; • convenience and ease of administration; • limitations or warnings contained in the labeling; • the timing of market introduction of our product as well as competitive products; • other potential advantages of alternative treatment methods; and • inadequate sales, marketing and / or distribution support ~~, including as a result of limitations or restrictions resulting from COVID- 19~~. If our medicines fail to achieve or maintain market acceptance, we may not be able to generate significant revenues in future periods. We **face uncertainty** ~~are dependent upon a small number of customers for a significant portion of our revenue, and the loss of, or significant reduction in sales to, these customers would adversely affect our results of operations. In the U. S., we sell our CF products principally to a limited number of specialty pharmacy and specialty distributors, which subsequently resell our products to patients and health care providers. Internationally, we sell our products primarily through distributor arrangements and to a limited number of retail pharmacies or pharmacy chains,~~ as **to whether** ~~well~~ **cell** ~~as to hospitals~~ and **gene therapy treatments will gain the acceptance of the public** ~~clinics. We expect this significant customer concentration in CF to continue for~~ **or** the ~~foreseeable future~~ **medical community**. **The commercial success** ~~Our ability to generate and grow sales~~ of ~~our CF medicines~~ **cell and gene therapy treatments, including CASGEVY,** will depend ~~significantly~~ **, in part,** on the ~~extent to~~ **acceptance of physicians, patients, and third- party payors of gene therapy products in general, and our product candidates in particular, as medically necessary, cost- effective and safe. In particular, our success will depend upon physicians prescribing our therapies in lieu of existing treatments they are already familiar with and for** which **greater clinical data may be available. Moreover, physicians and patients may delay acceptance of cell and gene therapies until the therapies have been on the market for a certain amount of time. In addition, medical centers, including ATCs, that administer procedures accompanying treatment could experience capacity constraints, and** these **centers** ~~specialty distributors and specialty pharmacies~~ are ~~able~~ **subject** to ~~provide adequate distribution of our~~ **competing priorities that could delay patient access to procedures associated with cell and gene therapy** products ~~to patients and healthcare providers~~. **Negative public opinion or more restrictive government regulations may delay or impair** ~~The loss of any large customer, a significant reduction in sales we make to them~~ **the successful commercialization** ~~, any cancellation~~ of ~~orders they have made with us~~, **and demand** ~~or~~ **for** ~~any failure to pay for the products we have shipped to them could adversely affect our business~~, **cell** ~~financial condition,~~ and **gene therapies** ~~results of operations~~. Sales of our products depend in part upon the availability of reimbursement from third- party payors. Third- party payors include government health programs such as Medicare and Medicaid in the U. S. and the national health care systems in ex- U. S. markets, managed care providers, private health insurers and other organizations. The trend in the health care industry is cost containment, and efforts of third- party payors to contain or reduce health care costs may adversely affect our ability to establish or maintain appropriate prices for our products or any drugs that we may develop and commercialize. In the U. S., there have been, and we expect that there will continue to be, a number of federal and state proposals to implement governmental controls that are similar to those that currently exist in Europe. For example, the ACA required manufacturers of Medicare Part D brand name drugs to provide discounts on those drugs to Medicare Part D beneficiaries during the coverage gap; increased the rebates paid by pharmaceutical companies to state Medicaid programs on drugs covered by Medicaid; and imposed an annual fee, which increases annually, on sales by branded pharmaceutical manufacturers. Additionally, private payors, including health maintenance organizations and pharmacy benefit managers in the U. S., are adopting more aggressive utilization management techniques and are increasingly applying restrictive plan designs that can impact patients and manufacturers, and they continue to push for significant discounts and rebates from manufacturers. Additionally, on August 16, 2022, the **IRA** ~~Inflation Reduction Act~~ was enacted. ~~The law~~ **Among other things, the IRA** establishes a Drug Price Negotiation Program, under which the government may negotiate maximum fair prices for certain drugs covered by Medicare that do not have generic or biosimilar competition. The first set of maximum fair prices will be effective in 2026. Certain products are excluded from the negotiation program including drugs that have a single orphan drug designation and that are not approved for any other orphan or non- orphan diseases or conditions. We cannot predict with certainty whether there will be future legislative changes to the scope of these exclusions. The law also requires manufacturers to pay a rebate to Medicare if the price of a Medicare drug (under both Part B and Part D) increases faster than the rate of inflation. The law also redesigns the Part D benefit. The current Coverage Gap Discount Program, which requires manufacturers to provide a 70 % discount on brand drugs and biologics during the coverage gap phase, will be eliminated after the 2024 plan year. Starting in 2025, manufacturers of brand drugs and biologics will be required to provide a 10 % discount during the initial phase and a 20 % discount during the catastrophic phase of the Part D benefit. The **IRA** ~~Inflation Reduction Act~~ continues a trend in the ~~United States~~ **U. S.** toward reducing drug prices and limiting spending by the federal health care programs on drugs. We cannot predict how CMS will interpret the **IRA** ~~Inflation Reduction Act~~ or how the provisions of the law will affect our business once fully implemented, but it is possible that these changes or other legislative updates will have an adverse impact on our revenue. The **IRA** ~~Inflation Reduction Act~~ also requires the Secretary of the Department of Health and Human Services **(the " Secretary ")** to issue program guidance on numerous areas associated with implementation of the law' s requirements, including for drug price negotiation and inflation rebates. We cannot know what form this program guidance would take or how it would affect our business. It is possible the U. S. Congress or administration may take further actions to ~~control prescription drug pricing~~ **address health care costs and access to medicine, and specifically address coverage and reimbursement of cell and gene therapies**. For example, in October 2022, President Biden issued an Executive Order ~~,~~ directing the Center for Medicare and Medicaid Innovation (" CMMI "), to consider new healthcare payment and delivery models that would lower drug costs and promote access to innovative drug therapies for Medicare and Medicaid beneficiaries. ~~The Executive Order requires CMMI to~~ **In February 2023, the Secretary** ~~submit~~ **submitted** a report to the White House **describing three models that the Secretary selected for testing. Among the selected models is a Cell & Gene Therapy Access Model, under which CMS would structure and coordinate multi- state Medicaid outcomes- based agreements between participating states and**

manufacturers. The report also directs CMS to consider potential Medicare fee- for- service options to support cell and gene therapy access and affordability. In October 2023, CMMI further announced that it will move the start- date for the Cell & Gene Therapy Access Model from 2026 to 2025. On January 30, 2024, CMMI released additional information about the Cell & Gene Therapy Access Model, including the initial focus on ~~potential models~~ **cell and gene therapies for sickle cell disease. CMS intends to negotiate outcomes- based agreements with manufacturers between May 2024 and November 2024. In addition to the supplemental rebate negotiated under the outcomes- based agreement, participating manufacturers would be required to cover certain fertility preservation services and supports for ancillary services (e. g., travel, case management, behavioral health services). CMS is requesting that states submit an optional, non- binding letter of intent by April 2024. States may begin participating in the Cell & Gene Therapy Access Model on a rolling- basis, between January 2025 and January 2026** . Third- party payors throughout the world also have been attempting to control drug spending in light of the global economic pressures ~~, including due to COVID- 19~~ . In reimbursement negotiations, many payors are requesting price discounts and caps on total expenditures and limiting both the types and variety of drugs that they will cover if they are not able to secure them. Some payors restrict reimbursement to certain patient groups or by indication. As part of these negotiations, many ex- U. S. government payors also are requiring companies to establish product cost- effectiveness as a condition of reimbursement. These cost- effectiveness reviews may overlook many of the benefits provided by innovative medicines, and for the most part, have not taken into account the specific circumstances of products that treat rare diseases. This has led to conclusions that certain medicines, including our products in certain jurisdictions, are not cost-effective. As a result, certain countries have declined to reimburse, or delayed their reimbursement of, some of our products. Although not mandated in the U. S., various organizations have started advocating for cost- effectiveness analyses in the U. S. as well as value- based contracting in which the amount of reimbursement for a product is based on patient outcomes and other clinical or economic metrics related to the performance of such product. If U. S. payors were to adopt such assessments and make negative coverage determinations or utilize value- based contracts that result in penalties to, or lower rates of, reimbursement, it could adversely affect our product revenues. Our business would be materially adversely affected if we are not able to obtain or maintain coverage and reimbursement of our products from third- party payors on a broad, timely, or satisfactory basis, or if such coverage is subject to overly broad or restrictive utilization management controls. The increasing availability and use of innovative specialty pharmaceuticals for rare diseases, combined with their higher cost as compared to other types of pharmaceutical products, is generating significant third- party payor interest in developing cost- containment strategies targeted to this sector. Government regulations in both U. S. and ex- U. S. markets could further limit the prices that can be charged for our products and may limit our commercial opportunity. The increasing use of cost- effectiveness assessments in markets around the world and the financial challenges faced by many governments may lead to significant adverse effects on our business. There also has been an increase in state legislation and regulations related to drug pricing and drug pricing transparency. In the U. S., various states, including Nevada, Maryland, Louisiana, New York, California, Washington, Massachusetts, New Jersey, Connecticut, Vermont, New Hampshire, Utah, Minnesota, Oregon, Colorado, New Mexico, Virginia, Maine, Texas, North Dakota, ~~and~~ West Virginia, **Florida, and New Jersey** have passed legislation requiring companies to disclose extensive information relating to drug prices, drug price increases, and spending on research, development, and marketing, among other things. Although it is not always clear what states will do with the collected information, some laws were designed to obtain additional product discounts. Additionally, certain states have enacted laws establishing ~~Prescription Drug Affordability Boards (“~~ PDABs ~~”)~~ . Some state PDABs either have the authority or have defined a pathway where they may be granted the authority ~~,~~ to establish upper payment limits for prescription drugs ~~— although to date~~ , ~~none of~~ **including Colorado, Maryland, Washington, and Minnesota. Under** the ~~states have exercised~~ **Washington law, the PDAB cannot select for an affordability review drugs that are solely for the treatment of an orphan- designated disease or condition. In August 2023, the Colorado PDAB selected five drugs for an affordability review, including TRIKAFTA; in December, it found TRIKAFTA to be not unaffordable, and** ~~this~~ **thus** ~~authority~~ **not eligible for an upper payment limit. We cannot, however, predict whether future reviews by the Colorado PDAB, or any other PDAB, will come to the same conclusion about TRIKAFTA or any of our other therapies, or the amount of any potential upper payment limit** . We may continue to see more state action requiring additional disclosures or other actions **. Additional state actions, including the importation of drugs from other countries, also may affect the availability and accessibility of our medicines. For example, on January 5, 2024, the FDA authorized Florida’ s Agency for Health Care Administration’ s drug importation program under section 804 of the Federal Food, Drug, and Cosmetic Act, which eventually would allow Florida to import certain prescription drugs from Canada. The importation of drugs from Canada or other countries that potentially could compete with our medicines could create increased pressure on our revenue and profitability** . In addition, we could see increased federal activity related to drug pricing and transparency requiring disclosures or other actions instead of, or in addition to, state requirements. Similar initiatives also are occurring in, or being considered by, some of our ex-U. S. markets, including Italy and Brazil. Complying with these laws can be expensive and requires significant personnel and operational resources. Furthermore, any additional required discounts would adversely affect the pricing of, and revenues from, our products. Finally, while we seek to comply with all statutory and regulatory requirements, we face increased enforcement activity by the U. S. federal government, state governments, and private payors against pharmaceutical and biotechnology companies for pricing and reimbursement- related issues as well as inquiries from the U. S. Congress. Other federal activities seeking to specifically address drug pricing and reimbursement include: • rulemaking related to importation of prescription drugs from Canada, as well as guidance related to importation of prescription drugs from other foreign countries; • attempts to establish reference pricing for certain physician- administered drugs; • executive orders relating to drug pricing that are intended to broadly impact the pharmaceutical industry; • changes to the federal anti- kickback statute safe harbors that eliminate anti-kickback statute discount safe harbor protection for certain manufacturer rebate arrangements; and • legislation relating to drug

