**Risk Factors Comparison 2024-02-28 to 2023-02-22 Form: 10-K**

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Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward- looking statements made by us or on our behalf in this Annual Report on Form 10- K and other filings with the Securities and Exchange Commission (the " SEC "), press releases, communications with investors, and oral statements. Actual future results may differ materially from those anticipated in our forward- looking statements. We undertake no obligation to update any forward- looking statements, whether as a result of new information, future events, or otherwise. Risks Related to Our Financial Position and Need for Additional Capital We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. Since inception, we have incurred significant operating losses. Our net losses were $ **153. 2 million, $** 220. 4 million, **and** $ 192. 5 ~~million, and $ 116. 0~~ million for the years ended December 31, **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~ , respectively. As of December 31, ~~2022~~ **2023** , we had an accumulated deficit of $ 1. ~~1~~ **23** billion. We have financed our operations primarily through public offerings of our common stock, our collaboration with Bristol Myers Squibb Company (" BMS ") through its wholly owned subsidiary, Juno Therapeutics, Inc. (" Juno Therapeutics "), and payments under our former strategic alliance with Allergan Pharmaceuticals International Limited ( ~~which was acquired by AbbVie Inc. in May 2020 and is referred to~~ together with its affiliates ~~as ,~~ " Allergan "). We have devoted substantially all of our efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we: ~~●~~ • progress the clinical development of ~~EDIT~~ **reni** - ~~301~~ **cel** to treat severe sickle cell disease (" SCD ") and transfusion- dependent beta- thalassemia (" TDT "); ~~●~~ **• advance our in vivo programs as we progress towards preclinical proof- of- concept for an undisclosed in vivo indication in 2024; •** continue our current research programs ~~, including ex vivo treatments for hemoglobinopathies and in vivo gene editing medicines,~~ and our preclinical and clinical development of product candidates from our current research programs; ~~●~~ • seek to identify additional research programs and additional product candidates; ~~●~~ • initiate preclinical testing and clinical trials for any product candidates we identify and develop; ~~●~~ • maintain, expand, and protect our intellectual property portfolio and provide reimbursement of third- party expenses related to our patent portfolio; ~~●~~ • seek marketing approvals for any of our product candidates that successfully complete clinical trials; • ~~● ultimately~~ establish a sales, marketing, and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval; ~~●~~ • further develop our genome editing platform; ~~●~~ • hire additional clinical, quality control, and scientific personnel; ~~●~~ • add operational, financial, and management information systems and personnel, including personnel to support our product development; ~~●~~ • acquire or in- license other medicines and technologies; ~~● validate a~~ **and • establish, expand or contract for** commercial- scale current Good Manufacturing Practices (" cGMP ") manufacturing **capabilities. We** ~~facility; and ●~~ continue to **progress** ~~operate as a public company. We are in the early stages of~~ the clinical development of ~~EDIT~~ **reni** - **cel, but** ~~301 and expect that~~ it ~~will~~ **may** be ~~many~~ years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must develop and eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical testing and clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing, and selling those medicines for which we may obtain marketing approval, and satisfying any post- marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Other than ~~EDIT~~ **reni** - ~~301~~ **cel** , we are currently only in the preclinical testing stages for our most advanced research programs. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investments in us. We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce, or eliminate our research and product development programs or commercialization efforts. We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate **preclinical studies and** clinical trials of, and seek marketing approval for, product candidates. In addition, if we obtain marketing approval for any product candidates we develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. **We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate.** Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and product development programs or future commercialization efforts. We expect that our existing cash, cash equivalents ~~,~~ and marketable securities ~~at~~ **on** December 31, ~~2022~~ **2023 , together with the near- term annual license fees** and ~~anticipated interest income~~ **the contingent upfront payment payable under our license agreement with Vertex Pharmaceuticals, Incorporated (" Vertex "),** will ~~enable us to~~ fund our operating expenses and capital expenditure requirements into ~~2025~~ **2026 . As of December 31, 2023, our right to contingent payments under our collaboration agreements with BMS and Vor Bio, as well as our contingent upfront**

**payment and annual license fees with Vertex, are our only significant committed potential external source of funds** . Our future capital requirements will depend on many factors, including: ~~● •~~ **the costs of progressing the clinical development of reni- cel to treat SCD and TDT; •** the scope, progress, results, and costs of **clinical trials,** drug discovery, preclinical development, laboratory testing, and clinical or natural history study trials for ~~the~~ **other** product candidates we develop; **•** ~~● the costs of progressing the clinical development of EDIT- 301 to treat SCD and TDT; ●~~ the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property- related claims; **•** ~~52 ●~~ the costs, timing, and outcome of regulatory review of the product candidates we develop; ~~● •~~ **the costs of establishing and maintaining a supply chain for the development and manufacture of our product candidates; •** the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for any product candidates for which we receive regulatory approval; ~~● •~~ the success of our collaboration with BMS ~~; ● ,~~ **including** whether BMS exercises any of its options to extend the research program term and / or to additional research programs under our collaboration; ~~● •~~ our ability to establish and maintain additional collaborations on favorable terms, if at all; ~~● •~~ the extent to which we acquire or in- license other medicines and technologies; ~~● •~~ the costs of reimbursing our licensors for the prosecution and maintenance of the patent rights in- licensed by us; and ~~● the costs of operating as a public company~~ **• our ability to establish and maintain healthcare coverage and adequate reimbursement for any product candidates for which we receive regulatory approval** . Identifying potential product candidates and conducting preclinical testing and clinical trials is a time- consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully identify and develop product candidates and those are approved, we **will require significant additional amounts in order to launch and commercialize our product candidates and** may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for ~~many~~ years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We ~~do not~~ have ~~any~~ **limited** significant committed **potential** external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders may be materially diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, **would result in increased fixed payment obligations and** may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates, or we may have to grant licenses on terms that may not be favorable to us. Our ~~short~~ **limited** operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability. We were founded and commenced operations in the second half of 2013. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates, undertaking preclinical studies and initiating **and conducting** clinical trials. Except for ~~EDIT~~ **reni** ~~-~~ ~~301~~ **cel** , all of our research programs are still in the preclinical or research stage of development, and the risk of failure of all of our research programs is high. We have not yet demonstrated an ability to successfully complete any clinical trials, including large- scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial- scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for ~~53successful~~ **successful** commercialization. In addition, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown factors **. Our limited operating history, particularly in light of the rapidly evolving genome editing field, may make it difficult to evaluate our current business and predict our future performance. Our relatively short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early- stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer** . We expect that our financial condition and operating results will continue to fluctuate significantly from quarter- to- quarter and year- to- year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance. We have never generated revenue from product sales and may never be profitable. Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. We do not anticipate generating revenues from product sales for ~~the next several~~ years, if ever. Even if one or more of the product candidates we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U. S. Food and Drug Administration (the " FDA "), the European Medicines Agency (the " EMA "), or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Risks Related to Discovery, Development, and ~~CommercializationWe~~ **Commercialization We** are dependent on the success of our lead product candidate, ~~EDIT~~ **reni** ~~-~~ ~~301~~ **cel** , which is in clinical development. Clinical trials of product candidates may not be successful. If we are unable to complete the clinical development of, obtain marketing approval for, or successfully commercialize this product candidate, either alone or

with a collaborator, or if we experience significant delays in doing so, our business would be substantially harmed. **We** ~~In January 2023, we implemented a strategic reprioritization of our portfolio to focus on hemoglobinopathies and in vivo gene editing, and in connection with that paused patient enrollment in our clinical EDIT- 101 program, terminated our AAV IRD platform, and divested our preclinical wholly owned iNK programs. As a result, we~~ have one ongoing clinical- stage program, ~~EDIT~~ **reni** - ~~301~~ **cel** . We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of ~~EDIT~~ **reni** - ~~301~~ **cel** for the treatment of SCD and TDT. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize ~~EDIT~~ **reni** - ~~301~~ **cel** . Because our business is significantly dependent upon this one product candidate, any setback in the clinical development or the obtaining of regulatory approval for ~~EDIT~~ **reni** - ~~301~~ **cel** would have a material adverse effect on our business and prospects. The success of our ~~EDIT~~ **reni** - ~~301~~ **cel** program will depend on several factors, including the following: ~~•~~ • successful enrollment and completion of our RUBY **Phase 1 / 2 / 3 clinical trial of reni- cel for the treatment of SCD and our EdiTHAL** Phase 1 / 2 clinical trial of ~~EDIT~~ **reni** - **cel** ~~301 for the treatment of SCD and our EDITHAL Phase 1 / 2 clinical trial of EDIT- 301~~ for the treatment of TDT, as well as any additional clinical trials of ~~EDIT~~ **reni** - ~~301~~ **cel** that we undertake; ~~•~~ • safety, tolerability and efficacy profiles that are satisfactory to the FDA, or any comparable foreign regulatory authority for marketing approval; ~~•~~ • timely receipt of marketing approvals from applicable regulatory authorities; ~~•~~ • the performance of our future collaborators, if any; • ~~54~~ ~~•~~ the extent of any required post- marketing approval commitments to applicable regulatory authorities; ~~•~~ • establishment **and maintenance** of supply arrangements with third- party raw materials suppliers and manufacturers **for clinical development and, if approved, commercialization of our product candidates** ; ~~•~~ • establishment **and maintenance** of arrangements with third- party manufacturers to obtain finished drug products that are appropriately packaged for sale; ~~•~~ • **successful development of our internal manufacturing processes and transfer to larger- scale facilities operated by either a contract manufacturing organization or by us;** • obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally; ~~•~~ • protection of our rights in our intellectual property portfolio; ~~•~~ • successful launch of commercial sales following any marketing approval; ~~•~~ • a continued acceptable safety profile following any marketing approval; ~~•~~ • commercial acceptance by patients, the medical community and third- party payors following any marketing approval; and ~~•~~ • our ability to compete with other therapies ~~, including therapies that are further advanced in clinical development~~ . Many of these factors are beyond our control, including the outcome of clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize ~~EDIT~~ **reni** - ~~301~~ **cel** , on our own or with any future collaborator, or experience delays as a result of any of these or other factors, our business would be substantially harmed. We intend to identify and develop product candidates based on a **relatively** novel genome editing technology, which makes it difficult to predict the time and cost of product candidate development. ~~No~~ **Only one** therapeutic ~~products~~ **product** that ~~utilize~~ **utilizes** genome editing technology ~~have~~ **has** been approved in the United States or in Europe. We have concentrated our research and development efforts on our genome editing platform, which uses CRISPR technology. Our future success depends on the successful development of this **relatively** novel genome editing therapeutic approach. ~~To~~ **In 2023, the first and, to** date, ~~no~~ **only, approved** therapeutic product that utilizes genome editing, including CRISPR technology, **was** ~~has been~~ approved in the United States ~~or~~ **and** Europe. It is difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our genome editing platform, or any similar or competitive genome editing platforms, will result in the identification, development, and regulatory approval of any medicines. There can be no assurance that any development problems we experience in the future related to our genome editing platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process or transferring that process to commercial partners. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we develop on a timely or profitable basis, if at all. Regulatory requirements governing genetic medicines, and in particular any novel genetic medicines we may develop, have changed frequently and may continue to change in the future. Regulatory requirements governing genetic and cellular medicines, and in particular any novel genetic medicine products we may develop, have changed frequently and may continue to change in the future **. We are aware of a limited number of genetic medicines that have received marketing authorization from the FDA and EMA. Even with respect to more established products in the genetic medicine field, the regulatory landscape is still developing. For example, the FDA has established the Office of Therapeutic Products (" OTP ") to oversee the review of genetic medicines and related products. It has also established the Cellular, Tissue and Gene Therapies Advisory Committee to advise the Center for Biologics Evaluation and Research on its review of gene therapy products. The FDA has also issued guidance documents** , including **a March 2022** ~~, for example, the~~ draft guidance ~~document titled~~ **entitled** " Human Gene Therapy Products Incorporating Human Genome Editing " ~~issued by~~ **outlining the agency' s current recommendations regarding information that should be provided in an Investigational New Drug application (" IND ") in order to assess the safety and quality of the investigational product. Nonetheless,** the FDA **' s regulatory requirements governing** ~~in March 2022. We are aware of a limited number of~~ genetic **and cellular** medicines **continue** ~~that have received marketing authorization from the FDA and EMA. Even with respect~~ to **evolve** ~~more established products in the genetic medicine field, the regulatory 55landscape is still developing. For example, the FDA has established the Office of Tissues~~ and **we** ~~Advanced Therapies (formerly the Office of Cellular, Tissue and Gene Therapies) within CBER to consolidate the review of genetic medicines and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Genetic medicine clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH also are potentially subject to review by the Office of Biotechnology Activities' Recombinant DNA Advisory Committee,~~