pricing, including enhanced transparency measures into drug pricing. We expect government scrutiny over drug pricing, reimbursement, and distribution to continue. Potential future government regulation of drug prices or reimbursement creates uncertainties about our portfolio and could have a material adverse effect on our operations. **Moreover, antitrust and / or competition laws are increasingly being used to scrutinize pricing on high- value medicines. Defending against an antitrust or competition claim can be expensive and requires significant personnel and operational resources, may ultimately lead to a reduction in the prices of our products, and can ultimately result a material adverse effect on profitability and our business overall. Additionally, governmental efforts to pursue compulsory licensing, including the Biden Administration' s proposed framework to pursue so- called " march in " rights, could affect our pricing strategy and result in an adverse impact on our revenue.** The U. S. government, individual states and some foreign jurisdictions also have been aggressively pursuing legislative and regulatory reforms that could affect our ability to sell products. For example, in the U. S., there have been federal legislative and administrative efforts to repeal, substantially modify, or invalidate some or all of the provisions of the ACA, which could affect coverage and payment for medicines. The federal government additionally has proposed and enacted legislation leading to aggregate reductions of Medicare payments to providers, which ultimately could affect utilization of medicines. Other reforms include the Bipartisan Budget Act of 2018, which contained various provisions that affect coverage and reimbursement of drugs, including an increase in the discount that manufacturers of Medicare Part D brand name drugs must provide to Medicare Part D beneficiaries during the coverage gap from 50 % to 70 %. Under the **IRA** ~~Inflation Reduction Act~~, the coverage gap phase and the associated coverage gap discount program will be eliminated after the 2024 plan year. Starting in 2025, there will be a new Part D manufacturer discount program, which requires a 10 % discount in the initial phase and a 20 % discount in the catastrophic phase of the benefit. The **IRA** ~~Inflation Reduction Act~~ also authorizes the government to negotiate maximum fair prices for certain Medicare drugs. It also establishes mandatory rebates for Part B and Part D drugs with prices that increase faster than inflation. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other health care funding, which could negatively affect our customers and accordingly, our financial operations. Moreover, payment methodologies may be subject to changes in health care legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. Adoption of new health care reform legislation at the federal or state level could affect demand for, or pricing of, our products or product candidates if approved for sale. We cannot, however, predict the ultimate content, timing, or effect of any health care reform legislation or action, or its impact on us, including increased compliance requirements and costs, all of which may adversely affect our future business, operations, and financial results. In most ex- U. S. markets, the pricing and reimbursement of therapeutic and other pharmaceutical products is subject to governmental control and government authorities are making greater efforts to limit or regulate the price of drug products. The reimbursement process in ex- U. S. markets can take a significant time to conclude and reimbursement decisions are made on a country ~~-~~by ~~-~~country or region ~~-~~by ~~-~~region basis. Further, many ex- U. S. governments are introducing new legislation focusing on cost containment measures in the pharmaceutical industry. The final form of these laws and the relevant practical application is unknown at this time, but may lead to lower prices, paybacks or other forms of discounts or special taxes. Our medicines treat life- threatening conditions and address relatively small patient populations, and our research and development programs are primarily focused on developing medicines to treat similar diseases. Both government and private payors are targeting these types of **therapies** ~~high cost medicines~~, in some cases refusing to pay for them. We have experienced challenges in obtaining timely reimbursement for our products in various countries outside the U. S ~~. For example, we obtained reimbursement for ORKAMBI and SYMKEVI in England in the fourth quarter of 2019, four years after ORKAMBI' s initial approval in 2015~~. Our future product revenues, including from TRIKAFTA / KAFTRIO, depend on, among other things, our ability to maintain reimbursement in ex- U. S. markets for our products. There is no assurance that coverage and reimbursement will be available outside of the U. S. for our ~~four~~ **five** approved medicines or any future medicine, and, even if it is available, whether the timing or the level of reimbursement will be sufficient to allow us to market our medicines. Adverse pricing limitations or a delay in obtaining coverage and reimbursement would decrease our future net product revenues and harm our business ~~It is difficult to predict what third party payors,including U.S.or ex- U.S.governments or private insurance companies,will decide with respect to reimbursement for CASGEVY and the other novel cell and genetic therapies in our pipeline.Additionally,reimbursement rates for cell and genetic therapies approved before ours could create an~~ adverse environment for reimbursement of any therapies we ultimately commercialize.The administration of our products may require procedures for the collection of cells from patients,followed by other procedures either before or after delivery of the cell or genetic therapy.The manner and level at which reimbursement is provided for these services also is important.Inadequate reimbursement for such services may ~~discourage~~ **adversely affect** physicians **'** ~~from recommending~~ decisions to recommend any product for which we obtain approval in the future and ~~impair~~ our ability to market or sell the associated cell or **genetic therapy.Given there are only a few approved cell and genetic therapy products,it also is difficult to determine how long it will take or reasonably estimate the costs to develop,manufacture,and commercialize cell or genetic therapies.In addition,our cell- based therapies include approaches involving devices,which are subject to additional regulatory requirements** . Our business depends upon the successful development and commercialization of product candidates. These product candidates are in various stages of development and must satisfy rigorous standards of safety and efficacy before they can be approved for sale by the FDA or comparable foreign regulatory authorities. To satisfy these standards, we must allocate resources among our various development programs and must engage in expensive and lengthy testing of our product candidates. Discovery and development efforts for new pharmaceutical and biological products, including new combination therapies, are resource- intensive and may take 10 to 15 years or longer for each product candidate. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Despite our efforts, our product candidates may not: • offer therapeutic or other improvement over existing competitive therapies; • show the level of safety and efficacy, including the

level of statistical significance, required by the FDA or other regulatory authorities for approval of a drug or biologic; • meet applicable regulatory standards; • be capable of being produced in commercial quantities at acceptable costs; or • if approved for commercial sale, be successfully marketed as pharmaceutical or biological products. We have recently completed and / or have ongoing or planned clinical trials for several of our product candidates. The strength of our product portfolio and pipeline will depend in large part upon the outcomes of these clinical trials, including those evaluating TRIKAFTA / KAFTRIO **and vanzacaftor / tezacaftor / deutivacaftor** in younger children with CF, ~~our~~ **VX- 522 in** CF ~~pipeline products~~, ~~exa- cel and~~ VX-548 in **neuropathic** pain **, and VX- 880 and VX- 264 in T1D** . Failure to advance product candidates through clinical development could impair our ability to ultimately commercialize products, which could materially harm our business and long-term prospects. Results of our clinical trials and findings from our nonclinical studies, including toxicology findings in nonclinical studies conducted concurrently with clinical trials, could lead to abrupt changes in our development activities, including the possible cessation of development activities associated with a particular product candidate or program. For example, in October ~~2020~~ **2023** , we decided not to progress VX- ~~814~~ **864** , a drug candidate for the treatment of AATD, into further development ~~based~~ **due to** ~~on~~ **non - serious rash events** ~~safety and pharmacokinetic data observed~~ in **some patients** ~~a Phase 2 clinical trial~~ . Moreover, clinical data are often susceptible to varying interpretations, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their product candidate. Furthermore, results from our clinical trials may not meet the level of statistical significance or otherwise provide the level of evidence or safety and efficacy required by the FDA or other regulatory authorities for approval of a product candidate. Finally, clinical trials are expensive and require significant operational resources to implement and maintain. Many companies in the pharmaceutical and biotechnology industries, including our company, have suffered significant setbacks in later- stage clinical trials even after achieving promising results in earlier- stage clinical trials. For example, the results from completed preclinical studies and clinical trials may not be replicated in later clinical trials, and ongoing clinical trials for our product candidates may not be predictive of the results we may obtain in later- stage clinical trials or of the likelihood of approval of a product candidate for commercial sale. In addition, from time to time, we report interim, topline, and preliminary data from our clinical trials, which is based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change. Interim or preliminary data from a clinical trial may not be predictive of final results from the clinical trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment and treatment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. The ability of third parties to review and / or analyze data from our clinical trials, including as a result of government disclosure, also may increase the risk of commercial confidentiality breaches and result in enhanced scrutiny of our clinical trial results. For example, Clinical Trial Regulation (EU) No. 536 / 2014, and the EMA policy on publication of clinical data for medicinal products for human use, both permit the EMA to publish clinical information submitted in marketing authorization applications. Third party review and scrutiny could result in public misconceptions regarding our drugs and product candidates. These publications could also result in the disclosure of information to our competitors that we might otherwise deem confidential, which could harm our business. The time required to complete clinical trials and to satisfy the FDA and other countries' regulatory review processes is uncertain and typically takes many years. Our analysis of data obtained from nonclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We also may encounter unanticipated delays or increased costs due to government regulation from future legislation or administrative action or changes in governmental policy during the period of drug development, clinical trials and governmental regulatory review. We may seek a Fast Track, Priority Review, Breakthrough Therapy, and / or RMAT designation for some of our product candidates. Product candidates that receive one or more of these designations may be eligible for, among other things, a priority regulatory review. Each of these designations is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for Fast Track, Priority Review, Breakthrough Therapy and / or RMAT designation, the FDA may disagree and instead determine not to make such designation. The receipt of one or more of these designations for a product candidate does not guarantee a faster development process, review or approval compared to products developed or considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our products or product candidates qualifies for Fast Track, Priority Review, Breakthrough Therapy and / or RMAT designation, the FDA may later decide to withdraw such designation if it determines that the product or product candidate no longer meets the conditions for qualification. Any failure to obtain regulatory approvals for a product candidate would prevent us from commercializing that product candidate. Any delay in obtaining required regulatory approvals could materially adversely affect our ability to successfully commercialize a product candidate. Furthermore, any regulatory approval to market a product may be subject to limitations that we do not expect on the indicated uses for which we may market the product. Any such limitations could reduce the size or demand of the market for the drug. We also are subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third- party reimbursement. Non- U. S. jurisdictions have different approval procedures than those required by the FDA, and these jurisdictions may impose additional testing requirements for our product candidates. The foreign regulatory approval process includes all of the risks associated with the FDA approval process described above, as well as risks attributable to the satisfaction of foreign requirements. Approval by the FDA does not ensure approval by regulatory authorities outside the U. S. and approval by a foreign regulatory authority does

not ensure approval by the FDA. In addition, although the FDA may accept data from clinical trials conducted outside the U. S., acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population also must adequately represent the U. S. population, and the data must be applicable to the U. S. population and U. S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U. S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the U. S., it would likely result in the need for additional trials, which would be costly and time- consuming and delay or permanently halt our development of the applicable product candidate. We cannot predict whether or not we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or regulatory authorities to delay or suspend clinical trials, or delay the analysis of data from our completed or ongoing clinical trials. Among the factors that could delay our development programs are: • ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials and the number of clinical trials we must conduct; • failure or delay in reaching agreement on acceptable terms with prospective contract research organizations (" CROs ") and clinical trial sites; • failure to add or delay in adding a sufficient number of clinical trial sites and obtaining institutional review board or independent ethics committee approval at each clinical trial site; • suspension or termination of clinical trials of product candidates for various reasons, including non- compliance with regulatory requirements; • clinical trial sites deviating from clinical trial protocol or dropping out of a clinical trial; • delays in enrolling volunteers or patients into clinical trials, including as a result of low numbers of patients that meet the eligibility criteria for the trial; • a lower than anticipated retention rate of volunteers or patients in clinical trials; • the need to repeat clinical trials as a result of unfavorable or inconclusive results, unforeseen complications in testing or clinical investigator error; • inadequate supply or deficient quality of product candidate materials or other materials necessary for the conduct of our clinical trials; • unfavorable FDA or foreign regulatory authority inspection and review of a manufacturing facility that supplied clinical trial materials or its relevant manufacturing records or a clinical trial site or records of any clinical or preclinical investigation; • unfavorable or inconclusive scientific results from clinical trials; • serious and unexpected treatment- related side- effects experienced by participants in our clinical trials or by participants in clinical trials being conducted by our competitors to evaluate product candidates with similar mechanisms of action or structures to therapies that we are developing; • favorable results in testing of our competitors' product candidates, or FDA or foreign regulatory authority approval of our competitors' product candidates; or • action by the FDA or a foreign regulatory authority to place a clinical hold or partial clinical hold on a trial or compound or deeming the clinical trial conduct as problematic. For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory, and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our estimates may be adversely affected and, as a result, our stock price may decline. Our ability to enroll patients in our clinical trials in sufficient numbers and on a timely basis is subject to a number of factors. Clinical trials are expensive and require significant operational resources. Delays in patient enrollment or unforeseen drop- out rates may result in increased costs and longer development times. The enrollment of patients further depends on many factors, including: • the proximity of patients to clinical trial sites; • the size of the patient population, the nature of the protocol, and the design of the clinical trial; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • the number of other clinical trials ongoing and competing for patients in the same indication; • our ability to obtain and maintain patient consents; • reporting of the preliminary results of any of our clinical trials; • the availability of effective treatments for the relevant disease and eligibility criteria for the clinical trial; • the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion; and • factors we may not be able to control, such as current or potential pandemics that may limit patients, principal investigators or staff or clinical site availability ~~(e. g., the COVID- 19 pandemic)~~ . We, our collaborators, the FDA, or other applicable regulatory authorities may suspend clinical trials of a product candidate at any time if we or they believe the healthy volunteers or patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons. Any such suspension could materially adversely affect the development of a particular product candidate and **our business. For cell and genetic therapy programs addressing rare genetic diseases with small patient populations, we may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical studies in an adequate and timely manner. Additionally, patients may be unwilling to participate in our clinical trials because of concerns that cell and genetic therapies are unsafe or unethical, negative publicity from adverse safety events in the biotechnology or gene therapy industries, or for other reasons, including competitive clinical studies for similar patient populations. Moreover, adverse developments in clinical trials conducted by others of cell and genetic therapy products or products created using similar technology, or adverse public perception of the field of cell and genetic therapies, may cause the FDA and other regulatory bodies to revise the requirements for approval of any cell or genetic therapy product candidates we may develop or limit the use of products utilizing technologies such as ours, either of which could materially harm** our business. We are subject to health care fraud and abuse laws, such as the FCA and the AKS, and other similar laws and regulations both in the U. S. and in non- U. S. markets. In the U. S., the Federal Anti- Kickback Statute prohibits knowingly and willfully offering, paying, soliciting, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the ordering, furnishing, arranging for or recommending of an item or service that is reimbursable, in whole or in part, by a federal health care program, such as Medicare or Medicaid. Because

of the broad scope of the prohibition, most financial interactions between pharmaceutical manufacturers and prescribers, purchasers, third party payors and patients would be subject to the statute. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, ~~the exceptions and safe harbors are narrow. Financial~~ **financial** interactions must ~~therefore~~ be structured carefully to qualify for protection or otherwise withstand scrutiny. Federal false claims laws, including the FCA, prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Pharmaceutical companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as providing free product to customers with the expectation that the customers would bill federal programs for the product; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in promotion for uses that the FDA has not approved, known as " off- label " uses, that caused claims to be submitted to Medicaid for those off- label uses; submitting inflated " best price " information to the Medicaid Rebate Program; and certain manufacturing- related violations. The scope of this and other laws may expand in ways that make compliance more difficult and expensive. The FDA and other regulatory agencies closely regulate the post- approval marketing and promotion of products to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. Although physicians are **generally** permitted, based on their medical judgment, to prescribe products for indications other than those approved by the ~~FDA~~ **applicable regulatory agency** , manufacturers are prohibited from promoting their products for such off- label uses. We market our products to eligible people with CF **, SCD, and TDT** for whom the applicable product has been approved and provide promotional materials and ~~training~~ **informational** programs to physicians regarding the use of each product in these patient populations. These eligible people do not represent all people with CF **, SCD, and TDT** . If ~~the FDA~~ **a regulatory agency** determines that our promotional materials ~~, training~~ , or other activities constitute off- label promotion, it could request that we modify our ~~training or~~ promotional materials or other activities, conduct corrective advertising, or subject us to regulatory enforcement actions, ~~including~~ **such as** the issuance of a warning or untitled letter, injunction, seizure, civil fines and criminal penalties. It also is possible that other federal, state, or foreign enforcement authorities might take action if they believe that the alleged improper promotion led to the submission and payment of claims for an off- label use, which could result in significant fines or penalties under other statutory authorities, such as laws prohibiting false claims for reimbursement. Even if it is later determined we were not in violation of these laws, we may be faced with negative publicity, incur significant expenses defending our actions, and have to divert significant management resources from other matters. In the U. S., federal and state laws regulate financial interactions between pharmaceutical manufacturers and healthcare providers, require disclosure to government authorities and the public of such interactions, and mandate the adoption of compliance standards or programs. For example, the so- called federal " sunshine law " requires pharmaceutical manufacturers to report annually to CMS payments or other transfers of value made by that entity to physicians **, physicians assistants, advanced practice registered nurses,** and teaching hospitals ~~(and additional categories of health care practitioners beginning with reports submitted on or after January 1, 2022)~~ . We also have similar reporting obligations with respect to financial interactions throughout the E. U. We expended significant efforts to establish, and are continuing to devote significant resources to maintain and enhance, systems and processes to comply with these regulations. Requirements to track and disclose financial interactions with health care providers and organizations increase government and public scrutiny of these financial interactions. Failure to comply with the reporting requirements could result in significant civil monetary penalties. The sales and marketing practices of our industry have been the subject of increased scrutiny from government authorities in the U. S. and other countries in which we market our products, and we believe that this trend will continue. Many of these laws have not been fully interpreted by the government authorities or the courts, and their provisions are subject to a variety of interpretations. While we have a corporate compliance program which, together with our policies and procedures, is designed to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems and the promotion of a culture of compliance, if we are found not to be in full compliance with these laws and regulations, our business could be materially harmed. We may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from federal health care programs and / or the curtailment or restructuring of our operations. Even if we successfully defend against government challenge, responding to the challenge may cause us to incur significant legal expenses and divert our management' s attention from the operation of our business. We participate in the Medicaid Drug Rebate Program, the 340B program, and a number of other federal and state government pricing programs in the U. S. to obtain coverage for our products by certain government health care programs. These programs require us to pay rebates or provide discounts to certain government payors or private purchasers in connection with our products when dispensed to beneficiaries of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing and rebate calculations that we report on a monthly and quarterly basis to the government agencies that administer the programs. The terms, scope and complexity of these government pricing programs change frequently. For example, regulations finalized in December 2020 created an alternative Medicaid rebate formula for " line extensions " of oral solid dosage forms. Moreover, in December 2020, CMS finalized changes to Medicaid Drug Rebate Program pricing calculations regarding the provision of co- payment assistance to patients that may be impacted by so- called accumulator programs operated by private insurers or pharmacy benefit managers. The portion of this rule dealing with manufacturer co- payment assistance was struck down by the U. S. District Court for the District of Columbia in May 2022 (and the deadline for an appeal has lapsed). ~~Consequently~~ **In May 2023** , ~~while this~~ **CMS issued a proposed** rule ~~has been vacated~~ , ~~it is possible that CMS~~ **which would withdraw the challenged accumulator adjustment regulations, consistent with the Court' s order. The rule also proposes significant changes, which, if finalized,** could ~~issue~~ **have an impact on our Medicaid rebate liability, impact our participation in the Medicaid Drug Rebate Program, and impose** new **reporting requirements** ~~rulemaking or guidance on this topic that would affect rebates owed under the Medicaid program or otherwise limit our ability to support our patient co- pay assistance program~~ . Additionally, the expansion of the

340B Drug Discount Program through the ACA has increased the number of purchasers who are eligible for significant discounts on branded drugs. These and future changes to government pricing programs, laws, and regulations may have a material adverse impact on our revenue and operations. We also may have reimbursement obligations or be subject to penalties if we fail to provide timely and accurate information to the government, pay the correct rebates, or offer the correct discounted pricing. Changes to the price reporting or rebate requirements of these programs would affect our obligations to pay rebates or offer discounts. For example, the removal of the current statutory 100 % of Average Manufacturer Price per- unit cap on Medicaid rebate liability for single source and innovator multiple source drugs, effective as of January 1, 2024, under the American Rescue Plan Act of 2021 may affect the amount of rebates paid on prescription drugs under Medicaid and the prices that are required to be charged to covered entities under the 340B Drug Discount Program. Additionally, the **IRA** ~~Inflation Reduction Act~~ requires manufacturers to pay rebates for Medicare Part B and Part D drugs with prices that increase faster than the rate of inflation. Responding to current and future changes to these and other Medicaid Drug Rebate Program requirements may reduce our net revenues and the complexity of compliance, will be time- consuming, and could have a material adverse effect on our results of operations. We have a number of regulated processes and systems that are required both prior to and following approval of our drugs and product candidates. These processes and systems are subject to continual review and periodic inspection by the FDA and other regulatory bodies. In addition, the clinical research organizations and other third parties that we work with in our non- clinical studies and clinical trials and our oversight of such parties are subject to similar reviews and periodic inspection by the FDA and other regulatory bodies. If compliance issues are identified at any point in the development and approval process, we may experience delays in filing for regulatory approval for our product candidates, or delays in obtaining regulatory approval after filing, if at all. Any later discovery of previously unknown problems or safety issues with approved drugs or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such drugs or manufacturing processes, withdrawal of drugs from the market, the imposition of civil or criminal penalties or a refusal by the FDA and / or other regulatory bodies to approve pending applications for marketing approval of new drugs or supplements to approved applications, any of which could have a material adverse effect on our business. In addition, we are party to agreements that transfer responsibility for complying with specified regulatory requirements, such as filing and maintenance of marketing authorizations and safety reporting or compliance with manufacturing requirements, to our collaborators and third- party manufacturers. If our collaborators or third- party manufacturers do not fulfill these regulatory obligations, any drugs for which we or they obtain approval may be subject to later restrictions on manufacturing or sale, which could have a material adverse effect on our business genetic therapy product to market would materially adversely affect our business,financial condition,results of operations and prospects.The regulatory approval process and clinical trial requirements for cell and genetic therapies can be more expensive and take longer than for other,better known or more extensively studied product candidates,and regulatory requirements governing cell and genetic therapy products have changed frequently and may continue to change in the future.For example,the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research (“ CBER ”) to consolidate the review of cell therapies and related products,and the Cellular,Tissue and Gene Therapies Advisory Committee to advise CBER on its review.These and other regulatory review agencies,committees and advisory groups,and the requirements and guidelines they promulgate,may lengthen the regulatory review process,require us to perform additional preclinical studies or clinical trials,increase our development costs,lead to changes in regulatory positions and interpretations,delay or prevent approval and commercialization of these treatment candidates or lead to significant post . We are subject to data privacy and security laws and regulations in various jurisdictions that apply to the collection, storage, use, sharing, and security of personal data, including health information, and impose significant compliance obligations. In addition, numerous other federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure and security of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. For example, the E. U. General Data Protection Regulation (“ GDPR ”) went into effect in 2018 and has imposed new obligations on us with respect to our processing of personal data and the cross- border transfer of such data, including higher standards of obtaining consent, more robust transparency requirements, data breach notification requirements, requirements for contractual language with our data processors, and stronger individual data rights. Different E. U. member states have interpreted the GDPR differently and many have imposed additional requirements, which add to the complexity of processing personal data in the E. U. The GDPR also imposes strict rules on the transfer of personal data to countries outside the E. U., including the U. S. and the U. K., and permits data protection authorities to impose large penalties for violations of the GDPR. The GDPR rules related to cross border data transfers continue to evolve based on E. U. court decisions and regulator guidance, which presents certain practical challenges to compliance. Regulators also continue to focus enforcement efforts on behavioral advertising and other online tracking technologies commonly used by companies. Compliance with these evolving rules is challenging, as country specific guidance and rules are continually changing and limited alternatives currently exist in the market. Compliance with the GDPR is a rigorous and time- intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any activities falling within the scope of the GDPR. In the U. S., California has passed the California Consumer Privacy Act (the “ CCPA ”), which went into effect on January 1, 2020. In November 2020, California also passed the California Privacy Rights Act (the “ CPRA ”), which expands and builds upon the consumer privacy rights of the CCPA. The CPRA came into effect January 1, 2023. Certain other states have also enacted legislation governing the protection of personal data and several other states and the federal government are actively considering similar proposed legislation **. A number of other states have also introduced privacy legislation, with some focusing specifically on health data** . Additionally, Brazil passed the General Data Protection Law, which went into effect in August 2020. While we continue