~~or the RAC; however, the NIH announced that the RAC~~ will ~~only publicly review clinical trials if~~ **need to monitor and adapt to these requirements as** ~~the~~ **they develop** ~~trials cannot be evaluated by standard oversight bodies and pose unusual risks~~. The same ~~applies~~ **is true for activities** in the European Union. The EMA' s Committee for Advanced Therapies (" CAT ") is responsible for assessing the quality, safety and efficacy of advanced- therapy medicinal products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a genetic medicinal candidate that is submitted to the **Committee for Human Medicinal Products (" CHMP ")** before ~~CHMP~~ **it** adopts its final opinion. In the European Union, the development and evaluation of a genetic medicinal product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for genetic medicinal products and require that we comply with these new guidelines. As a result, the procedures and standards applied to genetic medicines and cell therapy products may be applied to any product candidates we may develop, but that remains uncertain at this point. These regulatory review committees and advisory groups and the new ~~guidelines~~ **guidances** they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of any product candidates we may develop or lead to significant post- approval limitations or restrictions. As we advance any product candidates we may develop, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of these product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business. Although the FDA decides whether individual genetic medicine protocols may proceed, the **Recombinant DNA Advisory Committee (" RAC ")** public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or an exemption from in- depth, public review. If we were to engage an NIH- funded institution to conduct a clinical trial, that institution' s ~~IBC~~ **institutional biosafety committee** as well as its **institutional review board (" IRB ")** would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of genetic medicine products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any product candidates we may develop. Similarly, the EMA may issue new guidelines concerning the development and marketing authorization for genetic medicine products and require that we comply with these new guidelines. As we are initially seeking to identify and develop product candidates to treat diseases using novel technologies, there is heightened risk that the FDA, the EMA or other regulatory authority may not consider the clinical trial endpoints that we propose to provide clinically meaningful results. Even if the endpoints are deemed clinically meaningful, we may not achieve these endpoints to a degree of statistical significance, particularly because many of the diseases we are targeting with our platform have small patient populations, making development of large and rigorous clinical trials more difficult. Adverse developments in post- marketing experience or in clinical trials conducted by others of genetic medicines or cell therapy products may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for development or approval of any product candidates we may develop or limit the use of products utilizing non- viral genetic medicinal technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as the product candidates we may develop can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing non- viral genetic medicine technology in a ~~56timely~~ **timely** manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the commercialization of resulting products. In addition, ethical, social and legal concerns about genetic medicine, genetic testing and genetic research could result in additional regulations or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed their intentions to further regulate biotechnology. More restrictive regulations or claims that any product candidates we may develop are unsafe or pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of any product candidates we may develop under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be. As we advance any product candidates we may develop through clinical development, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. These regulatory review committees and advisory groups and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of any product candidates we may develop or lead to significant post- approval limitations or restrictions. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue. We may not be successful in our efforts to identify, develop, or commercialize potential product candidates. The success of our business depends primarily upon our ability to identify, develop, and commercialize products based on our genome editing platform. Other than ~~EDIT~~ **reni** - ~~301~~ **cel**, all of our ongoing product development programs are still in the preclinical or research stage of development. Our research programs, including those subject to our collaboration with BMS, may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have **smaller patient populations than initially estimated or may have** harmful

side effects or may have other characteristics that may make the products impractical to manufacture or commercialize, or unlikely to receive marketing approval. The occurrence of these events may force us to abandon our development efforts for a program or programs, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful ~~.~~ ~~For example~~ , **as was the case with** ~~in November 2022 we announced updated clinical data from~~ our Phase 1 / 2 BRILLIANCE trial of EDIT- 101 to treat Leber congenital amaurosis ~~. This data demonstrated a favorable safety profile and provided proof of concept. However~~ , **for which** ~~we were not able to identify any baseline characteristics of the treatment responder patients that could pre- select a responder patient population other~~ -- **the** ~~than zygosity. The~~ identified responder patient population was determined to be too small to progress the program independently ~~. We have since paused patient enrollment in this program~~ . The genome editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on CRISPR gene editing technology using Cas9 and Cas12a enzymes, but other genome editing technologies may be discovered that provide significant advantages over CRISPR / Cas9 or CRISPR / Cas12a, which could materially harm our business. To date, we have focused our efforts on genome editing technologies using CRISPR and the Cas9 and Cas12a (also known as Cpf1) enzymes. Other companies have previously undertaken research and development of genome editing technologies using zinc finger nucleases, engineered meganucleases, and transcription activator- like effector nucleases, but to date none has obtained marketing approval for a product candidate. There can be no certainty that ~~the~~ **these** ~~57CRISPR / Cas9 or CRISPR / Cas12a technology will lead to the development of genomic medicines, that~~ other genome editing technologies will not be considered better or more attractive for the development of medicines ~~or that either Cas9 or Cas12a, the two CRISPR associated proteins that we use, may be useful or successful in developing therapeutics. For example, Cas9 or Cas12a may be determined to be less attractive than other CRISPR enzymes, including CRISPR enzymes that have yet to be discovered~~ . Similarly, a new genome editing technology that has not been discovered yet may be determined to be more attractive than CRISPR. Moreover, if we decide to develop genome technologies other than CRISPR technology using a Cas9 or Cas12a enzyme, we cannot be certain we will be able to obtain rights to such technologies. Any of these factors could reduce or eliminate our commercial opportunity, and could have a material adverse effect on our business, financial condition, results of operations, and prospects. Except for ~~EDIT~~ **reni** - ~~301~~ **cel** , all of our product development programs are at the preclinical or research stage. Preclinical testing and clinical trials of product candidates may not be successful. If we are unable to commercialize any product candidates we develop or experience significant delays in doing so, our business will be materially harmed. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on our successful development and eventual commercialization of product candidates that we have identified or may identify in the future. Our research programs, including any with collaborators, may fail to identify potential product candidates for clinical development for a number of reasons, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the product candidates impractical to manufacture, unmarketable, or unlikely to receive marketing approval. Any potential product candidates we identify will require preclinical and clinical activities and studies, regulatory review and approval in each jurisdiction in which we intend to market the products, substantial investment, establishing manufacturing capabilities, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product. If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any product candidates we develop, we may need to abandon or limit our further clinical development of those product candidates. We have limited experience in evaluating product candidates in human clinical trials, having dosed our first patient in a clinical trial in 2020, and our proposed delivery modes, combined with CRISPR technology, have a limited history ~~, if any,~~ of being tested clinically. It is impossible to predict when or if any product candidates we develop will ultimately prove safe in humans, including ~~EDIT~~ **reni** - ~~301~~ **cel** . In the genomic medicine field, there have been several significant adverse events from gene therapy treatments in the past, including reported cases of leukemia and death. There can be no assurance that genome editing technologies will not cause severe or undesirable side effects. A significant risk in any genome editing product is that the edit will be " off- target " and cause serious adverse events, undesirable side effects, or unexpected characteristics. For example, off- target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA. We cannot be certain that off- target editing will not occur in any of our clinical studies. There is also the potential risk of delayed adverse events following exposure to genome editing therapy due to the potential for persistent biological activity of the genetic material or other components of products used to carry the genetic material. If any product candidates we develop are associated with serious adverse events, or undesirable side effects, or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk- benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects. If any of the product candidates we develop or the delivery modes we rely on cause undesirable side effects, it could delay or prevent their regulatory approval, limit the commercial potential, or result in significant negative consequences following any potential marketing approval. ~~58Our~~ -- **Our** product candidates that we are testing or may test in clinical trials, including ~~EDIT~~ **reni** - ~~301~~ **cel** , or that are developed may be associated with off- target editing or other serious adverse events, undesirable side effects, or unexpected characteristics. In addition to serious adverse events or side effects caused by any product candidate we develop and test, the administration process or related procedures also can cause undesirable side effects. If any such events occur, our clinical trials could be suspended or terminated. If we are unable to demonstrate that such adverse events were caused by factors other than our product candidate, the FDA, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates we are able to

develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product- related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations, and prospects significantly. If we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy (" REMS ") to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any of our product candidates, several potentially significant negative consequences could result, including: ~~•~~ • regulatory authorities may suspend or withdraw approvals of such product candidate; ~~•~~ • regulatory authorities may require additional warnings on the label; ~~•~~ • we may be required to change the way a product candidate is administered or conduct additional clinical trials; ~~•~~ • we could be sued and held liable for harm caused to patients; and ~~•~~ • our reputation may suffer. Any of these events could prevent us from achieving or maintaining market acceptance of any product candidates we may identify and develop and could have a material adverse effect on our business, financial condition, results of operations, and prospects. We have not extensively tested any of our proposed delivery modes and product candidates in clinical trials. Our proposed delivery modes, combined with our product candidates, have a limited history of being evaluated in human clinical trials. Any of our product candidates, including ~~EDIT~~ **reni** - **cel** ~~301 to treat SCD and TDT~~ , may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical trials. There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development. Any such adverse events may cause us to delay, limit, or terminate planned clinical trials, any of which would ~~59have~~ -- **have** a material adverse effect on our business, financial condition, results of operations, and prospects. Because we are developing product candidates for the treatment of diseases in which there is little clinical experience using new technologies, there is increased risk that the FDA, the EMA, or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze. During the regulatory review process, we will need to identify success criteria and endpoints such that the FDA, the EMA, or other regulatory authorities will be able to determine the clinical efficacy and safety profile of our product candidates. As we are seeking to identify and develop product candidates to treat diseases in which there is little clinical experience using new technologies, there is heightened risk that the FDA, the EMA, or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre- specified endpoints to a degree of statistical significance. This may be a particularly significant risk for many of the genetically defined diseases for which we plan to develop product candidates because many of these diseases have small patient populations, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. The FDA weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. Any product candidates we develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. ~~No~~ **Only one** genome editing therapeutic product has been approved in the United States or in Europe. If clinical trials of any product candidates we identify and develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates. Before obtaining marketing approval from regulatory authorities for the sale of any of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans of any such product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. We or our collaborators may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates we may identify and develop, including: ~~•~~ • delays in reaching a consensus with regulators on trial design; ~~•~~ • regulators, ~~institutional review boards (" IRBs ")~~ or independent ethics committees (" IECs ") not authorizing us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; ~~•~~ • delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective contract research organizations (" CROs ") and clinical trial sites; ~~•~~ • clinical trials of any product candidates we develop producing negative or inconclusive results, and us deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development or research programs; ~~•~~ • the number of patients required for clinical trials of any product candidates we develop may be larger than we anticipate **; the number of subjects willing to enroll may be smaller than required** ; enrollment of suitable participants in these clinical trials may be delayed or slower than we anticipate; or patients may drop out of these clinical trials at a higher rate than we anticipate; • ~~60~~ ~~•~~ our third- party contractors failing to

comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all; • regulators, IRBs, or IECs requiring that we or our investigators suspend or terminate clinical research or clinical trials of any product candidates we develop for various reasons, including noncompliance with regulatory requirements, a finding of undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites; • the supply or quality of any product candidates we develop or other materials necessary to conduct clinical trials of any product candidates we develop being insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing, and delivery of any product candidates we develop to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions; • occurrence of serious adverse events associated with any product candidates we develop that are viewed to outweigh their potential benefits; and • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols. If we or our collaborators are required to conduct additional clinical trials or other testing of any product candidates we develop beyond those that we currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other tests of any product candidates we develop, or if the results of these trials or tests are not positive or only modestly positive, or if there are safety concerns, we or our collaborators may: • be delayed in obtaining marketing approval for any such product candidates we develop, or not obtain marketing approval at all; • obtain approval for indications or patient populations that are not as broad as intended or desired; • obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings; • be subject to changes in the way the product is administered; • be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements; • have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy; • be sued; or • experience damage to our reputation. Product development costs will also increase if we or our collaborators experience delays in testing or marketing approvals. We do not know whether clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we develop, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize any product candidates we develop, any of which may harm our business, financial condition, results of operations, and prospects. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary ~~61regulatory~~ **regulatory** approvals could be delayed or prevented. We or our collaborators may not be able to initiate or continue clinical trials for any of our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. In addition, if patients are unwilling to participate in our genome editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy, or genome editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products, or for other reasons, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of any product candidates we develop may be delayed. Moreover, some of our competitors may have **approved products or** ongoing clinical trials for product candidates that would treat the same indications as any product candidates we develop, and patients who would otherwise be eligible for our clinical trials may instead **select the approved product or** enroll in clinical trials of our competitors' product candidates **. Both Vertex and bluebird bio, Inc. recently received regulatory approval for medicines for the treatment of sickle cell disease, the same indication as reni- cel. Eligible patients for our ongoing RUBY trial may select one of these approved medicines rather than enroll in our trial, and any negative publicity resulting from these approved medicines may impact our ability to recruit patients** . Patient enrollment is also affected by other factors, including: • severity of the disease under investigation; • size of the patient population and process for identifying patients; • design of the trial protocol; • availability and efficacy of approved medications for the disease under investigation; • availability of genetic testing for potential patients; • ability to obtain and maintain patient informed consent; • risk that enrolled patients will drop out before completion of the trial; • eligibility and exclusion criteria for the trial in question; • perceived risks and benefits of the product candidate under trial; • perceived risks and benefits of genome editing as a therapeutic approach; • efforts to facilitate timely enrollment in clinical trials; • patient referral practices of physicians; • ability to monitor patients adequately during and after treatment; • **and • proximity and availability of clinical trial sites for prospective patients. The eligibility criteria of our clinical trials further limits the pool of available trial participants. Additionally, the process of finding and diagnosing patients may prove costly. Future pandemics or** ~~the~~ **other** ~~ongoing~~ **global health crises may impact our ability to timely enroll trial participants and conduct our studies, as the** COVID- 19 pandemic **did** ~~; and • proximity and availability of clinical trial sites for prospective patients. The eligibility criteria of our clinical trials further limits the pool of available trial participants. Additionally, the process of finding and diagnosing patients may prove costly. The COVID- 19 pandemic, including related restrictions imposed by regulatory authorities and constraints on healthcare provider capacity, has previously impacted and may in the future impact our ability to timely enroll trial participants and conduct our studies~~ . Our ability to successfully initiate, enroll, and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including: • ~~62~~ difficulty in establishing or managing relationships with CROs and physicians; • different standards for the conduct of clinical trials; • different standard- of- care for patients with a particular disease; • inability to locate qualified local consultants, physicians, and partners; and • potential burden of complying with a variety of foreign laws, medical standards, and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment. Enrollment delays in our clinical trials may result in increased development costs for any of our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate ongoing or planned clinical trials, any of

which would have an adverse effect on our business, financial condition, results of operations, and prospects. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we focus on research programs and our product candidates for specific indications among many potential options. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations, and prospects. If we are unable to successfully identify patients who are likely to benefit from therapy with any medicines we develop, or experience significant delays in doing so, we may not realize the full commercial potential of any medicines we may develop. Our success may depend, in part, on our ability to identify patients who are likely to benefit from therapy with any of our medicines, which may require those potential patients to have their DNA analyzed for the presence or absence of a particular sequence. If we, or any third parties that we engage to assist us, are unable to successfully identify such patients, or experience delays in doing so, then: • our ability to develop any product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials; • any product candidates we develop may not receive marketing approval if safe and effective use of such product candidates depends on an in vitro diagnostic; and • we may not realize the full commercial potential of any product candidates we develop that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our medicines. As a result, we may be unable to successfully develop and realize the commercial potential of any product candidates we may identify and develop, and our business, financial condition, results of operations, and prospects would be materially adversely affected.

 **Even** if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate we develop, and any such approval may be for a more narrow indication than we seek. We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if any product candidates we develop meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non- approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process. Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require precautions or contra- indications with respect to conditions of use, or they may grant approval subject to the performance of costly post- marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we develop. Any of the foregoing scenarios could materially harm the commercial prospects for any product candidates we develop and materially adversely affect our business, financial condition, results of operations, and prospects. Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success. The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third- party payors, and others in the medical community. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including: • the efficacy and safety of such product candidates as demonstrated in clinical trials; • the potential and perceived advantages compared to alternative treatments; • the limitation to our targeted patient population and limitations or warnings contained in approved labeling by the FDA or other regulatory authorities; • the ability to offer our medicines for sale at competitive prices; • convenience and ease of administration compared to alternative treatments; • the clinical indications for which the product candidate is approved by the FDA, the European Commission, or other regulatory agencies; • public attitudes regarding genomic medicine generally and genome editing technologies specifically; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, as well as their willingness to accept a therapeutic intervention that involves the editing of the patient' s genome; • product labeling or product insert requirements of the FDA, the EMA, or other regulatory authorities, including any limitations or warnings contained in a product' s approved labeling; • relative convenience and ease of administration; •  the timing of market introduction of competitive products; • publicity concerning our products or competing products and treatments; • the strength of marketing and distribution support; • sufficient third- party coverage or reimbursement; and • the prevalence and severity of any side effects. If any of our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues, and we may not become profitable. Adverse public perception of genomic medicines, and genome editing in particular, may negatively impact regulatory approval of, or demand for, our potential products. Our potential therapeutic products involve editing the human genome. The clinical and commercial success of our potential products will depend in part on public understanding and acceptance of the use of genome editing therapy for the prevention or treatment of human diseases **. To date, only one genome editing therapy has been approved for sale by the FDA** . Public attitudes may be influenced by claims that genome editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical

trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. In addition, genome editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of genome editing technology to human embryos or the human germline. For example, academic scientists in several countries, including the United States, have reported on their attempts to edit the genome of human embryos as part of basic research and, in November 2018, Dr. Jiankui He, a Chinese biophysics researcher who was an associate professor in the Department of Biology of the Southern University of Science and Technology in Shenzhen, China, announced he had created the first human genetically edited babies, twin girls and helped create a second gene- edited pregnancy. The announcement was negatively received by the public, in particular by those in the scientific community. In the United States, germline editing for clinical application has been expressly prohibited since enactment of a December 2015 U. S. FDA ban on such activity. Prohibitions are also in place in the United Kingdom, across most of Europe, in China, and many other countries around the world. In the United States, the NIH has announced that it would not fund any use of genome editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey- Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Basic research on embryos is more tightly controlled in many other European countries. Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of genome editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any products we may develop. If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any of our product candidates, we may not be successful in commercializing those product candidates if and when they are approved. ~~65We~~ **We** do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved. There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel. Factors that may inhibit our efforts to commercialize our medicines on our own include: • our inability to recruit and retain adequate numbers of effective sales and marketing personnel; • the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines; • the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and • unforeseen costs and expenses associated with creating an independent commercialization organization. If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to market and sell any medicines we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. We face significant competition in an environment of rapid technological change, and our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours. The development and commercialization of new drug products is highly competitive. Moreover, the biotechnology and pharmaceutical industries, including in the gene therapy, genome editing and cell therapy fields, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. We will face competition with respect to any of our product candidates now and in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. **For example, in late 2023 and early 2024, the FDA approved Vertex' s CASGEVYTM (exagamglogene autotemcel), a Cas9 genome- edited cell medicine, for the treatment of SCD and TDT. The FDA also approved in late 2023 bluebird bio' s LYFGENIATM (lovotibeglogene autotemcel), a cell- based gene therapy, for the treatment of SCD. If reni- cel is approved for marketing, these therapies will be directly competitive with reni- cel, our Cas12a genome- edited medicine for the treatment of SCD and TDT.** ~~66Our~~ -- **Our** platform and product focus is the development of therapies using CRISPR

technology specifically for genome editing. Other companies developing CRISPR Cas9 or Cas12a technology or therapies using CRISPR Cas9 or Cas12a technology include Artisan Bio, **AvenCell Therapeutics,** Caribou Biosciences, CRISPR Therapeutics, EdiGene, ERS Genomics, Excision Biotherapeutics, ~~Graphite Bio,~~ Inscripta, Intellia **Therapeutics, Kamau** Therapeutics, Sigma- Aldrich, ToolGen, and Vertex Pharmaceuticals. In addition, there have been and may continue to be discoveries of new CRISPR- based gene editing technologies. There are additional companies developing therapies using related CRISPR genome editing technologies, including other CRISPR nucleases, base editing, prime editing and gene writing. These companies include **Amber Bio,** Arbor Biotechnologies, Beam Therapeutics, Chroma Medicine, Emendo Biotherapeutics **, Epic Bio** , Integra Therapeutics, KSQ Therapeutics, Locus Biosciences, Mammoth Biosciences, Metagenomi, Poseida Therapeutics, Prime Medicine, Scribe Therapeutics, Tessera Therapeutics, Tome Biosciences, Tune Therapeutics, and Verve Therapeutics. There are also companies developing therapies using transcription activator- like effector nucleases, meganucleases, Mega- TALs and zinc finger nucleases. These companies include 2Seventy Bio, Allogene Therapeutics, bluebird bio, Cellectis, Precision Biosciences, and Sangamo Therapeutics. In addition to competition from other genome editing therapies, gene therapies or cell medicine therapies, any products that we may develop may also face competition from other types of therapies, such as small molecule, antibody, protein, oligonucleotide, or ribonucleic acid therapies. ~~There are also companies developing therapies related to our development programs.~~ For hemoglobinopathies, these companies include Acceleron Pharma, **Agios Pharmaceuticals** ~~Aruvant Therapeutics, Beam Therapeutics, bluebird bio, Cellectis, CRISPR Therapeutics, EdiGene~~ , Global Blood Therapeutics, ~~Graphite Bio, Intellia Therapeutics,~~ Novartis Pharmaceuticals, ~~Sangamo Therapeutics,~~ and Vertex ~~Pharmaceuticals~~ . Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non- competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we develop against competitors. In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and / or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. If we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third- party reimbursement practices, or healthcare reform initiatives, which would harm our business. The regulations that govern marketing approvals, pricing, and reimbursement for new medicines vary widely from country to country. Some countries require approval of the sale price of a medicine before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a medicine in a particular country, but then be subject to price regulations that delay our commercial launch of the medicine, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the medicine in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any of our product candidates obtain marketing approval. Our ability to commercialize any medicines successfully also will depend in part on the extent to which ~~67reimbursement~~ -- **reimbursement** for these medicines and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Government authorities and third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. For example, the Inflation Reduction Act of 2022 (the " IRA ") includes several measures intended to lower the cost of prescription drugs and related healthcare reforms, including limits on price increases and subjecting an escalating number of drugs to annual price negotiations with The Centers for Medicare & Medicaid Services. We cannot be sure whether additional legislation or rulemaking related to the IRA will be issued or enacted, or what impact, if any, such changes will have on the profitability of any of our drug candidates, if approved for commercial use, in the future. Increasingly, third- party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any medicine that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval. There may be significant delays in obtaining reimbursement for newly approved medicines, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any medicine will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for