to address the implications of the new data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges. Each law is also subject to various interpretations by courts and regulatory agencies, creating even more uncertainty. While we have a global privacy program that addresses such laws and regulations, our efforts to comply with the evolving data protection rules may be unsuccessful. We must devote significant resources to understanding and complying with the changing landscape in this area. Failure to comply with data protection laws may expose us to risk of enforcement actions taken by data protection authorities, private rights of action in some jurisdictions, and potential significant penalties if we are found to be non- compliant. Failure to comply with the GDPR and applicable national data protection laws of European Economic Area member states could lead to fines of up to € 20, 000, 000 or up to 4 % of the total worldwide annual revenue of the preceding financial year, whichever is higher. Some of these laws and regulations also carry the possibility of criminal sanctions. For example, while we are not directly subject to the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act (" HIPAA "), we could be subject to penalties, including criminal penalties if we knowingly obtain or disclose individually identifiable health information from a HIPAA- covered health care provider or research institution that has not complied with HIPAA' s requirements for disclosing such information. In addition, the commercialization of cell and gene therapies requires the collection and processing of a greater amount of personal data than traditional therapies, potentially increasing risk. Furthermore, the number of government investigations related to data security incidents and privacy violations **, with a specific focus on online data sharing,** continue to increase and government investigations typically require significant resources and generate negative publicity, which could harm our business and our reputation. The COVID- 19 pandemic has added further complexity to the processing of personal data. For example, safety measures and government health regulations intended to protect our employees, contractors, and other visitors to our sites may require the collection of certain personal data. Although we are focused on ensuring that personal data is properly protected, our efforts may be unsuccessful and we could unintentionally be subject to unauthorized access or disclosure of such personal data. If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected. Our research and development efforts involve the regulated use of hazardous materials, chemicals, and various controlled and radioactive compounds. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state, federal and foreign regulations, the risk of loss of, or accidental contamination or injury from, these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We also are subject to numerous environmental, health, and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood- borne pathogens, and the handling of biohazardous materials. Although we maintain workers' compensation insurance to cover us for costs we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We maintain insurance to cover pollution conditions or other extraordinary or unanticipated events relating to our use and disposal of hazardous materials that we believe is appropriate based on the small amount of hazardous materials we generate. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations. ~~Although we actively engage with~~ **as needed for manufacturing of our products.Supply disruptions may result from a number of factors,including shortages in product raw materials,labor or technical difficulties,** regulatory **inspections** ~~authorities,the timing of regulatory approvals for~~ **or restrictions,shipping** ~~each of these facilities may be delayed for~~ **or** ~~a variety of reasons~~ **customs delays,general global supply chain disruptions,or any other performance failure by us or any third- party manufacturer on which we rely** .We may **also** experience supply disruptions if regulatory agencies are unable to inspect the manufacturing facilities on which we rely. ~~In addition,we and the third parties with whom we engage are required to maintain compliance with quality regulations globally.An inability to maintain compliance with such regulations,including cGMP requirements,could cause significant disruptions to our business and operations.Additionally,establishing,managing and expanding our global manufacturing and supply chain requires a significant financial commitment and the creation and maintenance of our numerous third- party contractual relationships.We may not be able to agree on contractual terms with third parties as needed for manufacturing of our products.Although we attempt to manage the business relationships with our partners,we could be subject to supply disruptions outside of our control.Supply disruptions may result from a number of factors,including shortages in product raw materials,labor or technical difficulties,regulatory inspections or restrictions,shipping or customs delays,general global supply chain disruptions,or any other performance failure by us or any third- party manufacturer on which we rely.Additionally,unfavorable geopolitical events or situations could affect our ability to interact with or conduct business with specific vendors within our global supply network,or could prevent or delay the transportation of supplies or products to their planned destination.~~ Any such disruptions could disrupt sales of our products and / or the timing or advancement of our clinical trials. **While we have developed internal capabilities to supply product candidates for use in our clinical trials as well as our medicines for commercial sale,a majority of the manufacturing steps needed to produce our medicines,product candidates,and drug products are performed through a third- party manufacturing network.We expect that we will continue to rely on third parties to meet our commercial supply needs and a significant portion of our clinical supply needs for the foreseeable future.** If we or our third- party manufacturers become unable or unwilling to continue manufacturing product and we are not able to promptly identify another manufacturer,we could experience a disruption in the commercial supply of our then- marketed medicines,which would have a significant effect on patients,our business,and our product revenues.Similarly,a disruption in the clinical supply of product candidates could delay the completion of clinical trials and affect timelines for regulatory filings.We have a limited number of critical steps in our manufacturing process that are single sourced,including for commercialized products.To ensure the stability of our supply chains,we continue to develop ~~alternative~~ **alternatives** ~~suppliers~~ for our manufacturing processes.However,there can be no assurance that we will be able to

establish and maintain additional manufacturers or capacity for all of our product candidates and products on a timely basis or at all.In the course of providing its services,a contract manufacturer may develop process technology related to the manufacture of our products or product candidates that the manufacturer owns,either independently or jointly with us.This would increase our reliance on that manufacturer or require us to obtain a license from that manufacturer to have our products or product candidates manufactured by other suppliers utilizing the same process.We rely on third parties such as CROs to help manage certain pre-clinical work and our clinical trials and on medical institutions,clinical investigators,and clinical research organizations such as the Therapeutic Development Network,which is primarily funded by the Cystic Fibrosis Foundation,to assist in the design and review of,and to conduct our clinical trials,including enrolling qualified patients.In addition,we engage third party contractors to support numerous other research,commercial and administrative activities.Our reliance on these third parties for clinical development activities reduces our control over these activities but does not relieve us of our responsibilities.For example,we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the clinical trial.Moreover,the FDA requires us to comply with standards,commonly referred to as good laboratory practices and good clinical practices,for conducting,recording and reporting the results of pre- clinical and clinical trials to assure that data and reported results are credible and accurate and that the rights,integrity and confidentiality of trial participants are protected.Such standards,particularly with respect to newer cell and genetic therapies,will continue to evolve and subject us and third parties to new or changing requirements.If these third parties do not successfully carry out their contractual duties or meet expected deadlines,we may be required to replace them.Although we believe that there are a number of other third- party contractors we could engage to continue the activities,it may result in a delay of the affected clinical trial,drug development program or applicable activity.If clinical trials are not conducted in accordance with **our contractual expectations or regulatory requirements,action by regulatory authorities might significantly and adversely affect the conduct or progress of these clinical trials or in specific circumstances might result in a requirement that a clinical trial be redone.Accordingly,our efforts to obtain regulatory approvals for and commercialize our product candidates could be delayed.In addition,failure of any third- party contractor to conduct activities in accordance with our expectations,including as a result of COVID- 19,could adversely affect the relevant research,development,commercial or administrative activity** To achieve our long- term business objectives, we seek to license or acquire products, product candidates and other technologies that have the potential to complement our ongoing research and development efforts, access emerging technologies and license or acquire pipeline assets. These transactions may be similar to prior transactions, may be structured differently than prior transactions, or may involve larger transactions or later- stage assets. We have faced and will continue to face significant competition for the acquisition of rights to these types of products, product candidates and other technologies from a variety of other companies, some of which have significantly more financial resources and experience in business development activities than we have. In addition, non- profit organizations may be willing to provide capital to the companies that control additional products, product candidates or technologies, which may provide incentives for companies to advance these products, product candidates or technologies independently. Also, the cost of acquiring, in- licensing or otherwise obtaining rights to such products, product candidates or other technologies has grown dramatically in recent years and may be at levels that we cannot afford or that we believe are not justified by market potential. As a result, we may not be able to acquire, in- license or otherwise obtain rights to additional products, product candidates or other technologies on acceptable terms or at all. Effectively integrating acquired businesses, technologies and..... which could harm our financial condition. The risks that we face in connection with our current collaborations, including **with** CRISPR **, Moderna,** and Entrada, and any future collaborations, include the following: ~~• Our collaborators may change the focus of their development and commercialization efforts or may have insufficient resources or expertise to effectively develop, manufacture or commercialize our product candidates. • The ability of some of our therapies to reach their potential could be limited if collaborators are unable to effectively develop, manufacture or commercialize these therapies or product candidates or decrease or fail to increase development or commercialization efforts related to those therapies or product candidates. Our collaboration agreements allocate development, manufacturing and commercialization responsibilities between us and our collaborators and provide our collaborators with a level of discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations. • Our collaborators may have limited experience in developing, manufacturing and commercializing therapies, either generally, or in the specific therapeutic area. • Collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties.~~ • Collaborators may develop and commercialize, either alone or with others, drugs **or therapies** that are similar to or competitive with the products or product candidates that are the subject of their collaborations with us. • Disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities or costs for us with respect to product candidates, or might result in litigation or arbitration. Any such disagreements would divert management attention and resources and would be time- consuming and expensive. • Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation. • Collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. • Investigations and / or compliance or enforcement actions against a collaborator, which may expose us to indirect liability as a result of our partnership with such collaborator. **If** ~~• Our collaboration agreements are subject to termination under various circumstances. • We may be unable to control the resources our collaborators devote to our programs, products or product candidates, and the priorities and strategic objectives of our collaborators may not align precisely with ours. Additionally, if~~ a collaborator were to be involved in a business combination with a third party, it might de- emphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its

agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be harmed. ~~As~~ **Moreover, as** part of our ongoing strategy, we may seek additional collaborative arrangements ~~or external funding~~ for certain of our development programs and / or seek to expand existing collaborations to cover additional commercialization and / or development activities ~~. We have a number of research programs and clinical development programs, some of which are being developed in collaboration with a third party. At any time, we may determine that to continue development of a product candidate or program or successfully commercialize a drug we need to identify a collaborator or amend or expand an existing collaboration~~. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator' s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator' s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or other regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of the applicable intellectual property, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally ~~. Potentially, and depending on the circumstances, we may desire that a collaborator either agree to fund portions of a drug development program led by us, or agree to provide all of the funding and directly lead the development and commercialization of a program~~. No assurance can be given that any efforts we make to seek additional collaborative arrangements will be successfully completed on a timely basis or at all. **Effectively integrating acquired businesses** ~~If we elect to fund and undertake development or commercialization activities on our own~~ , **technologies** ~~we may need to obtain additional expertise~~ and ~~additional capital, which~~ **exclusive licenses is challenging. We** may not **realize the benefits anticipated from** ~~be available to us on acceptable terms or~~ **our** ~~at all~~ **external innovation transactions** . ~~If~~ Achieving the anticipated benefits of any transaction and successfully integrating acquired businesses or technologies involves a number of risks,including:• failure to successfully develop and commercialize the acquired products,product candidates or technologies or to achieve other strategic objectives;• delays or inability to progress preclinical programs into clinical development or unfavorable data from clinical trials evaluating the acquired or licensed product or product candidates;• difficulty in integrating the products,product candidates,technologies,business operations and personnel of an acquired asset or company;• disruption of our ongoing business and distraction of our management and employees from daily operations or other opportunities and challenges;• the potential loss of key employees of an acquired company;• entry into markets in which we **have no** ~~are unable to enter into acceptable collaborative relationships, one or more of our~~ **or limited direct prior experience** ~~development programs could be delayed or terminated and the possibility of our~~ **or** ~~receiving a return on~~ **where competitors in such markets have stronger market positions; • potential failure of the due diligence processes to identify significant problems, liabilities** ~~our~~ **or** ~~investment in the program could be impaired. We rely~~ **challenges of an acquired company, or acquired or licensed products, product candidate or technology, including problems, liabilities or challenges with respect to intellectual property, clinical or** ~~on~~ **non** ~~a worldwide network of~~ **- clinical data, safety, accounting practices, employee, or** third- party ~~manufacturers~~ **relations** and **other known and unknown liabilities; • liability for activities of the acquired company** ~~our~~ **or** ~~internal capabilities~~ **licensor before the acquisition or license** , including **intellectual property infringement claims, violations of laws, commercial disputes, tax liabilities, and other known and unknown liabilities; • exposure to litigation** ~~our~~ **or other claims** ~~own manufacturing facilities~~ in ~~Boston~~ **connection with** , ~~to manufacture product candidates for~~ **or** ~~clinical trials~~ **inheritance of claims or litigation risk as a result of an acquisition or license, including claims from terminated employees, customers, former equity holders or other third parties; and • difficulties in the integration of the acquired company' s departments, systems, including accounting, human resource and other administrative systems, technologies, books and records, and procedures,** as well as **in maintaining uniform standards, controls, including internal control over financial reporting required by the Sarbanes- Oxley Act of 2002 and related procedures and policies. Acquisitions, licensing arrangements and other strategic transactions are inherently risky, and ultimately, if we do not complete an announced acquisition, collaboration** ~~our~~ **or** ~~medicines~~ **strategic transaction** ~~for~~ **or** ~~commercial use~~ **integrate an acquired or licensed asset, business or technology successfully and in a timely manner, we may not realize the anticipated benefits of the strategic transaction** . We **may later incur impairment charges related to assets acquired in any such transaction. Even if we achieve the long- term benefits associated with our strategic transactions, our expenses and short- term costs may increase materially and adversely affect our liquidity and short- term net income. Future strategic transactions** could ~~be subject to significant supply interruptions as a~~ result **in increased operating expenses, potentially dilutive issuances** of ~~disruptions~~ **equity securities, the incurrence of debt, the creation of contingent liabilities, impairment expenses related** to **goodwill,** ~~third party or our~~ **or impairment** ~~internal manufacturing capabilities. Our supply chain for~~ **or amortization expenses related to other intangible assets** ~~sourcing raw materials and manufacturing drug product ready for distribution~~ , **all** ~~including obtaining necessary supplies, is a multi- step international endeavor. Third- party contract manufacturers, including some in China, perform different parts~~ of **which could harm** ~~our manufacturing process. Contract manufacturers may supply us with raw materials, convert these raw materials into drug substance and / or~~ **our financial condition** ~~convert the drug substance into final dosage form~~ . **If our patents do not protect our** ~~Third parties are used for packaging, warehousing and distribution of~~ products ~~. In cell and genetic therapies, third parties also will be used to both manufacture and deliver our~~ **or** ~~therapies, which requires significant investment by us to secure capacity at third parties with expertise to meet our requirements. This capacity may be limited by the number of other clinical trials and commercial manufacturing ongoing for other companies seeking similar support. If third parties are unwilling or~~ **our products infringe** unable to meet our requirements, including..... the creation and maintenance of our numerous third- party **patents** ~~contractual relationships. Although we attempt to manage the business relationships with companies in our supply chain~~ , we could be subject to ~~supply disruptions outside of~~ **litigation which could result in injunctions preventing us from selling our products, substantial damages,** ~~our~~ **or circumvention of**

our patents by ~~control. In addition, we may not be able to agree on contractual terms with~~ third parties as needed for manufacturing of our products....., development, commercial or administrative activity . We own and / or control numerous issued patents and pending patent applications in the U. S., as well as counterparts in other countries. Our success will depend, in significant part, on our ability to obtain and defend U. S. and foreign patents covering our products, their uses and our processes, to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. We cannot be certain that any patents will issue from our pending patent applications or, even if patents issue or have issued, that the issued claims will provide us with adequate protection against competitive products or otherwise be commercially valuable. ~~Due to evolving legal standards relating to the patentability, validity, and enforceability of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents in the U. S. The Leahy- Smith America Invents Act (the " Leahy- Smith Act "), made a number of significant changes to U. S. patent law in 2011. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. For example, the first to file provisions limit the rights of an inventor who is the first to invent an invention but is not the first to file an application claiming that invention.~~ U. S. and foreign patent applications typically are maintained in confidence for a period of time after they initially are filed with the applicable patent office. Consequently, we cannot be certain that we were the first to ~~invent, or the first to~~ file patent applications on ~~,~~ our products or product candidates or their use. If ~~a third party also has filed a U. S. patent application relating to our products or product candidates, their uses, or a similar invention, we may have to participate in legal or administrative proceedings to determine priority of invention. For applications governed by the Leahy- Smith Act, if~~ a third- party has an earlier filed ~~U. S.~~ patent application relating to our ~~products~~ **product** or product candidates, their uses, or a similar invention, we may be unable to obtain an issued patent from our application **. Due to evolving legal standards relating to the patentability, validity, and enforceability of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under these patents, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions** . The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability. Our patents may be challenged by third parties and certain of our patents have been challenged. This could result in the patent being deemed invalid, unenforceable or narrowed in scope, or the third party may circumvent any such issued patents **, including through compulsory licensing mechanisms** . Also, our pending patent applications may not issue, and we may not receive any additional patents. Our patents or patents we license might not contain claims that are sufficiently broad to prevent others from developing competing products. For instance, issued patents, or patents that may issue in the future, (i) relating to our small molecules may be limited to a particular molecule or molecules and may not cover similar molecules that have similar clinical properties, and (ii) relating to cell or genetic therapies may not cover similar technologies that would allow competitors to achieve similar results. Consequently, our competitors may independently develop competing products that do not infringe our patents or other intellectual property. ~~In addition, CRISPR only has co- exclusive rights to the patent rights that protect the core CRISPR / Cas9 gene- editing technology.~~ The laws of many foreign jurisdictions do not protect intellectual property rights to the same extent as in the U. S. and many companies in our segment of the pharmaceutical industry have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions **, including through compulsory licensing** , our business could be substantially harmed. Because of the extensive time required for the discovery, development, testing and regulatory review of product candidates, it is possible that a patent may expire before a product candidate can be commercialized, or a patent may expire or remain in effect for only a short period following commercialization of such product candidate. This would result in a minimal or non- existent period of patent exclusivity. If our product candidates are not commercialized significantly ahead of the expiration date of any applicable patent, or if we have no patent protection on such product candidates, then, to the extent available we would rely on other forms of exclusivity, such as data exclusivity or orphan drug exclusivity. ~~Uncertainty over intellectual property in the pharmaceutical and biotechnology industry has been the source of litigation and other disputes that are inherently costly and unpredictable.~~ There is considerable uncertainty within our industry about the validity, scope, and enforceability of many issued patents in the U. S. and elsewhere in the world, and, to date, the law and practice remains in ~~substantial~~ flux both in the agencies that grant patents and in the courts. We cannot currently determine the ultimate scope and validity of patents which may be granted to third parties in the future or which patents might be asserted as being infringed by the manufacture, use and sale of our products. There has been, and we expect that there may continue to be, significant litigation in the pharmaceutical industry regarding patents and other intellectual property rights. Litigation, arbitrations, administrative proceedings, and other legal actions with private parties and governmental authorities concerning patents and other intellectual property rights may be protracted, expensive, and distracting to management. Competitors may sue us as a way of delaying the introduction of our products or to remove our products from the market. Any litigation, including litigation related to Abbreviated New Drug Applications (" ANDA "), litigation related to 505 (b) (2) applications, interference proceedings to determine priority of inventions, derivations proceedings, inter partes review, oppositions to patents in foreign countries, litigation against our collaborators or similar actions, may be costly and time consuming and could harm our business. We expect that litigation may be necessary in some instances to determine the validity and scope of certain of our proprietary rights. Litigation may be necessary in other instances to determine the validity, scope or non- infringement of certain patent rights claimed by third parties to be pertinent to the manufacture, use or sale of our products. Ultimately, the outcome of such litigation could adversely affect the validity and scope of our patent or other proprietary rights, hinder our ability to manufacture and market our products, or result in the assessment of significant monetary damages against us that may exceed amounts, if any, accrued in our consolidated financial statements. On July 24, 2020, we filed a lawsuit against Sun Pharmaceutical Industries Limited (" Sun ") in the U. S. District Court for the