new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the medicine and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost medicines and may be incorporated into existing payments for other services. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government- funded and private payors for any approved medicines we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines, and our overall financial condition. Due to the novel nature of our technology and the potential for some of our product candidates to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for these product candidates. The pricing and reimbursement of any of our product candidates, if approved, must be adequate to support the necessary commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to any of our product candidates, e. g., for administration of our product to patients, is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products. In addition, it may be necessary for us to develop new reimbursement models in order to realize adequate value. Payors may not be able or willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations, and prospects could be adversely affected. We expect the cost of a single administration of **our** genomic medicine products to be substantial, when and if they achieve regulatory approval **. For example, Vertex has announced that the list price for its recently approved Cas9 genome- edited cell medicine for the treatment of SCD and TDT is $ 2. 2 million, while bluebird bio' s recently approved cell- based gene therapy for SCD has a list price of $ 3. 1 million** . We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any such product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of any product candidates we develop will be paid by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers, and other third- party payors. Coverage and reimbursement by a third- party payor may depend upon several factors, including the third- party ~~68payor~~ -- **payor** ' s determination that use of a product is: • a covered benefit under its health plan; • safe, effective, and medically necessary; • appropriate for the specific patient; • cost- effective; and • neither experimental nor investigational. Obtaining coverage and reimbursement for a product from third- party payors is a time- consuming and costly process that could require us to provide to the payor supporting scientific, clinical, and cost- effectiveness data. There is significant uncertainty related to third- party coverage and reimbursement of newly approved products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any of our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any product candidates we develop will be harmed ~~. If the market opportunities for any of our product candidates are smaller than we believe they are, our revenues may be adversely affected, and our business may suffer. If the target patient population for a product candidate we develop is small, we will need to successfully identify patients and achieve a significant market share to maintain profitability and growth. Some of our programs may focus on treatments for rare genetically defined diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe, and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with our products, or may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition, results of operations, and prospects~~ . Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any medicines that we may develop. We face an inherent risk of product liability exposure related to the testing in human clinical trials of any of our product candidates and will face an even greater risk if we commercially sell any medicines that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • decreased demand for any product candidates or medicines that we may develop; • injury to our reputation and significant negative media attention; • withdrawal of clinical trial participants; • significant time and costs to defend the related litigation; • substantial monetary awards to trial participants or patients; • loss of revenue; ~~and69~~ -- **and** • the inability to commercialize any medicines that we may develop. Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage if we successfully commercialize any medicine. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those

governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third- party facilities. We also could incur significant costs associated with civil or criminal fines and penalties. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our commercial general liability and umbrella liability policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Any third- party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Genomic medicines are novel, and our product candidates can be complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products, or otherwise harm our business. Our product candidates can require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, or insufficient inventory. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical- grade materials that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. ~~70In~~ **In** addition, the FDA, the EMA, and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA, or other regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials, including the ongoing ~~Phase 1 / 2~~ clinical ~~trial~~ **trials** for ~~EDIT~~ **reni** - ~~301~~ **cel**, or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations, and prospects. We also may encounter problems hiring and retaining the experienced scientific, quality control, and manufacturing personnel needed to manage our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements. Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall, or restriction on the use of biologically derived substances in the manufacture of any product candidates we develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations, and prospects. Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in third- party manufacturing process or facilities also could restrict our ability to ensure sufficient clinical material for any clinical trials we may be conducting or are planning to conduct and meet market demand for any products we commercialize. Risks Related to Our Dependence on Third ~~PartiesWe~~ -- **Parties We** expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we develop or for development of certain of our research programs. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates or research programs. We anticipate seeking third- party collaborators for the research, development, and commercialization of certain of the product candidates we develop or for development of certain of our research programs. Our likely collaborators include large and mid- size pharmaceutical companies, regional and national pharmaceutical companies, and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them and, if applicable, whether they exercise any additional options to commercialize a product. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs or any of our product candidates and alliance arrangements we may enter into under which our research programs or product candidates may be involved pose the following risks to us: ● Collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations. ● Collaborators may not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial ~~71results --~~ **results**, changes in the collaborator' s strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities. ● Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing. ● Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our medicines or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours. ● Collaborators with marketing and distribution rights to one or more medicines may not commit sufficient resources to the marketing and distribution of such medicine or medicines. ● Collaborators may not properly obtain, maintain, enforce, or defend our intellectual property or proprietary rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. ● Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources. ● We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control. ● Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. ● Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated. If our collaborations do not result in the successful development and commercialization of products, or if one of our collaborators terminates its agreement with us, we may not receive any milestone or royalty payments under such collaborations. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval, and commercialization described in this Annual Report on Form 10- K apply to the activities of our collaborators. If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans. Our product development and research programs and the potential commercialization of any of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates and research programs, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates or programs. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement ~~72for --~~ **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 or similar regulatory authorities outside the United States, 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 technology, 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. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us. We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators or allies. For example, under our amended and restated collaboration with BMS, we may not use directly or indirectly, or license others to use, genome editing technology in connection with any research, development, manufacture, commercialization or other exploration of certain T cells, subject to certain exceptions, as more fully described in " Part I — Business — Our Collaborations and Licensing Strategy " of this Annual Report on Form 10- K. Collaborations are also complex and time- consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue. We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing. We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may

terminate their engagements with us at any time. If we need to enter into alternative arrangements, our product development activities would be delayed. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government- sponsored database, ClinicalTrials. gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines. We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any ~~73performance --~~ **performance** failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue. We contract with third parties for the manufacture of materials for our research programs, preclinical studies and clinical trials and expect to continue to do so and for commercialization of any product candidates that we develop. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts. We have a limited ability to manufacture materials for our research programs and preclinical studies and we do not operate any significant manufacturing facilities. ~~We~~ **While we currently perform some manufacturing for our internal programs, as well as cell processing for reni- cel, we** primarily rely on third- party contract manufacturing organizations (" CMOs ") for the manufacture of our **other** materials for preclinical **studies** and clinical ~~studies~~ **trials** and expect to continue to do so and for commercial supply of any product candidates that we develop and for which we or our collaborators obtain marketing approval. **If** ~~Even though~~ we **were to experience an unexpected loss or interruption of supply for any of our product candidates, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials. Further, our product candidates are composed of multiple components and require specialized formulations for which scale- up and manufacturing could be difficult. We** have **limited experience in such scale- up and manufacturing requiring us to depend on a limited number of third parties, who may not be able to deliver in a timely manner, or at all. In order to develop products, apply for regulatory approvals, and commercialize our products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. Additionally, our product candidates have not yet been manufactured for commercial use. If any of our product candidates become approved for commercial sale, we will need to** ~~established --~~ **establish** ~~supply agreements with~~ **either internal or third- party manufacturing capacity. Manufacturing partner requirements may require us to fund capital improvements, perhaps on behalf of third parties, to support the scale- up of manufacturing and related activities. We may not be able to establish scaled manufacturing capacity for an approved product in a timely or economic manner, if at all. If we or our** third- party manufacturers **are unable to provide commercial quantities of such an approved product** , ~~reliance~~ **we will have to successfully transfer manufacturing technology to a different manufacturer. Engaging a new manufacturer for such an approved product could require us to conduct comparative studies or utilize other means to determine bioequivalence of the new and prior manufacturers' products, which could delay or prevent our ability to commercialize such an approved product. If we or any of these manufacturers is unable or unwilling to increase its manufacturing capacity or if we are unable to establish alternative arrangements** on ~~third- party~~ **a timely basis or on acceptable terms, the development and commercialization of such an approved product may be delayed or there may be a shortage in supply. Any inability to** ~~manufacturers --~~ **manufacture** ~~entails additional risks, including: ● the possible breach of the manufacturing agreement by the third party; ● the possible termination or~~ **our** ~~nonrenewal of~~ **product candidates or future approved drugs in sufficient quantities when needed would seriously harm our business. While we are exploring alternative suppliers for certain critical materials,** ~~the~~ **there can be no assurance** ~~agreement by the third party at a time~~ that ~~is costly or~~ **our efforts will be successful** ~~inconvenient for us; and ● reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting~~ . Third- party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Our current and anticipated future dependence upon others for the manufacture of any of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis. Risks Related to Our Intellectual Property If we are unable to obtain and maintain patent protection for any products we develop and for our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any of our product candidates, and our

technology may be adversely affected. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our CRISPR platform technology and any proprietary product candidates and technology we develop. We seek to protect our proprietary position by in- licensing intellectual property relating to our platform technology and filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business. If we or our licensors and / or collaborators are unable to obtain or maintain patent protection with respect to our CRISPR platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed. ~~74No~~ **No** consistent policy regarding the scope of claims allowable in the field of genome editing, including CRISPR technology, has emerged in the United States. The scope of patent protection outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in- licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. The patent prosecution process is expensive, time- consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non- disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we hold or in- license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non- infringing manner. For example, we are aware that third parties have suggested the use of the CRISPR technology in conjunction with a protein other than Cas9 or Cas12a. Our owned and in- licensed patents may not cover CRISPR technology in conjunction with a protein other than Cas9 or Cas12a. If our competitors commercialize the CRISPR technology in conjunction with a protein other than Cas9 or Cas12a, our business, financial condition, results of operations, and prospects could be materially adversely affected. The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Our licensors are currently, and we or our licensors may in the future become, subject to a third- party pre- issuance submission of prior art to the United States Patent and Trademark Office (the " USPTO ") or opposition, derivation, revocation, re- examination, post- grant and inter partes review, or interference proceedings and other similar proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third- party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post- grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. As discussed below, some of our in- licensed patents are subject to interference, opposition and ex parte re- examination proceedings and therefore subject to these risks. In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our owned and in- licensed patents and patent applications are, and may in the future be, co- owned with third parties. If we are unable to obtain an exclusive license to ~~75any --~~ **any** such third party co- owners' interest in such patents or patent applications, such co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co- owners of our owned and in- licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. Furthermore, our owned and in- licensed patents and patent applications may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in- licensed patent rights and technology was funded in part by the U. S. government. As a result, the U. S. government has certain rights to such patent rights and technology. These rights may permit the U. S. government to disclose our confidential information to third parties and to exercise march- in rights to use or allow third parties to use our licensed technology. Any exercise by the government of any of the foregoing rights could harm our competitive position, business, financial condition, results of

operations, and prospects. Our rights to develop and commercialize our technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others. We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our genome editing technology, including our CRISPR technology, and product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. For example, pursuant to our license agreements with The Broad Institute, Inc. (" Broad "), and Broad and the President and Fellows of Harvard College (" Harvard "), the licensors may, under certain circumstances, grant a license to the patents that are the subject of such license agreements to a third party. Such third party would have full rights to the patent rights that are the subject of such licenses, which could impact our competitive position and enable a third party to commercialize products similar to our future product candidates and technology. The terms of these license agreements are described more fully under " Part I — Business — Our Collaborations and Licensing Strategy " in this Annual Report. In addition, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, pursuant to each of our intellectual property licenses with Broad and Harvard, our licensors retain control of preparation, filing, prosecution, and maintenance, and, in certain circumstances, enforcement and defense of their patents and patent applications. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. Additionally, we are required to reimburse our licensors for all of their expenses related to the prosecution, maintenance, enforcement and defense of patents and patent applications that we in- license from them, and we anticipate that our obligation to reimburse our licensors for expenses related to these matters will continue to be substantial. Our licensors may have relied on third party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications we in- license. For example, certain patent applications licensed to us by Broad are co- owned with NIH. Broad does not and does not purport to grant any rights in NIH' s interest in these patent applications under our agreement. If other third parties have ownership rights to our in- licensed patents and patent applications, they may be able to license such patents and patent applications to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. Some of our in- licensed patents are subject to priority and validity disputes. In addition, our owned and in- licensed patents, patent applications and other intellectual property may be subject to further priority and validity disputes, ~~76and~~ -- **and** other similar intellectual property proceedings including inventorship disputes. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of the product candidates we develop, which could have a material adverse impact on our business. Certain U. S. patents and a U. S. patent application directed to CRISPR / Cas9 that are co- owned by the Broad Institute and the Massachusetts Institute of Technology (" MIT "), and in some cases Harvard (collectively referred to as " Broad "), and in- licensed by us were involved in a first interference with a U. S. patent application that is co- owned by the University of California, the University of Vienna, and Emmanuelle Charpentier (collectively referred to " CVC "). An interference is a proceeding in United States Patent and Trademark Office (the " USPTO ") before the Patent Trial and Appeal Board of the USPTO (" PTAB ") to determine priority of invention of the subject matter of patent claims filed by different parties. In this first interference, the PTAB made a judgment of no interference- in- fact in favor of the Broad, which was upheld on appeal. This decision was final and bars any further interference between the same parties for claims to the same invention that was considered in the interference. As a result of this decision, the U. S. patents and application that we in- license from the Broad and others were not modified or revoked. On June 24, 2019, the PTAB declared a second interference between certain pending U. S. patent applications that are co- owned by CVC and certain U. S. patents and a U. S. patent application that are co- owned by Broad and in- licensed by us. Most of the Broad U. S. patents and the patent application that are involved in the second interference were also part of the first interference. The invention that was considered in the first interference related to a method involving contacting a target DNA in a eukaryotic cell with certain defined CRISPR / Cas9 components for the purpose of cleaving or editing that target DNA molecule or modulating transcription of at least one gene encoded thereon. The second interference is directed to a different invention, namely a eukaryotic cell comprising a target DNA and certain defined CRISPR / Cas9 components including a single molecule guide RNA that are capable of cleaving or editing the target DNA molecule. On September 10, 2020, the PTAB granted Broad' s motion for priority benefit while denying CVC priority benefit to their two earliest provisional patent applications. As a result, Broad entered the priority phase of the interference as " Senior Party " while CVC remained the " Junior Party " for purposes of determining which entity was the first to invent the inventions at issue. On February 28, 2022, the PTAB issued a decision regarding the priority phase of the interference determining that Broad was the first entity to invent the claims at issue. This decision has been appealed by CVC and the Broad has cross- appealed. It is uncertain when or in what manner the U. S. Court of Appeals for the Federal Circuit will act on these appeals. On December 14, 2020, the PTAB, declared two new interferences involving a pending U. S. patent application that is owned by ToolGen, Inc. (the " ToolGen application "). One of the two interferences is between the ToolGen application and certain U. S. patents and U. S. patent applications that are co- owned by Broad and in- licensed by us. Most of the Broad U. S. patents and patent applications that are involved in the interference with ToolGen are also part of the second interference with CVC. The other ToolGen interference is between the same ToolGen application and the U. S. patent

applications that are co- owned by CVC and involved in the second interference with Broad. The claims in ToolGen' s patent application relate to a mammalian cell with a CRISPR / Cas system comprising a codon optimized nucleic acid encoding a Cas9 polypeptide with a nuclear localization signal and a single- molecule guide RNA that, together, are capable of forming a Cas9 / RNA complex that mediates double stranded cleavage of a target nucleic acid sequence. On September 28, 2022, the PTAB suspended both of these interferences until the U. S. Court of Appeals for the Federal Circuit issues a mandate in the pending appeals related to the second interference between Broad and CVC. On June 21, 2021, the PTAB declared two new interferences involving a pending U. S. patent application owned by Sigma- Aldrich (the " Sigma- Aldrich application "). One of the two new interferences is between the Sigma- Aldrich application and certain U. S. patents and U. S. patent applications that are co- owned by Broad and in- licensed by us. The other Sigma interference is between the same Sigma- Aldrich application and the U. S. patent applications that are co- owned by CVC. Most of the Broad U. S. patents and patent applications that are involved in the interference with Sigma- Aldrich are also part of the concurrent interferences with CVC and ToolGen. The claims in Sigma- Aldrich' s application relate to a method for modifying a chromosomal sequence in a eukaryotic cell by integrating a donor sequence into that ~~77chromosomal~~ -- **chromosomal** sequence. These methods use a CRISPR / Cas9 system comprising a Cas9 polypeptide with a nuclear localization signal, a guide RNA, and a donor sequence that, together, are capable of mediating double stranded cleavage and repair of a target nucleic acid sequence leading to integration of the donor sequence into the chromosomal sequence. On December 14, 2022, the PTAB suspended both of these interferences until the U. S. Court of Appeals for the Federal Circuit issues a mandate in the pending appeals related to the second interference between Broad and CVC. As a result of these declarations of interference, five parallel adversarial proceedings in the USPTO before the PTAB have been initiated – the patent interferences between Broad and CVC, Broad and ToolGen, CVC and ToolGen, Broad and Sigma- Aldrich, and CVC and Sigma- Aldrich. We cannot predict with any certainty how long each interference proceeding will take. It is also possible that other third parties may seek to become a party to these interferences. Our owned and in- licensed patents and patent applications are, or may in the future become, subject to validity disputes in the USPTO and other foreign patent offices. For example, a request for ex parte re- examination was filed with the USPTO on February 16, 2016 against a U. S. patent that we have in- licensed from Broad, which is involved in certain of the interferences. The request for ex parte re- examination was granted on May 9, 2016 thereby initiating a re- examination procedure between the USPTO and The Broad Institute, acting on behalf of itself and MIT. The PTAB has suspended the re- examination noting that it has jurisdiction over any file that involves a patent involved in an interference. It is uncertain when the PTAB will lift the suspension. If The Broad Institute is unsuccessful during the re- examination, the patent in question may be revoked or narrowed, which could have a material adverse effect on the scope of our rights under such patent. We or our licensors may also be subject to claims that former employees, collaborators, or other third parties have an interest in our owned or in- licensed patents or patent applications, or other intellectual property rights as an inventor or co- inventor. If we are unable to obtain an exclusive license to any such third- party co- owners' interest in such patents, patent applications or other intellectual property rights, such co- owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co- owners to enforce any patents, including any patents that issue from patent applications, against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on the conduct of our business, financial condition, results of operations, and prospects. We or our licensors are subject to and may in the future become a party to similar proceedings or priority disputes in Europe or other foreign jurisdictions. For example, certain European patents that we have in- licensed from Broad have been revoked in their entirety by the European Patent Office Opposition Division (the " Opposition Division "). Certain other European patents that we have in- licensed from Broad were maintained with amended patent claims. Certain of these decisions have been appealed by both Broad and the opposing party (s), and it is uncertain when or in what manner the Boards of Appeal will act on these appeals. The Opposition Division has also initiated opposition proceedings against certain other European patents that we have in- licensed from Broad. The European Patent Office opposition proceedings may involve issues including, but not limited to, procedural formalities related to filing the European patent application, priority, and the patentability of the involved claims. In view of certain arguments made by the third parties against the revoked patents and similar arguments made by the third parties against other in- licensed European patents under opposition, the opposition proceedings may lead to the revocation of certain additional in- licensed European patents. The loss of priority for, or the loss of, these European patents could have a material adverse effect on the conduct of our business. One or more of the third parties that have filed oppositions against these European patents or other third parties may file future oppositions against other European patents that we in- license or own. There may be other oppositions against these European patents that have not yet been filed or that have not yet been made available to the public. If we or our licensors are unsuccessful in any patent related disputes, including interference proceedings, patent oppositions, re- examinations, or other priority, inventorship, or validity disputes to which we or they are subject (including any of the proceedings discussed above), we may lose valuable intellectual property rights through the loss of one or more patents owned or licensed or our owned or licensed patent claims may be narrowed, invalidated, or held unenforceable. In addition, if we or our licensors are unsuccessful in any inventorship disputes to which we or they are subject, we may lose valuable intellectual property rights, such as exclusive ownership of, or the exclusive right to use, ~~78our~~ -- **our** owned or in- licensed patents and patent applications. If we or our licensors are unsuccessful in any interference proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or may be non- exclusive or may not be available at all. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we develop. The loss of exclusivity or the narrowing of our owned and in- licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could result in a material adverse effect on our business,

financial condition, results of operations, or prospects. Even if we are successful in any interference proceeding or other priority, inventorship, or validity disputes, it could result in substantial costs and be a distraction to our management and other employees. We may not be able to protect our intellectual property and proprietary rights throughout the world. Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. In addition, our intellectual property license agreements may not always include worldwide rights. For example, certain U. S. patent applications licensed to us by Broad include The University of Tokyo (" Tokyo ") and NIH as joint applicants. Broad has only granted a license to us with respect to its interests and to Tokyo' s interests in these U. S. patent applications but not to any foreign equivalents thereof. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents and our intellectual property rights or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing ~~79partners~~ **partners** to pay these fees due to U. S. and non- U. S. patent agencies. The USPTO and various non- U. S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non- compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business. We have entered into license agreements with third parties and may need to obtain additional licenses from our existing licensors and others to advance our research or allow commercialization of product candidates we develop. It is possible that we may be unable to obtain any additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our current technology, including CRISPR genome editing technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and / or other forms of compensation to third parties, which could be significant. In each of our license agreements, and we expect in our future agreements, we are responsible for bringing any actions against any third party for infringing on the patents we have licensed. Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. Disputes may arise regarding intellectual property subject to a licensing agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement; • the sublicensing of patent and other rights under our collaborative development relationships; • our diligence obligations under the license agreement and what activities satisfy those diligence

obligations; • the inventorship and ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and • the priority of invention of patented technology. In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, including the amount, if any, that may become due and payable to our ~~80licensors~~ -- **licensors** in connection with sublicense income. If these events were to occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. We may not be successful in obtaining necessary rights to any product candidates we develop through acquisitions and in- licenses. We currently have rights to intellectual property, through licenses from third parties, to identify and develop product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of genome editing technology and filing patent applications potentially relevant to our business. For example, we are aware of third party patents and patent applications that may be construed to cover our CRISPR technology and product candidates. In order to avoid infringing these third party patents, or patents that issue from these third party patent applications, we may find it necessary or prudent to obtain licenses from such third party intellectual property holders. We may also require licenses from third parties for certain non- CRISPR technologies including certain delivery methods that we are evaluating for use with product candidates we develop. In addition, with respect to any patents we co- own with third parties, we may require licenses to such co- owners' interest in such patents. However, we may be unable to secure such licenses or otherwise acquire or in- license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our CRISPR technology and product candidates we develop. For example, certain methods for editing cells, guide RNA modifications and delivery modes, including certain adeno-associated virus vector technologies, that we are evaluating for us for use are covered by patents held by third parties. If we are unable to successfully obtain rights to required third party intellectual rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Issued patents covering our technology and product candidates could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad. If we or one of our licensors or our collaborators were to initiate legal proceedings against a third party to enforce a patent covering a product candidate we develop or our technology, including CRISPR genome editing technology, the defendant could counterclaim that such patent is invalid or unenforceable. Third parties have raised challenges to the validity of certain of our in- licensed patent claims and may in the future raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These and other proceedings could result in the revocation or cancellation of, or amendment to our patents in such a way that they no longer cover our technology or platform, or any product candidates that we develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects. The intellectual property landscape around genome editing technology, including CRISPR, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. The field of genome editing, especially in the area of CRISPR technology, is still in its infancy, and no such products have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to our owned and in- licensed, and other third party, intellectual property and proprietary rights in the future. Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, ~~81market~~ -- **market** , and sell any product candidates that we develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. We are subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and any product candidates we develop, including interference, re- examination, post- grant review, inter partes review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the EPO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. We are aware of certain third party patents and patent applications in this landscape that may be asserted to encompass our CRISPR / Cas9 technology. In particular, we are aware of several separate families of U. S. patents and / or U. S. patent applications and foreign counterparts which relate to CRISPR / Cas9 technology, where the earliest priority dates of each family pre- date the priority dates of our in-licensed patents and patent applications, including patent families filed by Vilnius University, by the University of California, the University of Vienna, and Emmanuelle Charpentier, by ToolGen, and by Sigma- Aldrich. Each of these patent families are owned by a different third party and contain claims that may be construed to cover components and uses of CRISPR / Cas9 technology. If we are not able to obtain or maintain a license on commercially reasonable terms to any third- party patents that cover our product candidates or activities, such third parties could potentially assert infringement claims against us, which could have a material adverse effect on the conduct of our business. Even if we believe third- party intellectual property claims are