District of Delaware alleging infringement of **our** U. S. Patent No. 10, 646, 481 (~~the~~ " **the** ' 481 patent "). The lawsuit follows our receipt of a Notice Letter on June 11, 2020, advising that Sun had submitted an ANDA to the FDA seeking approval to manufacture and market a generic version of the 150 mg tablet of KALYDECO ~~®~~ in the U. S. The Notice Letter indicated that Sun submitted a " Paragraph IV " certification to the FDA in which Sun asserts that the' 481 patent is invalid or would not be infringed by Sun' s generic product. The' 481 patent, which expires on August 13, 2029, was issued on May 12, 2020, and listed in the Orange Book with respect to **the** KALYDECO ~~® tablets~~ **tablet** on June 1, 2020. **By letter dated June 5, 2023,** Sun ~~does not appear~~ **notified us that it had amended its ANDA** to ~~challenge~~ **include a Paragraph IV certification with respect to** our ~~other~~ U. S. **Patent No. 11, 564, 916 (" the' 916** ~~patents~~ **patent ")** ~~covering KALYDECO tablets~~, ~~the latest of~~ which ~~expires~~ **issued** on ~~August 5~~ **January 31** , ~~2027~~ **2023 , is related to the' 481 patent and was listed in the FDA' s Orange Book on February 28, 2023. On June 16, 2023, we filed a lawsuit against Sun in the U. S. District Court for the District of Delaware alleging infringement of the' 916 patent. In December 2023, we settled the case against Sun. The terms of the settlement are confidential** . On July 13, 2021, we filed a lawsuit against Lupin Limited and Lupin Pharmaceuticals, Inc. (collectively, " Lupin ") in the U. S. District Court for the District of Delaware alleging infringement of the' 481 patent. The lawsuit follows our receipt of a Notice Letter on June 2, 2021 **,** advising that Lupin had submitted an ANDA to the FDA seeking approval to manufacture and market a generic version of the 150 mg tablet of KALYDECO in the U. S. The Notice Letter indicated that Lupin submitted a " Paragraph IV " certification to the FDA in which Lupin asserts that the' 481 patent is invalid or would not be infringed by Lupin' s generic product. **By letter dated April 25, 2023,** Lupin ~~does not appear~~ **notified us that it had amended its ANDA** to ~~challenge our~~ **include a Paragraph IV certification with respect to** ~~other~~ **the' 916 patent. On May 26, 2023, we filed a lawsuit against Lupin in the** U. S. **District Court for the District of Delaware alleging infringement of the' 916** ~~patents~~ **patent** ~~covering KALYDECO tablet~~ **. In November 2023, we settled the case against Lupin. The terms of the settlement agreement are confidential** . On June 2, 2022, we filed a lawsuit against Aurobindo Pharma Limited (" Aurobindo ") ~~,~~ in the U. S. District Court for the District of Delaware alleging infringement of the' 481 patent. The lawsuit follows our receipt of a Notice Letter on April 21, 2022, advising that Aurobindo had submitted an ANDA to the FDA seeking approval to manufacture and market a generic version of the 150 mg tablet of KALYDECO in the U. S. The Notice Letter indicated that Aurobindo submitted a " Paragraph IV " certification to the FDA in which Aurobindo asserts that the' 481 patent is invalid or would not be infringed by Aurobindo' s generic product. **By letter dated April 12, 2023,** Aurobindo ~~does not appear~~ **notified us that it had amended its ANDA** to ~~challenge our~~ **include a Paragraph IV certification with respect to** ~~other~~ **the' 916 patent. On May 26, 2023, we filed a lawsuit against Aurobindo in the** U. S. **District Court for the District of Delaware alleging infringement of the' 916** ~~patents~~ **patent** ~~covering KALYDECO ® tablet~~ **. In November 2023, we settled the case against Aurobindo** . The **terms** ~~lawsuits against Sun, Lupin, and Aurobindo described above regarding the 150mg tablet~~ of ~~KALYDECO and~~ the **settlement agreement are confidential** ~~' 481 patent have been consolidated by the Delaware court. A scheduling order has been entered by the court and trial is set for February 2024. We intend to vigorously enforce our intellectual property rights relating to KALYDECO tablet and the' 481 patent~~ . On July 22, 2022, we filed a lawsuit against Lupin in the U. S. District Court for the District of Delaware alleging ~~the~~ infringement of the ~~'~~ **'** 481 patent and ~~the~~ U. S. Patent Nos. 8, 883, 206 (~~the~~ " **the** ' 206 patent "), 10, 272, 046 (~~the~~ " **the** ' 046 patent "), and 11, 147, 770 (~~the~~ " **the** ' 770 patent "). The lawsuit follows our receipt of a Notice Letter on June 9, 2022, advising that Lupin had submitted an ANDA to the FDA seeking approval to manufacture and market a generic version of KALYDECO ~~®~~ granules in the U. S. The Notice Letter indicated that Lupin submitted a " Paragraph IV " certification to the FDA in which Lupin asserts that the' 481 patent, the' 206 patent, and the' 046 patent are invalid or would not be infringed by Lupin' s generic product. **By letter dated April 25, 2023, Lupin notified us that it had amended its ANDA to include a Paragraph IV certification with respect to the' 916 patent. On May 26, 2023, we filed a lawsuit against Lupin in the U. S. District Court for the District of Delaware alleging infringement of the' 916 patent. On October 11, 2023, U. S. Patent No. 11, 752, 106 (the "' 106 patent ") was listed in the Orange Book as covering KALYDECO granules. We have not yet received notification that Lupin has submitted a " Paragraph IV " certification for the' 106 patent.** Other than the' 770 patent, which was listed in the Orange Book on April 14, 2022, Lupin does not appear to challenge our other U. S. patents covering KALYDECO granules, the last of which expires on August 5, 2027 **. Therefore, regardless of the outcome of the litigation, Lupin cannot receive final approval of its ANDA before that date** . A scheduling order has been entered by the court and trial is set for ~~September~~ **April** ~~2024~~ **2025** . We intend to vigorously enforce ~~its~~ **our** intellectual property rights relating to KALYDECO granules and the' 481,' 206,' 046 ~~and~~ **,** ' 770 **,' 916, and' 106** patents. CRISPR has licensed certain rights to a worldwide patent portfolio that covers various aspects of the CRISPR / Cas9 editing platform technology including, for example, compositions of matter and methods of use in targeting or cutting DNA from Dr. Emmanuelle Charpentier, one of the named inventors of this patent portfolio. The patent portfolio also has named inventors who assigned their rights to the CVC Group. For example, in connection with their collaboration, Novartis and Intellia Therapeutics, Inc. have reportedly obtained a license to this patent portfolio in certain fields. Both the CVC Group and ~~the~~ Broad ~~Institute~~ have obtained granted patents that purport to cover aspects of CRISPR / Cas9 editing platform technology. Patents and patent applications in this patent portfolio have been the subject of numerous contentious proceedings in the U. S., Europe, and other jurisdictions, including interference proceedings in the USPTO between the CVC Group and (separately) ~~the~~ Broad ~~Institute~~ , Sigma- Aldrich and ToolGen. On February 28, 2021, the USPTO issued a decision in Interference No. 106, 115, concluding that ~~the~~ Broad ~~Institute~~ invented certain applications of CRISPR / Cas9 technology in eukaryotic cells before the CVC Group. The CVC Group has appealed the decision to the U. S. Court of Appeals for the Federal Circuit. If the decision is upheld on appeal (including a potential subsequent appeal to the Supreme Court), ~~the~~ Broad ~~Institute~~ would maintain its granted patents directed to those applications CRISPR / Cas9 technology in eukaryotic cells, and the CVC Group' s pending patent applications directed to that subject matter would not proceed to grant. We can give no assurances to the ultimate outcome of these proceedings or the disputes between the CVC Group and ~~the~~ Broad ~~Institute~~ ,

Sigma- Aldrich and ToolGen. In **December 2023, we entered into an agreement with Editas, providing us a non- exclusive sublicense to certain patents relating to CRISPR / Cas9 technology owned by Broad and Harvard, which are licensed to Editas. In** addition to ~~the~~ Broad ~~Institute~~ , other third parties have filed patent applications claiming CRISPR / Cas9- related inventions and may allege that they invented one or more of the inventions claimed by the CVC Group. Thus, the USPTO may, in the future, declare an interference between certain CVC Group patent applications and one or more patent applications. ~~The Broad Institute, as well as other third~~ **Third** parties ~~,~~ could seek to assert ~~its~~ **their patents, if** issued ~~patents~~ **,** against us based on our CRISPR / Cas9- based activities, including commercialization. Defense of these claims, regardless of their merit, could involve substantial litigation expense and could result in a substantial diversion of management and other employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we could be unable to further develop and commercialize **CASGEVY** ~~exa- cel~~ or other products that we may develop using the CRISPR / Cas9 technology we license from CRISPR. To the extent that valid present or future third- party patents or other intellectual property rights cover our products, product candidates or technologies, we or our strategic collaborators may seek licenses or other agreements from the holders of such rights to avoid or settle legal claims. Such licenses may not be available on acceptable terms, which may hinder our ability to, or prevent us from being able to, manufacture and market our products. Payments under any licenses that we are able to obtain would reduce our profits derived from the covered products. Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee' s former employer. Litigation may be necessary to defend against these claims. In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self- executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management. Risks Related To Our Operations We have expanded ~~operations,financial performance,and stock price will depend on future developments that are highly uncertain and cannot be predicted.If we fail to manage our operations effectively,our business may suffer.We have expanded~~ and are continuing to expand our global operations and capabilities,which has placed,and will continue to place,significant demands on our management and our operational,research and development and financial infrastructure.To effectively manage our business,we need to **continue to adapt as our business grows in scale and complexity across multiple disease states,modalities,and geographies,including by** :• implement and clearly ~~communicate~~ **communicating** our corporate- wide strategies;• ~~enhance~~ **enhancing** our operational and financial infrastructure,including **expansion of** our controls over **data,** records and information;• ~~enhance~~ **enhancing** our operational **,administrative** ,financial and management processes,including our cross- functional decision- making processes and our budget prioritization systems;• **effectively growing,** ~~train~~ **training** and ~~manage~~ **managing** our global employee base;and • ~~enhance~~ **expanding** our compliance **and legal resources.We have expanded** our international operations over the past several years to market our ~~CF~~ medicines and expand our research and development capabilities. New laws and industry codes in the E. U. and elsewhere have expanded transparency requirements regarding payments and transfers of value to healthcare professionals, requirements surrounding patient- level clinical trial data, the protection of personal data and increased sanctions for violations. Collectively, our expansion and these new requirements are adding to our compliance costs and potentially exposes us to sanctions in the event of an infringement or failure to report in these jurisdictions. In addition, a significant portion of our commercial supply chain, including sourcing of raw materials and manufacturing, is located in China and the E. U. Consequently, we are, and will continue to be, subject to risks related to operating in foreign countries, including risks relating to intellectual property protections and business interruptions ~~, including as a result of COVID- 19~~ . These risks are increased with respect to countries such as China that have substantially different local laws and business practices and weaker protections for intellectual property. Risks associated with operating a global biotechnology company include: • differing regulatory requirements for drug approvals and regulation of approved drugs in foreign countries; • varying reimbursement regimes and difficulties or the inability to obtain reimbursement for our products in foreign countries in a timely manner; • differing patient treatment infrastructures, particularly since our business is focused on the treatment of serious diseases that affect relatively smaller numbers of patients and are typically prescribed by specialist physicians; • collectability of accounts receivable; • changes in tariffs, trade barriers, and regulatory requirements, the risks of which appear to have increased in the current political environment; • economic weakness, including recession and inflation, or political instability in particular foreign economies and markets; • differing levels of enforcement and / or recognition of contractual and intellectual property rights; • complying with local laws and regulations, which can change significantly over time; • foreign taxes, including withholding of payroll taxes; • foreign currency fluctuations, which could result in reduced revenues or increased operating expenses, and other obligations incident to doing business or operating in another country; • workforce uncertainty in countries where labor unrest is more common than in the U. S.; • reliance on third- party vendors, distributors and suppliers; • import and export licensing requirements, tariffs, and other trade and travel restrictions; • global or regional public health emergencies that could affect our operations or business; • production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and • business interruptions resulting from geo- political actions, including war and terrorism. Our revenues