without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we develop and any other product candidates or technologies covered by the asserted third party patents. If we are found to infringe a third party' s intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing any product candidates we develop and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non- exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects. If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, it could have a material adverse effect on our business. Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 **(** ~~, or~~ the **"** Hatch- Waxman Amendments **")** . The Hatch- Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, an extension may not be granted because of, for example, failure to exercise due diligence during the testing phase or regulatory review process, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Further, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or if the term of any such extension is less than we request, we will be unable to rely on our patent position to forestall the marketing of competing products **and / or competitors may obtain approval of competing products** following our patent ~~expiration~~ **expirations** , and it could have a materially adverse effect on our business, financial condition, results of operations, and prospects. We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged ~~82trade~~ -- **trade** secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property. Many of our employees, consultants, and advisors are currently or 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, consultants, and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual' s current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects. If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know- how, technology, and other proprietary information and to maintain our competitive position. With respect to our technology platform, we consider trade secrets and know- how to be one of our primary sources of intellectual property. Trade secrets and know- how can be difficult to protect. In particular, we anticipate that with respect to our technology platform, these trade secrets and know- how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions. We seek to protect these trade secrets and other proprietary technology, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to them, such as our employees, collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time- consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed. If we do not obtain patent term extension and data exclusivity for any product candidates we develop, our business may

be materially harmed. Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we develop, one or more of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 (the " Hatch- Waxman Amendments "). The Hatch- Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the ~~83approved~~ -- **approved** drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed. Risks Related to Regulatory Approval and Other Legal Compliance Matters Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time- consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of any of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired. Any of our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third- party CROs to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate' s safety, purity, and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any of our product candidates may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post- approval commitments that render the approved medicine not commercially viable. **Further, changes in or the enactment of additional statutes, promulgation of regulations or issuance of guidance during preclinical or clinical development, or comparable changes in the regulatory review process for each submitted product application, may cause delays in the approval or rejection of an application. For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act (" FDORA "), Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other " pivotal study " of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late- stage clinical trials of FDA regulated products. Further, on January 31, 2022, the new Clinical Trials Regulation (EU) No 536 / 2014 became applicable in the European Union (" EU ") and replaced the prior Clinical Trials Directive 2001 / 20 / EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the EU (" EU Member State ") will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public. We have not previously secured authorization to conduct clinical studies in the EU pursuant to this new regulation and, accordingly, there is a risk that we may be delayed in commencing any such studies.** If we experience delays in obtaining approval or if we fail to obtain approval of any of our product candidates, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired. We may seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review designations in the US, and PRIME Designation in the EU, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process. We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination ~~84with~~ -- **with** one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical

development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life- threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product' s application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. In the EU, we may seek PRIME designation for some of our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA' s role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the EU or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the EU and the applicant intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims. The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA' s grant of a marketing authorization. If approved, our product candidates that are licensed and regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway. The Biologics Price Competition and Innovation Act of 2009, (" BPCIA "), was enacted as part of the Patient Protection and Affordable Care Act, (" ACA "), to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as " interchangeable " based on its similarity to an approved biologic. Under the BPCIA, a reference biological product is granted 12 years of ~~data~~ **regulatory** ~~85exclusivity~~ -- **exclusivity** from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product In addition, the licensure of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12- year period of exclusivity, another company may still develop and receive approval of a competing biologic, so long as its BLA does not reply on the reference product, sponsor' s data or submit the application as a biosimilar application. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty, and any new policies or processes adopted by the FDA could have a material adverse effect on the future commercial prospects for our biological products. We believe that any of the product candidates we develop as a biological product under a BLA should qualify for the 12- year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non- biological products will depend on a number of marketplace and regulatory factors that are still developing. Nonetheless, the approval of a biosimilar to our product candidates would have a material adverse impact on our business due to increased competition and pricing pressure. We may not be able to obtain orphan drug exclusivity for one or more of our product candidates, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity

period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified. In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200, 000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In particular, the concept of what constitutes the" same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies. In September 2021, the FDA issued final guidance describing its current thinking on when a gene therapy product is the " same " as another product for purposes of orphan exclusivity. Under the guidance, if either the transgene or vector differs between two gene therapy products in a manner that does not reflect " minor " differences, the two products would be considered different drugs for orphan drug exclusivity purposes. The FDA will determine whether two vectors from the same viral class are the same on a case- by- case basis and may consider additional key features in assessing sameness. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition. On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017 (" FDARA "). FDARA, among other things, codified the FDA' s pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act ~~86unambiguously~~ -- **unambiguously** requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Further, under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by the FDA. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term " same disease or condition " means the designated " rare disease or condition " and could not be interpreted by the FDA to mean the " indication or use. " Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the " indication or use. " Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, FDA announced that, in matters beyond the scope of that court order, FDA will continue to apply its existing regulations tying orphan- drug exclusivity to the uses or indications for which the orphan drug was approved. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. Failure to obtain marketing approval in foreign jurisdictions would prevent any of our product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue. In order to market and sell any of our product candidates in the European Union and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue. ~~Additionally~~ **Further** , **we could face heightened risks with respect to obtaining marketing authorization in** the ~~United Kingdom left~~ **UK as a result of** the ~~European Union on January 31, 2020~~ **withdrawal of the UK from the EU** , commonly referred to as Brexit **. The UK is no longer** , ~~and, effective January 1, 2021, the United Kingdom ceased to be~~ part of the European Single Market and **EU** ~~European Union~~ Customs Union ~~. A co- operation agreement was signed between the United Kingdom and the European Union in December 2020, which entered into force on May 1, 2021. The agreement addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. As both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal. Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, the consequences of Brexit and the impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom remains unclear~~ . As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency **(“** ~~, or the~~ MHRA ~~,~~ **”)** became responsible for supervising medicines and medical devices in Great Britain **(" GB")** , comprising England, Scotland and Wales under domestic law, whereas ~~Northern Ireland will continue to be subject to European Union rules~~ under **the terms of** the Northern Ireland Protocol **, Northern Ireland is currently subject to EU rules** . The ~~MHRA will rely on~~ **UK and EU have however agreed to** the **Windsor**

**Framework which fundamentally changes** ~~Human Medicines Regulations 2012 (SI 2012 / 1916) (as amended), or~~ the ~~HMR, as~~ **existing system under** the ~~basis for~~ **Northern Ireland Protocol, including with respect to the** ~~regulating~~ **regulation** ~~medicines. The HMR has incorporated into the domestic law~~ of ~~the body of European Union law instruments governing~~ medicinal products ~~that pre- existed prior to~~ **in the UK Once implemented, the changes introduced by the Windsor Framework will see the MHRA be responsible for approving all medicinal products destined for the UK market (i. e., GB and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. In addition, foreign regulatory authorities may change** ~~the~~ **their** ~~United Kingdom~~ **approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission** ' s ~~withdrawal from~~ **proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by** the European **Parliament** ~~Union. Any delay in obtaining, or an~~ **and European Council and** ~~inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in~~ the ~~87United Kingdom for our product candidates~~ **proposals may therefore be substantially revised before adoption** , which ~~could~~ **is not anticipated before early 2026. The revisions may however have a** ~~significantly~~ **significant impact on the pharmaceutical industry** and ~~materially harm~~ our business **in the long term** . We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets (such as the ongoing conflict between Ukraine and Russia); compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States. Even if we, or any collaborators we may have, obtain marketing approvals for any of our product candidates, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue. Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post- approval clinical data, labeling, advertising, and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post- marketing testing and surveillance to monitor the safety or efficacy of the medicine **. Further, our ability to develop and market new drug products may be impacted by ongoing litigation challenging the FDA' s approval of mifepristone. Specifically, on April 7, 2023, the U. S. District Court for the Northern District of Texas stayed the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various conditions adopted under a REMS. In reaching that decision, the district court made a number of findings that may negatively impact the development, approval and distribution of drug products in the U. S. Among other determinations, the district court held that plaintiffs were likely to prevail in their claim that FDA had acted arbitrarily and capriciously in approving mifepristone without sufficiently considering evidence bearing on whether the drug was safe to use under the conditions identified in its labeling. Further, the district court read the standing requirements governing litigation in federal court as permitting a plaintiff to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS based on a showing that the plaintiff or its members would be harmed to the extent that FDA' s drug approval decision effectively compelled the plaintiffs to provide care for patients suffering adverse events caused by a given drug. On April 12, 2023, the district court decision was stayed, in part, by the U. S. Court of Appeals for the Fifth Circuit. Thereafter, on April 21, 2023, the U. S. Supreme Court entered a stay of the district court' s decision, in its entirety, pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit and the disposition of any petition for a writ of certiorari to or the Supreme Court. The Court of Appeals for the Fifth Circuit held oral argument in the case on May 17, 2023 and, on August 16, 2023, issued its decision. The court declined to order the removal of mifepristone from the market, finding that a challenge to the FDA' s initial approval in 2000 is barred by the statute of limitations. But the court did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that FDA authorized in 2016 and 2021 were arbitrary and capricious. On September 8, 2023, the Justice Department and a manufacturer of mifepristone filed petitions for a writ of certiorari, requesting that asked the U. S. Supreme Court to review the appeals court decision. On December 13, 2023, the Supreme Court granted these petitions for writ of certiorari for the appeals court decision** . Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more of our product candidates, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post- approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post- approval regulations may have a negative effect on our business, operating results, financial condition,

and prospects. Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U. S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. **In addition** ~~If a prolonged government shutdown occurs~~ , **disruptions may result from events similar** ~~it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future 88government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. Separately, in response~~ to the COVID- 19 pandemic **. During the COVID- 19 pandemic** , a number of companies announced **receipt of** ~~in 2020 and 2021 that they had received~~ complete response letters due to the FDA' s inability to complete required inspections for their applications. **In** ~~As of May 26, 2021,~~ the **event** ~~FDA noted it was continuing to ensure timely reviews~~ of **a similar public health emergency** ~~applications for medical products during the ongoing COVID- 19 pandemic~~ in **the future** ~~line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However~~ , the FDA may not be able to continue its current pace and review timelines could be extended ~~, thus the FDA may be unable to complete such required inspections during the review period~~ . Regulatory authorities outside the ~~U. S.~~ **United States facing similar circumstances** may **adopt similar restrictions or other policy measures in response to a similar public health emergency and may also** experience delays in their regulatory activities. ~~If~~ **Accordingly, if** a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets. ~~Any~~ **Even if our** product ~~candidate~~ **candidates receive regulatory** ~~for which we obtain marketing~~ approval ~~could~~ **, they will** be subject to **significant post-** ~~restrictions or withdrawal from the market~~ **marketing** ~~, and we may be subject to substantial penalties if we fail to comply with~~ regulatory requirements ~~or if we experience unanticipated problems with our medicines, when~~ and **oversight** ~~if any of them are approved~~ . **Any** ~~The FDA and other~~ regulatory ~~agencies closely~~ **approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and ongoing surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations** ~~regulate~~ **related** ~~the~~ **to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome** post- approval **study or risk management requirements and regulatory inspection. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, EMA or foreign regulatory authorities approve our product candidates, the manufacturing processes, labelling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-** marketing **information** and ~~promotion of medicines to ensure~~ **reports, registration, as well as ongoing compliance with cGMPs and good clinical practices (GCP) for any clinical trials** that ~~they~~ **we conduct post- approval. In addition, manufacturers of drug products and their facilities** are **subject to continual review** ~~marketed only for the approved indications~~ and ~~in accordance with~~ **periodic, unannounced inspections by** the ~~provisions of the approved labeling. The~~ FDA **, EMA** and other regulatory ~~agencies impose stringent restrictions on~~ **authorities for compliance with cGMP regulations and standards. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug** ~~manufacturers~~ **manufacturing establishments are subject to registration** ~~' communications regarding off- label use,~~ and **listing requirements even** if **a drug** ~~we do not market our~~ **or** ~~medicines~~ **biologic undergoes further manufacture, preparation, propagation, compounding,** ~~for~~ **or processing at a separate establishment outside** ~~their~~ **the U. S. prior** ~~approved indications, we may be subject~~ to ~~enforcement action~~ **being imported** ~~for~~ **or offered** ~~off- label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Product, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or~~ **for import into the U** ~~allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws~~ . ~~In addition, later~~ **S. If we or a regulatory authority** ~~discovery~~ **discover** ~~of~~ previously unknown problems with **a product, such as adverse events of unanticipated severity** ~~our~~ **or** ~~medicines~~ **frequency** , **or problems with the facilities where the product is** ~~manufacturers~~ **manufactured** , ~~or~~ **a regulatory authority may impose restrictions on that product, the** manufacturing **facility** ~~processes,~~ or **us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition,**

failure to comply with **FDA, EMA and other comparable foreign** regulatory requirements ~~,~~ may ~~yield various results~~ **subject our company to administrative or judicially imposed sanctions** , including: ~~●~~ **• delays in or the rejection of product approvals; •** restrictions on ~~such medicines, manufacturers, or~~ **our** ~~manufacturing processes~~ **ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials** ; ~~●~~ **•** restrictions on the ~~labeling~~ **products, manufacturers** or **manufacturing process** ~~marketing of a medicine~~ ; **•** ~~● restrictions on the distribution or use of a medicine; ● requirements to conduct post- marketing clinical trials; ● receipt of~~ warning or untitled letters; ~~●~~ **• civil and criminal penalties; • injunctions; • suspension or** withdrawal of **regulatory** ~~the medicines from the market; ● refusal to approve pending applications or supplements to approved applications that we submit; ● recall of medicines; ● fines, restitution, or disgorgement of profits or revenue; 89 ● suspension or withdrawal of marketing~~ approvals; ~~●~~ **• product seizures, detentions or import bans; • voluntary or mandatory product recalls and publicity requirements; • total or partial** suspension of ~~any ongoing~~ **production; • imposition of restrictions on operations, including costly new manufacturing requirements; • revisions to the labelling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings; • imposition of a REMS, which may include distribution or use restrictions; and • requirements to conduct additional post- market** clinical trials ~~; ● refusal~~ to ~~permit~~ **assess** the **safety** ~~import or export~~ of ~~our medicines; ●~~ **the product. The FDA strictly regulates marketing, labeling, advertising, and promotion of** ~~product~~ **products** ~~seizure; that are placed on the U. S. market,~~ and ~~● injunctions or~~ **the relevant foreign regulatory agencies do the same in** ~~the~~ **their** ~~imposition~~ **respective jurisdictions. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of** ~~of~~ **off** ~~civil or criminal penalties~~ **- label uses and a company that is found to have improperly promoted off- label uses may be subject to significant liability** . ~~Any~~ **The FDA, EMA and other regulatory authorities' policies may change and additional** government **regulations may be enacted that** ~~investigation of alleged violations of law~~ could **prevent, limit or delay regulatory approval** ~~require us to expend significant time and resources in response and could generate negative publicity. The occurrence~~ of **our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U. S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose** any **marketing approval that we** ~~event or penalty described above~~ may ~~inhibit~~ **have obtained and we may not achieve** ~~our~~ **or sustain profitability** ~~ability to commercialize any product candidates we develop and adversely affect our business, financial condition, results of operations, and prospects~~ . Our relationships with healthcare providers, physicians, and third- party payors will be subject to applicable anti- kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings. Healthcare providers, physicians, and third- party payors play a primary role in the recommendation and prescription of any of our product candidates for which we obtain marketing approval. Our future arrangements with third- party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following: ~~●~~ **•** the federal healthcare anti- kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid; ~~●~~ **•** the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per- claim penalties; ~~●~~ **•** the federal Health Insurance Portability and Accountability Act of 1996, as further amended by the Health Information Technology for Economic and Clinical Health Act, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses, and health care providers; ~~●~~ **•** the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services; ~~●~~ **•** the federal transparency requirements under the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians, other ~~90healthcare~~ **healthcare** providers and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations; and ~~●~~ **•** analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third- party payors, including private insurers, and certain state laws that require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and

Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti- bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician' s employer, his or her competent professional organization, and / or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Enacted and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products. ~~91In~~ **In** March 2010, President Obama signed into law the ~~Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively the "~~ ACA ~~")~~. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $ 1. 2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation' s automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2 % per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act (the " CARES Act "). **Under current** ~~Pursuant to subsequent~~ legislation, ~~however, these~~ -- **the actual reductions in Medicare payments may vary up to 4 %. The Consolidated Appropriations Act (the " CAA "), which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the CAA delays the 4 % Statutory Pay- As- You- Go Act of 2010 (PAYGO) sequester for two years, through the end of calendar year 2024. Triggered by the enactment of the American Rescue Plan Act of 2021, the 4 % cut to the Medicare program would have taken effect in January 2023. The CAA' s health care offset title includes Section 4163, which extends the 2 % Budget Control Act of 2011** Medicare sequester **for six months into fiscal year 2032 and lowers the payment** ~~reductions~~ **reduction percentages in fiscal** ~~were suspended and reduced through the end of June 2022, with the full 2 % cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five~~ years **2030** ~~. These laws may result in additional reductions in Medicare~~ and **2031** ~~other healthcare funding and otherwise affect the prices we may obtain for any of our products or product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used~~. Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts for Jobs Act ~~, or TCJA,~~ in 2017, Congress repealed the " individual mandate. " The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. ~~Further, on December 14, 2018, a U. S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well.~~ In June 2021, the U. S. Supreme Court dismissed ~~this action after finding that~~ the **most recent judicial** ~~plaintiffs did not have standing to~~ challenge **to the ACA brought by several states without specifically ruling on** the constitutionality of the ~~ACA~~ **statute**. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and

strengthen that access. Under this Order, federal agencies are directed to re- examine: policies that undermine protections for people with pre- existing conditions ~~, including complications related to COVID- 19~~ ; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. ~~This Executive Order also directed the U. S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID- 19 pandemic.~~ The prices of prescription pharmaceuticals in the United States and foreign jurisdictions is subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed. The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U. S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician- administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, **the Centers for Medicare & Medicaid Services (“** CMS **”)** issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to ~~92incorporate~~ -- **incorporate** value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence- based care. In addition, in October 2020, **Department of Health and Human Services (“** HHS **”)** and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program ~~, or~~ **(“** SIP ~~,~~ **”)** to import certain prescription drugs from Canada into the United States. ~~The final rule is currently~~ **That regulation was challenged in a lawsuit by** the ~~subject~~ **Pharmaceutical Research and Manufacturers** of ~~ongoing litigation,~~ **America (“ PhRMA ”)** but ~~at least six~~ **the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Nine** states ( ~~Vermont,~~ Colorado, Florida, Maine **, New Hampshire** , New Mexico, **North Dakota, Texas, Vermont** and **Wisconsin** ~~New Hampshire~~ ) have passed laws allowing for the importation of drugs from Canada ~~with~~ **. Certain of** ~~the~~ **these** ~~intent of developing SIPs for review~~ **states have submitted Section 804 Importation Program proposals** and **are awaiting FDA** approval ~~by~~ **. On January 5, 2023,** the FDA **approved Florida’ s plan for Canadian drug importation** . Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The **final** ~~implementation of the~~ rule **would also eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point- of- sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but** has been delayed by **Congress** ~~the Infrastructure Investment and Jobs Act~~ to January 1, ~~2026~~ - **2032** ~~in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point- of- sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which has been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act~~ . On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs ~~the Department of Health and Human Services, or~~ HHS ~~,~~ to create a plan within 45 days to combat “ excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging. ” On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments. **On** ~~More recently, on~~ August 16, 2022, the ~~Inflation Reduction Act of 2022, or~~ IRA ~~,~~ was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in ~~2023~~ **2025** ); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of ~~the Department of Health and Human Services (~~ HHS ~~)~~ to implement many of these provisions through guidance, as opposed to regulation, for the initial years. Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single- source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high- cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further

heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated " maximum fair price " under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out- of- pocket drug costs at an estimated $ 4, 000 a year in 2024 and, thereafter beginning in 2025, at $ 2, 000 a year. ~~93At~~ **On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA' s Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U. S. Chamber of Commerce (the " Chamber "), Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. At** the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures **. In addition, in some countries, including member states of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take a significant amount of time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low- priced and high- priced member states, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product and / or our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or government authorities may lead to further pressure on the prices or reimbursement levels. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the commercial launch of our product and / or product candidates could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a material adverse effect on our business** . Our employees, principal investigators, consultants, and commercial partners may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants, and partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions. Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs. We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. The Foreign Corrupt Practices Act (" FCPA ") prohibits any U. S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also

obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti- bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be ~~94improper~~ -- **improper** payments to government officials and have led to FCPA enforcement actions. Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non- U. S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U. S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long- term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U. S. exchanges for violations of the FCPA' s accounting provisions. We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations. We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally- identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the U. S., EU and UK. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects. There are numerous U. S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to **the Health Insurance Portability and Accountability Act of 1996 (“** HIPAA **”)** establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future. If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems. In 2018, California passed into law the California Consumer Privacy Act (the “ CCPA ”), which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA' s requirements are similar to those found in the General Data Protection Regulation (the “ GDPR ”), including requiring businesses to provide notice to data subjects regarding the information collected about ~~95them~~ -- **them** and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt- out of “ sales ” of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act (the “ CPRA ”), which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR- like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition **to California** , **at least eleven** other states ~~, including Virginia, Colorado, Utah, and Connecticut already~~

have passed ~~state~~ **comprehensive** privacy laws **similar to the CCPA and CPRA** . **These** ~~Virginia' s privacy law~~ **laws** ~~also went into~~ **are either in** effect **or** ~~on January 1, 2023, and the laws in the other three states~~ will go into effect ~~later in~~ **sometime before the end of 2026. Like the CCPA and CPRA,** ~~the~~ **these** ~~year~~ **laws create obligations related to the processing of personal information, as well as special obligations for the processing of " sensitive " data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2023 legislative sessions that will go into effect in 2024 and beyond, including New Hampshire and New Jersey** . Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law **. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data and additional states (including Vermont) are considering such legislation for 2024** . These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. Similar to the laws in the U. S., there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area (" EEA "), and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross- border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and / or fines of up to 20 million Euros or up to 4 % of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill. The GDPR places restrictions on the cross- border transfer of personal data from the EU to countries that have not been found by the EC to offer adequate data protection legislation, such as the U. S. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union (the " CJEU ") invalidated the EU- U. S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U. S. The CJEU decision also drew into question the long- term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U. S. While we were not self- certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the U. S. generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners. ~~Additionally~~ **Following the CJEU decision** , in October 2022, President ~~Joe~~ Biden signed an executive order to implement the EU- U. S. Data Privacy Framework, which would serve as a replacement to the EU- US Privacy Shield. The EC initiated the process to adopt an adequacy decision for the EU- US Data Privacy Framework in December 2022 ~~. It is unclear if~~ **, and has now adopted** ~~and~~ **an** ~~when~~ **adequacy decision to permit data transfers from** the **EU to the US going forward. This development permits data transfers at this point under this** ~~framework~~ **Framework** ~~will be finalized~~ and ~~whether it will be~~ **more broadly has made international data transfers more straightforward, but these provisions are being** challenged in court. ~~The uncertainty around this issue may further impact our business operations in the EU.~~ Following ~~the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. As with other issues related to~~ Brexit, there are open questions about how personal data will be protected in the ~~UK~~ **U. K.** and whether personal information can transfer from the EU to the ~~UK~~ **U** . ~~It~~ **K. Following the withdrawal of the U. K. from the EU, the U. K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U. K. and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the U. K. that " implements " and complements the GDPR has achieved Royal Assent on May 23, 2018 and** is ~~still~~ **now effective in the U. K., it is** unclear whether transfer of data from the ~~European Economic Area, or~~ EEA ~~,~~ to the ~~UK~~ **U. K.** will remain lawful under **the** GDPR. The ~~United Kingdom~~ **U. K.** government has already determined that it considers all European Union **27** and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the ~~United Kingdom~~ **U. K.** to the **EU** ~~European Union~~ / EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the ~~UK~~ **U. K.** as being " essentially adequate " for purposes of data transfer from the EU to the ~~UK~~ **U. K.** , although this decision may be re-evaluated in the future. **The UK and the United States also have agreed on a framework for personal data to be transferred between the UK and the United States, called the U. K.- U. S. Data Bridge. The U. K.- U. S. Data Bridge may be challenged in the future.** ~~96Beyond~~ -- **Beyond** GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions. While we continue to address the implications of the recent changes to 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, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it