are subject to foreign exchange rate fluctuations due to the global nature of our operations. Although we have foreign currency forward contracts to hedge certain forecasted product revenues denominated in foreign currencies, our efforts to reduce currency exchange losses may not be successful. As a result, currency fluctuations among our reporting currency, the U. S. dollar, and the currencies in which we do business will affect our operating results, often in unpredictable ways. In addition, our international operations are subject to regulation under U. S. law. For example, the FCPA prohibits U. S. companies and their representatives from offering, promising, authorizing or making payments to foreign officials for the purpose of obtaining or retaining business abroad. In many countries, the health care professionals we regularly interact with may meet the definition of a foreign government official for purposes of the FCPA. We also are subject to import / export control laws. Failure to comply with domestic or foreign laws could result in various adverse consequences, including the possible delay in approval or refusal to approve a product, recalls, seizures, withdrawal of an approved product from the market, the imposition of civil or criminal sanctions, the prosecution of executives overseeing our international operations and corresponding bad publicity and negative perception of our company in foreign countries. Due to the highly technical nature of our drug discovery and development activities, we require the services of highly qualified and trained scientists who have the skills necessary to conduct these activities. In addition, we need to attract and retain employees with experience in development, marketing and commercialization of medicines and therapies, including cell and genetic therapies. We **provide stock- related compensation benefits to all of our key employees that vest over time and therefore induce them to remain with us and** have entered into employment agreements with some executives ~~and provide stock- related compensation benefits to all of our key employees that vest over time and therefore induce them to remain with us~~ . However, the employment agreements can be terminated by the executive on relatively short notice. The value to employees of stock- related benefits that vest over time can be significantly affected by movements in our stock price and business performance, and may, at any point in time, be insufficient to counteract more lucrative offers from other companies. We face intense competition for our personnel from our competitors and other companies throughout our industry, especially with respect to employees with expertise in cell or genetic therapies. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Moreover, the growth of local biotechnology companies and the expansion of major pharmaceutical companies into the Boston area has increased competition for the available pool of skilled employees, especially in technical fields. The high cost of living can make it difficult to attract employees to our global headquarters in Boston and our international headquarters in London. Current job market dynamics, caused in part by the effects of COVID- 19 and other macro- level events, with many employers unable to fill existing openings at all levels of their organizations, could result in significant increases to our costs to recruit and retain employees. Challenges could adversely affect our operations and financial results if we do not have sufficient staff to perform necessary functions. In addition, the available pool of skilled employees would be further reduced if immigration laws change in a manner that increases restrictions on immigration. Our ability to continue to commercialize our products and achieve our research and development objectives depends on our ability to respond effectively to these demands. If we are unable to hire and retain qualified personnel, there could be a material adverse effect on our business. We maintain and rely extensively on information technology systems and network infrastructures for the effective operation of our business. In the course of our business, we collect, store, and transmit confidential information (including personal information and intellectual property), and it is critical that we do so in a secure manner to maintain the confidentiality ~~and~~ **,** integrity **, and availability** of such confidential information. A disruption, infiltration, or failure of our information technology systems or any of our data centers as a result of software or hardware malfunctions, computer viruses, cyber- attacks, employee theft or misuse, power disruptions, natural disasters, floods or accidents could cause breaches of data security and loss of critical data, which in turn could materially adversely affect our business and subject us to both private and governmental causes of action. While we have implemented security measures to minimize these risks to our data and information technology systems and have adopted a business continuity plan to deal with a disruption to our information technology systems, there can be no assurance that our efforts to protect our data and information systems will prevent breakdowns or breaches in our systems that could adversely affect our business. In addition, ~~our~~ **we maintain cyber** liability **insurance, however, this** insurance may not be sufficient ~~in type or amount~~ to cover ~~us against claims related to security~~ **the financial, legal, business or reputational losses that may result from an interruption or** ~~breaches~~ **breach of** ~~, cyber- attacks or~~ **our** ~~other related liabilities~~ **systems and those of critical third parties** . Cyber- attacks are increasing in their frequency, sophistication, and intensity, and are becoming increasingly difficult to detect. They are often carried out by well- resourced and skilled parties, including nation states, organized crime groups, " hacktivists " and employees or contractors acting carelessly or with malicious intent. Cyber- attacks include deployment of harmful malware and key loggers, ransomware, denial- of- service attacks, malicious websites, the use of social engineering, and other means to affect the confidentiality, integrity and availability of our technology systems and data. Cyber- attacks also include manufacturing, hardware or software supply chain attacks, which could cause a delay in the manufacturing of products or products produced for contract manufacturing or lead to a data privacy or security breach. Our key business partners face similar risks, and any security breach of their systems could adversely affect our security. In addition, our increased use of cloud technologies heightens these third party and other operational risks, and any failure by cloud or other technology service providers to adequately safeguard their systems and prevent cyber- attacks could disrupt our operations and result in misappropriation, corruption, or loss of confidential or propriety information. **A significant portion of our workforce continues to leverage hybrid work.** Risk of cyber- attack is increased with employees working remotely. Remote work increases the risk we may be vulnerable to cybersecurity- related events such as phishing attacks and other security threats. We are subject to risks associated with..... enhance our compliance and legal resources. Our business has a substantial risk of product liability claims and other litigation liability. We are or may be involved in various legal proceedings, including securities / shareholder matters and claims related to product liability, intellectual property, employment law, **competition law,** data privacy, and breach of contract. Such proceedings may involve claims for, or the possibility of, damages or fines and

penalties involving substantial amounts of money or other relief, including ~~but not limited to~~ civil or criminal fines and penalties. If any of these legal proceedings were to result in an adverse outcome, it could have a material adverse effect on our business. With respect to product liability and clinical trial risks, in the ordinary course of business we are subject to liability claims and lawsuits, including potential class actions, alleging that our products or product candidates have caused, or could cause, serious adverse events or other injury. We have product liability insurance and clinical trial insurance in amounts that we believe are adequate to cover this risk. However, our insurance may not provide adequate coverage against all potential liabilities. If a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as pay uncovered damage awards resulting from a claim brought successfully against us and these damages could be significant and have a material adverse effect on our financial condition. Furthermore, whether or not we are ultimately successful in defending any such claims, we might be required to direct significant financial and managerial resources to such defense and adverse publicity is likely to result. If our facilities were to experience a catastrophic loss, our operations would be seriously harmed. Most of our operations, including our research and development activities, are conducted in a limited number of facilities. If any of our major facilities were to experience a catastrophic loss, due to an earthquake, severe storms, fire or similar event, our operations could be seriously harmed. For example, our corporate headquarters, as well as additional leased space that we use for certain logistical and laboratory operations and manufacturing, are located in a flood zone along the Massachusetts coast. We have adopted ~~a~~ business continuity ~~plan~~ **plans** to address most crises. However, if we are unable to fully implement our business continuity plans, we may experience delays in recovery of data and / or an inability to perform vital corporate functions, which could result in a significant disruption in our research, development, manufacturing and / or commercial activities, large expenses to repair or replace the facility and / or the loss of critical data, which could have a material adverse effect on our business. The use of social media platforms **and artificial intelligence tools** presents risks and challenges. Social media is being used by third parties to communicate about our products and product candidates and the diseases our therapies are designed to treat. We believe that members of the ~~CF community~~ **communities supporting serious diseases** may be more active on social media as compared to other patient populations due to the demographics of ~~this~~ **those** patient ~~population~~ **populations** . Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product or a product candidate, which could result in reporting obligations. In addition, our employees may engage on social media in ways that may not comply with legal or regulatory requirements, which may give rise to liability, lead to the loss of trade secrets and other intellectual property, or result in public disclosure of protected personal information. There is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. **Negative sentiment about us or our business shared over social media, or misinformation disseminated from fraudulent accounts impersonating our employees or our business, or otherwise, could harm our business and reputation, whether or not it is based in fact.** Certain data protection regulations, such as the GDPR, apply to personal data contained on social media. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur harm to our business, including damage to our reputation **. Similar risks relating to inappropriate disclosure of sensitive information or inaccurate information appearing in the public domain may also apply from our employees engaging with and use of new artificial intelligence tools, such as ChatGPT** . Our stock price may fluctuate. Market prices for securities of companies such as ours are highly volatile. From January 1, ~~2022~~ **2023** to December 31, ~~2022~~ **2023** , our common stock traded between $ **282.** ~~214~~ **21** ~~. 66~~ and $ ~~324~~ **413** . ~~75~~ **00** per share. The market for our stock, like that of other companies in the biotechnology industry, has experienced significant price and volume fluctuations. The future market price of our securities could be significantly and adversely affected by factors such as: • the information contained in our quarterly earnings releases, including updates regarding our commercialized products or our product candidates, our net product revenues and operating expenses for completed periods and financial guidance regarding future periods; • announcements of FDA actions with respect to our therapies or those of our competitors, or regulatory filings for our therapies or those of our competitors, or announcements of interim or final results of clinical trials or nonclinical studies relating to our therapies or those of our competitors **; • announcements we make or commentary by public equity analysts with respect to clinical development of the product candidates in our pain program** ; • developments in domestic and international governmental policy or regulation, for example, relating to drug pricing and tax reform; • technological innovations or the introduction of new drugs by our competitors; • government regulatory action; • public concern as to the safety of drugs developed by us or our competitors; • developments in patent or other intellectual property rights or announcements relating to these matters; • information disclosed by third parties regarding our business or products; • developments relating specifically to other companies and market conditions for pharmaceutical and biotechnology stocks or stocks in general; • business development, capital structuring or financing activities; and • general worldwide or national economic, political and capital market conditions, including as a result of ~~the COVID- 19 pandemic,~~ inflation and rapid fluctuations in interest rates. Following periods of volatility in the market price of a company' s securities, stockholder derivative lawsuits and securities class action litigation are common. Such litigation, if instituted against us or our officers and directors, could result in substantial costs and a diversion of management' s attention and resources. Our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate globally. Our effective tax rate may be different than experienced in the past due to numerous factors, including changes in the mix of our profitability from country to country, tax authority examinations / audits of our tax filings, adjustments to the value of our uncertain tax positions, changes in accounting for income taxes, and changes in tax laws or modifications of treaties in various jurisdictions. Any of these factors could cause us to experience an effective tax rate that is significantly different from previous periods or our current expectations. On December 12, 2022, E. U. member states reached an agreement to implement the minimum tax component (" Pillar Two ") of the Organization for Economic Co- operation and Development' s (the "