the potential for significant penalties if we are found to be non- compliant. Similarly, failure to comply with federal and state laws in the U. S. regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government- imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects. Risks Related to Employee Matters, Managing Growth, Public Health and Information ~~TechnologyOur~~ --- **Technology Our** future success depends on our ability to attract and retain key executives and to attract, retain, and motivate qualified personnel. We are highly dependent on the principal members of our management and scientific teams. Each of these individuals is employed " at will, " meaning we or the individual may terminate the employment relationship at any time. We do not maintain " key person " insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development, and commercialization objectives. ~~Additionally, we are actively trying to recruit a candidate for the role of Chief Scientific Officer. Any inability to fill this position in an expedient manner may have a material adverse effect on our business.~~ Recruiting and retaining qualified scientific, clinical, manufacturing, and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. In addition, our ability to recruit and retain qualified personnel could be impacted by other factors, such as remote or hybrid working arrangements, which could impact employees' productivity and morale, as well as any failure to succeed in preclinical or clinical trials. The inability to recruit or the loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives. We face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, ~~including the COVID- 19 pandemic,~~ which could significantly disrupt our operations, impact our financial results or otherwise adversely impact our business. Significant outbreaks of contagious diseases, and other adverse public health developments, could have a material impact on our business operations and operating results. Any public health crises ~~, including the COVID- 19 pandemic,~~ or related healthcare staffing shortages, supply chain restrictions, or other issues, may result in disruptions that could adversely impact our operations, research and development, including preclinical studies, clinical trials and manufacturing activities, including: ~~• 97 •~~ delays or disruptions in clinical trials that we may be conducting, including patient screening, patient enrollment, patient dosing, clinical trial site activation, and study monitoring; ~~•~~ • delays or disruptions in preclinical experiments and IND- and clinical trial application- enabling studies due to restrictions related to our staff being on site; ~~•~~ • interruption or delays in the operations of the FDA, EMA and comparable foreign regulatory agencies; ~~•~~ • interruption of, or delays in, receiving, supplies of drug substance and drug product from our CMOs or delays or disruptions in our pre- clinical experiments or clinical trials performed by CROs due to staffing shortages, production and research slowdowns or stoppages and disruptions in delivery systems or research; ~~•~~ • limitations imposed on our business operations by local, state, or federal authorities to address such pandemics or similar public health crises could impact our ability to conduct preclinical or clinical activities, including conducting IND- and ~~CTA~~ **clinical trial application** - enabling studies or our ability to select future development candidates; and ~~•~~ • business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations, cyber security and data accessibility, or communication or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors. Our clinical trials for ~~EDIT~~ **reni** - ~~301~~ **cel** , as well as timely completion of preclinical activities and initiation of planned clinical trials for other product candidates, is dependent upon the availability of, for example, preclinical and clinical trial sites, researchers and investigators, regulatory agency personnel, and materials, which may be adversely affected by a public health crisis and related government responses ~~. A resurgence or other negative developments relating to the COVID- 19 pandemic may require us to restrict access to our offices and laboratories for an extended period of time, or to pause or suspend preclinical research and our clinical trials; and, further, may cause delays or restrictions at healthcare facilities or disrupt our manufacturing and supply chain or those of our third- party suppliers and manufacturers. In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile in part as a result of the COVID- 19 pandemic. As a result, we may face difficulties raising additional capital through sales of our common stock or such sales may be on unfavorable terms~~ . We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage, however, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business and our results of operation and financial condition. We expect to expand our manufacturing, clinical, development, and regulatory capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. We expect growth in the number of our employees and the scope of our operations, particularly in the areas of manufacturing, clinical development, drug development, and regulatory affairs, and, if any product candidates receive marketing approval, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we

may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. ~~98Security~~ -- **Security** breaches and other disruptions to our information technology structure could compromise our information, disrupt our business and expose us to liability, which would cause our business and reputation to suffer. In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, as well as our proprietary business information and that of our suppliers and business partners, employee data, and we may collect personally identifiable information of clinical trial participants in connection with clinical trials. We also rely to a large extent on information technology systems to operate our business, including our financial systems. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. Similarly, our business partners and other third- party providers possess certain elements of our sensitive data. The secure maintenance of this information is important to our operations and business strategy. Despite our security measures, our information technology infrastructure (and those of our partners, vendors and third- party providers) may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. We, our partners, vendors, and other third- party providers could be susceptible to third party attacks on our, and their, information security systems, which attacks are of ever- increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. **We** ~~Furthermore, we~~ have implemented a hybrid work model, which may place our information technology infrastructure and data at increased risk as more of our employees work from home utilizing network connections outside our premises. **Additionally, sensitive data could be leaked, disclosed, or revealed as a result of or in connection with our employees', vendors' or partners' use of generative AI technologies.** We have invested in information technology security measures and the protection of confidential and sensitive information, but there can be no assurance that our efforts will prevent system failures, accidents or security breaches. While we believe we have not experienced any such material system failure, accident or security breach to date, any such event may substantially impair our ability to operate our business and would compromise our, and their, networks and the information stored could be accessed, publicly disclosed, lost, or stolen. In addition, if a ransomware attack or other cybersecurity incident occurs, either internally or at our vendors or third- party technology service providers, we could be prevented from accessing our data or systems, which may cause interruptions or delays in our business operations, cause us to incur remediation costs, subject us to demands to pay a ransom, or damage our reputation, regardless of whether we pay the ransom amount. Any such event, or other loss of information, could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation, any of which could adversely affect our business. Although we have general liability and cybersecurity insurance coverage, our insurance may not cover all claims, continue to be available on reasonable terms or be sufficient in amount to compensate us fully for potential significant losses; additionally, the insurer may disclaim coverage as to any claim. The successful assertion of one or more large claims against us that exceed or are not covered by our insurance coverage or changes in our insurance policies, including premium increases or the imposition of large deductible or co- insurance requirements, could materially harm our business, financial condition, results of operations and prospects. Risks Related to Our Common ~~StockThe~~ -- **Stock The** market price of our common stock may be volatile, which could result in substantial losses for our stockholders. Our stock price has been, and is likely to remain, volatile. For example, since January 1, ~~2021~~ **2022** , the trading price of our common stock on the Nasdaq Global Select Market has ranged from a low of $ ~~7~~ **6** . ~~71~~ **08** to a high of $ **27.** 99 ~~. 95~~ through January 31, ~~2023~~ **2024** . Some of the factors that may cause the market price of our common stock to fluctuate include: ~~●~~ • the success of existing or new competitive products or technologies; ~~●~~ • the timing and results of **our RUBY and EdiTHAL** clinical trials for ~~EDIT~~ **reni** - ~~301~~ **cel** and any preclinical studies and clinical trials of any other product candidates that we develop; ~~●~~ • commencement or termination of collaborations for our product development and research programs; ~~●~~ • failure or discontinuation of any of our product development and research programs; • ~~99 ●~~ results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors; ~~●~~ • developments or changing views regarding the use of genomic medicines, including those that involve genome editing; ~~●~~ • regulatory or legal developments in the United States and other countries; ~~●~~ • developments or disputes concerning patent applications, issued patents, or other proprietary rights; ~~●~~ • the recruitment or departure of key personnel; ~~●~~ • the level of expenses related to any of our research programs, clinical development programs, or product candidates that we develop; ~~●~~ • the results of our efforts to develop additional product candidates or products; ~~●~~ • actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts; ~~●~~ • announcement or expectation of additional financing efforts; ~~●~~ • sales of our common stock by us, our insiders, or other stockholders; ~~●~~ • variations in our financial results or those of companies that are perceived to be similar to us; ~~●~~ • changes in estimates or recommendations by securities analysts, if any, that cover our stock; ~~●~~ • changes in the structure of healthcare payment systems; ~~●~~ • market conditions in the pharmaceutical and biotechnology sectors; ~~●~~ • general economic, industry, and market conditions; and ~~●~~ • the other factors described in this " Risk Factors " section. **The** ~~In recent years, the~~ stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management' s attention and resources from our business. If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock and trading volume could decline. The trading market for our common stock depends, in part, on the research and reports that

industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fail to regularly publish reports on us, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. ~~100Future~~ --- **Future** sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of stockholders and could cause our stock price to fall. We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. In addition, sales of a significant number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. We have registered substantially all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline. We incur costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices. As a public company we ~~have incurred~~ --- **incur**, and will continue to incur, significant legal, accounting, and other expenses ~~that we did not incur as a private company~~. The Sarbanes- Oxley Act of 2002, the Dodd- Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. **Our** ~~We have had to hire additional accounting, finance, and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our~~ management and other personnel devote a substantial amount of time towards maintaining compliance with these requirements. These requirements increase our legal and financial compliance costs and make some activities more time- consuming and costly. We have broad discretion in the use of our cash reserves and may not use them effectively **, including that we may be exposed to liquidity issues and other systemic financial risks at the financial institutions holding our cash and cash equivalents**. Our management has broad discretion to use our cash reserves and could use our cash reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline, and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value **. A portion of our cash may be held by financial institutions that may have been, or could in the future become, exposed to liquidity issues, bank failures or other systemic financial risks. Our uninsured cash deposits with such financial institutions may be at risk in the event they experience liquidity problems or other financial losses. We assess our banking relationships as we believe necessary or appropriate, but our business, our business partners, or industry as a whole may be adversely impacted in ways that we cannot predict at this time, including our ability to access cash in amounts adequate to finance or capitalize our current and / or projected business operations could be significantly impaired by factors that affect the financial institutions with which we have banking relationships, and in turn, us. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements (including cash management arrangements), disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. In addition, our vendors, such as our CMOs, CROs or business partners, may be susceptible to the foregoing liquidity or other financial risks and factors, which could, in turn, have a material adverse effect on our current and / or projected business operations and results of operations and financial condition**. We do not expect to pay any dividends for the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investments. We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be stockholders' sole source of gain for the foreseeable future. Provisions in our restated certificate of incorporation and amended and restated bylaws or Delaware law might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock. Provisions in our restated certificate of incorporation and amended and restated bylaws or Delaware law may ~~101discourage~~ --- **discourage**, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. These provisions include: limitations on the removal of directors; a classified board of directors so that not all members of our board of directors are elected at one time; advance notice requirements for stockholder proposals and nominations; the inability of stockholders to act by written consent or to call special meetings; the requirement that at least 75 % of the votes cast by all our stockholders approve the amendment or repeal of certain provisions of our amended and restated bylaws or restated certificate of incorporation; the ability of our board of directors to make, alter, or repeal our amended and restated bylaws; and the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock

ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors. In addition, Section 203 of the General Corporation Law of the State of Delaware prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15 % of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. The existence of the foregoing provisions could deter potential acquirers of our company, thereby reducing the likelihood that our stockholders could receive a premium for their shares of common stock in an acquisition. Our restated certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors and officers. Our restated certificate of incorporation provides that, unless our board of directors otherwise determines, the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to our company or our stockholders, any action asserting a claim against us or any of our directors or officers arising pursuant to any provision of the General Corporation Law of the State of Delaware or our restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us or any of our directors or officers governed by the internal affairs doctrine. This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors or officers, which may discourage such lawsuits against us and our directors and officers. This exclusive forum provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act of 1934, which provides for exclusive jurisdiction of the federal courts. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act of 1933, as amended (the " Securities Act "), inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder; provided, that with respect to claims under the Securities Act, our stockholders will not be deemed to have ~~102~~ **waived our compliance with the federal securities laws and the rules and regulations thereunder.**