OECD' s "), global international tax reform initiative **with effective dates of January 1, 2024 and 2025** . ~~It is expected~~ **On July 17, 2023, the OECD published Administrative Guidance proposing certain safe harbors** that **effectively extend certain effective dates to January 1, 2027.** E. U. member states ~~will implement~~ **need to adopt this Administrative Guidance in their local** Pillar Two **legislation** for **such safe harbors to apply** ~~tax years beginning after December 31, 2023~~ . In addition, the U. K. has independently released draft legislation to introduce the OECD' s Pillar Two reforms into U. K. law. ~~If implemented,~~ **We are continuing to evaluate the potential impact on future periods of the** Pillar Two ~~could result in changes in tax laws in jurisdictions~~ **guidance, pending legislative adoption by individual countries, including those** in which we do business ~~and adversely affect our provision for income taxes and our current rate~~ . We are subject to ongoing tax audits in various jurisdictions, and local tax authorities may disagree with certain positions we have taken and assess additional taxes. We regularly assess the probable outcomes of these audits to determine the appropriateness of our tax provision, and we have established contingency reserves for material tax exposures. However, there can be no assurance that we will accurately predict the outcomes of these disputes or other tax audits or that issues raised by tax authorities will be resolved at a financial cost that does not exceed our related reserves and the actual outcomes of these disputes and other tax audits could have a material impact on our results of operations or financial condition. Our quarterly operating results are subject to significant fluctuation. Our operating results have fluctuated from quarter to quarter in the past, and we expect that they will continue to do so in the future. Our revenues are primarily dependent on the amount of net product revenues from sales of our CF medicines. Our total net product revenues could vary on a quarterly basis based on, among other factors, the timing of orders from our significant customers. Additional factors that have caused quarterly fluctuations to our operating results in recent years include variable amounts of revenues ~~,~~ **;** expenses resulting from our significant investments in research and development **, acquired in- process research and development,** and commercialization activities ~~,~~ **;** changes in the fair value of our strategic investments, derivative instruments and contingent consideration liabilities ~~,~~ **;** charges for excess and obsolete inventories, interest income, interest expenses **;** and our provision for income taxes. Our revenues also are subject to foreign exchange rate fluctuations due to the global nature of our operations. Although we have foreign currency forward contracts to hedge forecasted product revenues denominated in foreign currencies, our efforts to reduce currency exchange losses may not be successful. As a result, currency fluctuations among our reporting currency, the U. S. dollar, and the currencies in which we do business may affect our operating results, often in unpredictable ways. Our quarterly results also could be materially affected by significant charges, which may or may not be similar to charges we have experienced in the past. Most of our operating expenses relate to our research and development activities, do not vary directly with the amount of revenues and are difficult to adjust in the short term. As a result, if revenues in a particular quarter are below expectations, we are unlikely to reduce operating expenses proportionately for that quarter. These examples are only illustrative and other risks, including those discussed in these " Risk Factors, " could also cause fluctuations in our reported financial results. Our operating results during any one period do not necessarily suggest the results of future periods. We expect that results from our clinical development activities and the clinical development activities of our competitors will continue to be released periodically, and may result in significant volatility in the price of our common stock. Any new information regarding our products and product candidates **,** or competitive products or potentially competitive product candidates **,** can substantially affect investors' perceptions regarding our future prospects. We, our collaborators, and our competitors periodically provide updates regarding drug **and therapy** development programs, typically through press releases, conference calls and presentations at medical conferences. These periodic updates often include interim or final results from clinical trials conducted by us or our competitors and / or information about our or our competitors' expectations regarding regulatory filings and submissions as well as future clinical development of our products or product candidates, competitive products or potentially competitive product candidates. The timing of the release of information by us regarding our drug **and therapy** development programs is often beyond our control and is influenced by the timing of receipt of data from our clinical trials and by the general preference among pharmaceutical companies to disclose clinical data during medical conferences. In addition, the information disclosed about our clinical trials, or our competitors' clinical trials, may be based on interim rather than final data that may involve interpretation difficulties and may in any event not accurately predict final results. The release of such information may result in volatility in the price of our common stock. General Risk Factors ~~We may need to raise additional capital that may not be available. We may need to raise additional capital in the future. Any potential public offering, private placement or debt financing may or may not be similar to the transactions that we entered into in the past. Any debt financing may be on terms that, among other things, include conversion features that could result in dilution to our then- existing security holders and restrict our ability to pay interest and dividends — although we do not intend to pay dividends for the foreseeable future. Any equity financings would result in dilution to our then- existing security holders. If adequate funds are not available on acceptable terms, or at all, we may be required to curtail significantly or discontinue one or more of our research, drug discovery or development programs, including clinical trials, incur significant cash exit costs, or attempt to obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain of our technologies, products or product candidates. Based on many factors, including general economic conditions, additional financing may not be available on acceptable terms, if at all.~~ Future indebtedness could materially and adversely affect our financial condition, and the terms of our credit agreements impose restrictions on our business, reducing our operational flexibility and creating default risks. In July 2022, we entered into a credit agreement providing for a $ 500. 0 million revolving credit facility and terminated an existing $ 500. 0 million credit agreement entered into in 2019. In September 2022, our $ 2. 0 billion credit agreement that was entered into in 2020 expired in accordance with its terms. Subject to certain conditions, our current credit agreement provides that we may request the borrowing capacity be increased by an additional $ 500. 0 million for a total of $ 1. 0 billion. If we borrow under our current credit agreement or any future credit agreements, such indebtedness could have important consequences to our business, including increasing our vulnerability to general adverse financial, business, economic and industry conditions, as well as other factors that are beyond our control. The credit agreement requires that we comply with

certain financial covenants, including a consolidated leverage ratio covenant. Further, the credit agreement includes negative covenants, subject to exceptions, restricting or limiting our ability and the ability of our subsidiaries to, among other things, incur additional indebtedness, grant liens, engage in certain investment, acquisition and disposition transactions, and enter into transactions with affiliates. As a result, we may be restricted from engaging in business activities that may otherwise improve our business. Failure to comply with the covenants could result in an event of default that could trigger acceleration of our indebtedness, which would require us to repay all amounts owed under the credit agreements and / or our finance leases and could have a material adverse effect on our business. Additionally, our obligations under the credit agreement are unconditionally guaranteed by certain of our domestic subsidiaries. **If we incur additional indebtedness, the risks related to our business and our ability to service or repay our indebtedness would increase.** Issuances of additional shares of our common stock could cause the price of our common stock to decline. As of December 31, ~~2022~~ **2023**, we had 257. ~~0~~ **7** million shares of common stock issued and outstanding. As of December 31, ~~2022~~ **2023**, we also had ~~2~~ **3**. ~~9~~ **0** million unvested restricted stock units (" RSUs "), 1. 2 million unvested performance stock units (" PSUs "), and outstanding options to purchase ~~2~~ **1**. ~~5~~ **9** million shares of common stock with a weighted- average exercise price of $ ~~146. 11~~ **151 . 37** per share. The majority of our unvested RSUs are likely to vest based on our employees' continued employment. The number of PSUs that vest is dependent on a potential range of shares issuable pursuant to certain financial and non- financial milestones, and our employees' continued employment. Outstanding vested options are likely to be exercised if the market price of our common stock exceeds the applicable exercise price. In the future, we expect to issue a limited number of additional options to our directors. In addition, we may issue additional common stock or restricted securities in the future as part of financing activities or business development activities and any such issuances may have a dilutive effect on our then- existing shareholders. Sales of substantial amounts of our common stock in the open market, or the availability of such shares for sale, could adversely affect the price of our common stock. The issuance of restricted common stock or common stock upon exercise of any outstanding options would be dilutive, and may cause the market price for a share of our common stock to decline. There can be no assurance that we will repurchase shares of common stock or that we will repurchase shares at favorable prices. In February 2023, our Board of Directors approved a share repurchase program (the " ~~2023~~ Share Repurchase Program ") pursuant to which we are authorized to repurchase up to $ 3. 0 billion of our common stock **from time to time through open market or privately negotiated transactions**. Our stock repurchases will depend upon, among other factors **, market conditions**, our cash balances and potential future capital requirements, results of operations, financial condition, and other factors that we may deem relevant. We can provide no assurance that we will repurchase stock at favorable prices, if at all. We have adopted provisions in our articles of ~~incorporation~~ **organization** and by- laws and are subject to Massachusetts corporate laws that may frustrate any attempt to remove or replace members of our board or to effectuate certain types of business combinations involving ~~Vertex~~ **us**. Provisions of our articles of ~~incorporation~~ **organization**, by- laws and Massachusetts state laws may frustrate any attempt to remove or replace members of our current Board of Directors and may discourage certain types of business combinations involving ~~Vertex~~ **us**. Our by- laws ~~grant~~ **allow** the **Board of** ~~directors~~ **Directors** ~~a right~~ to adjourn any meetings of shareholders prior to the time the meeting has been convened. We may issue shares of any class or series of preferred stock in the future without shareholder approval and upon such terms as our Board of Directors may determine. The rights of the holders of common stock will be subject to, and may be adversely affected by, the rights of the holders of any class or series of preferred stock that may be issued in the future. Massachusetts state law also prohibits us from engaging in specified business combinations with an interested stockholder **, subject to certain exceptions,** unless the combination is approved or consummated in a prescribed manner, ~~and prohibits~~ **places restrictions on** voting by any shareholder who acquires 20 % or more of the ~~outstanding~~ **aggregate shareholder** voting ~~stock~~ **power** without ~~shareholder~~ approval **by non- interested shareholders**. As a result, shareholders or other parties may find it difficult to remove or replace our directors or to effectuate certain types of business combinations involving ~~Vertex~~ **us**. SPECIAL NOTE REGARDING FORWARD- LOOKING STATEMENTS This Annual Report on Form 10- K, including the descriptions of our Business set forth in Part I, Item 1, our Risk Factors set forth in Part I, Item 1A, and our Management' s Discussion and Analysis of Financial Condition and Results of Operations set forth in Part II, Item 7, contains forward- looking statements. Forward- looking statements are not purely historical and may be accompanied by words such as " anticipates, " " may, " " forecasts, " " expects, " " intends, " " plans, " " potentially, " " believes, " " seeks, " " estimates, " and other words and terms of similar meaning. Such statements may relate to: • our expectations regarding the amount of, timing of, and trends with respect to our financial performance, including revenues, costs and expenses, and other gains and losses; • our expectations regarding clinical trials, including expectations for patient enrollment, development timelines, the expected timing of data from our ongoing and planned clinical trials, and regulatory authority filings and other submissions for our therapies; • our ability to maintain and obtain adequate reimbursement for our products **and product candidates**, our ability to launch, commercialize and market our products or any of our other therapies for which we obtain regulatory approval **, including CASGEVY,** and our ability to obtain label expansions for existing therapies; • our expectations regarding our ability to continue to grow our CF business by increasing the number of people with CF eligible and able to receive our medicines and providing improved treatment options for people who are already eligible for one of our medicines; • the data that will be generated by ongoing and planned clinical trials and the ability to use that data to advance compounds, continue development or support regulatory filings **, including from the multiple ascending dose portion of the Phase 1 / 2 clinical trial of VX- 522, the durable efficacy and effectiveness of CASGEVY as one- time functional cure for people with SCD and TDT, and the benefit risk profile supporting VX- 548 as a transformative option for acute pain as compared to existing agents, and that our triple combinations of vanzacaftor / tezacaftor / deutivacaftor will provide additional clinical benefits to people with CF who have at least one mutation in their CFTR; • our beliefs and plans with respect to the potential near- term launch of our triple combinations of vanzacaftor / tezacaftor / deutivacaftor for treatment of CF and for VX- 548 for the treatment of acute pain**; • our beliefs regarding the support provided by clinical trials and preclinical and nonclinical studies of

our therapies for further investigation, clinical trials or potential use as a treatment; • our plans to continue investing in our research and development programs, including anticipated timelines for our programs, and our strategy to develop our pipeline programs, alone or with third party- collaborators; • our beliefs regarding the approximate patient populations for the disease areas on which we focus; • the potential benefits and therapeutic scope of our acquisitions and collaborations, including our acquisition of ViaCyte and its potential to accelerate development of our stem- cell based T1D programs ~~; •~~ **, and our collaboration with CRISPR for** ~~the~~ **their** ~~establishment,~~ **gene- editing technology to accelerate the** development ~~and maintenance~~ of ~~collaborative relationships, including potential milestone payments or~~ **our** ~~other obligations~~ **hypoimmune cell therapies for T1D** ; • potential business development activities, including the identification of potential collaborative partners or acquisition targets; • **the establishment, development and maintenance of collaborative relationships, including potential milestone payments or other obligations; •** our ability to expand and protect our intellectual property portfolio and otherwise maintain exclusive rights to products; • potential fluctuations in foreign currency exchange rates and the effectiveness of our foreign currency management program; • our expectations regarding the amount of cash to generated by operations, our cash balance and expected generation and interest income; • our expectations regarding our provision for or benefit from income taxes and the utilization of our deferred tax assets; • our ability to use our research programs to identify and develop new product candidates to address serious diseases and significant unmet medical needs; • **the effectiveness of our governance, plans and strategy with respect to managing cybersecurity risks and other threats to our information technology systems; •** our plans to expand, strengthen, and invest in our global supply chains and manufacturing infrastructure and capabilities, including for cell and gene therapies; • our ability to attract and retain skilled personnel; • our expectations involving governmental cost containment and other regulatory efforts; • our expectations surrounding the competitive landscape facing our products and product candidates ~~; • our expectations regarding the effect of COVID- 19 on, among other things, our financial performance, liquidity, business and operations, including manufacturing, supply chain, research and development activities and pipeline programs~~ ; and • our liquidity and our expectations regarding the possibility of raising additional capital. Forward- looking statements are subject to certain risks, uncertainties, or other factors that are difficult to predict and could cause actual events or results to differ materially from those indicated in any such statements. These risks, uncertainties, and other factors include, but are not limited to, those described in our Risk Factors, set forth in Part I, Item 1A, and elsewhere in this report and those described from time to time in our future reports filed with the Securities and Exchange Commission. Any such forward- looking statements are made on the basis of our views and assumptions as of the date of the filing and are not estimates of future performance. Except as required by law, we undertake no obligation to publicly update any forward- looking statements. The reader is cautioned not to place undue reliance on any such statements. **61**