Risk Factors Comparison 2023-03-29 to 2022-03-04 Form: 10-K

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An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Annual Report on Form 10- K, including our financial statements and related notes hereto, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment. We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have incurred net losses in each year since our inception in 1992, including net losses from continuing operations of $ ~~562~~ **266** . 6 million for the year ended December 31, ~~2021~~ **2022** . As of December 31, ~~2021~~ **2022** , we had an accumulated deficit of $ 3. ~~72~~ **99** billion. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to generate revenues. We have devoted significant financial resources to research and development, including our clinical and preclinical development activities, which we expect to ~~continue for~~ **directionally decrease as we focus on bringing our therapies to patients in** the ~~foreseeable future~~ **commercial setting** . To date, we have financed our operations primarily through the sale of equity securities **and priority review vouchers,** and, to a lesser extent, through collaboration agreements and grants from governmental agencies and charitable foundations. We ~~have~~ **did** not ~~generated~~ - **generate** material revenues from the sale of **ZYNTEGLO** ~~beti- cel~~ in the European Union ~~,~~ and **only recently** ~~we do not expect to generate meaningful product revenues in the foreseeable future until we obtain marketing approval for products in the United States and following any potential commercial launch~~ **launched ZYNTEGLO and SKYSONA in the US** . **Our** ~~Following marketing approval, our~~ future revenues will depend upon the size of any markets in which our ~~potential~~ products **and product candidates** have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third- party payers and adequate market share for our potential products in those markets. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we: • continue ~~our research and clinical development~~ **to invest in lovo- cel in anticipation** of **the submission of** our ~~product candidates~~ **BLA and subsequent FDA review** ; • ~~establish~~ **grow our** capabilities to support our commercialization efforts **for ZYNTEGLO and SKYSONA** , including **continuing to** ~~establishing~~ --- **establish** a sales, marketing and distribution infrastructure in the United States ~~, and to commercialize products for which we may obtain marketing approval~~ ; • obtain, build and expand manufacturing capacity, including capacity at third- party manufacturers; • **attract and retain skilled personnel; •** initiate additional research, preclinical, clinical or other programs as we seek to identify and validate additional product candidates; • acquire or in- license other product candidates and technologies; • maintain, protect and expand our intellectual property portfolio; ~~• attract and retain skilled personnel;~~ and • experience any delays or encounter issues with any of the above. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline. There is substantial doubt regarding our ability to continue as a going concern. We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our **commercial programs,** product development efforts or other operations ~~. We are currently advancing our late- stage programs in severe genetic diseases through clinical development~~ . Developing and commercializing gene therapy products is expensive, and we do not expect to generate meaningful product revenues in the foreseeable future ~~until we obtain marketing approval for products in the United States and following any potential commercial launch. As of December 31, 2021, our cash, cash equivalents and marketable securities were $ 396. 6 million. As of completion of the separation, we had restricted cash, cash and cash equivalents, and marketable securities of approximately $ 507. 2 million~~ . Based on our current business plan **as of the date of our consolidated financial statements appearing elsewhere in this Annual Report on Form 10- K** , there is substantial doubt regarding our ability to continue as a going concern ~~for a period~~ **. See Part II, Item 7. " Management' s Discussion and Analysis** of ~~one year after the date that our financial~~ **Financial** ~~statements~~ **Condition and Results of Operations — Liquidity and Capital Resources " of this Annual Report on Form 10- K for a discussion of our expected cash runway both including our restricted cash of $ 45. 4 million and excluding this restricted cash. Our restricted cash is currently unavailable for use, and there is no assurance as to when** ~~for~~ **or** ~~the year ended December 31~~ **if our restricted cash will become available for use. Furthermore** , ~~2021 are issued~~ **pursuant to the terms of certain agreements we have in place, we could be required to further increase our restricted cash due, in part, to recent concerns related to the stability of the banking sector, which would consequently reduce the amount of cash available to fund our operations. Accordingly, we will need to raise additional funding in order to execute on our current business plans and strategy, including prior to becoming profitable** . Our fundraising efforts to raise additional funding may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our ~~potential~~ products ~~following marketing approval if and when obtained~~ . In addition, we cannot guarantee that financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment

obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. **Moreover, as a result of recent volatile market conditions, the cost and availability of capital has been and may continue to be adversely affected. Concern about the stability of the banking sector has generally led many lenders and institutional investors to reduce, and in some cases, cease to provide credit to businesses and consumers. Continued turbulence in the U. S. market and economy may adversely affect our liquidity and financial condition, including our ability to access the capital markets to meet liquidity needs. In addition, we maintain the majority of our cash and cash equivalents in accounts with major financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position.** If we are unable to obtain funding on a timely basis, or if revenues from collaboration arrangements or product sales are less than we have projected, we may be required to further revise our business plan and strategy, which may result in us significantly curtailing, delaying or discontinuing one or more of our research or development programs or the commercialization of any product candidates or may result in our being unable to expand our operations or otherwise capitalize on our business opportunities. As a result, our business, financial condition and results of operations could be materially affected. ~~Our future success depends on our ability to retain key employees and to attract, retain and motivate qualified personnel. We are highly dependent on our executive team and key employees, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are " at- will " employees. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and our turnover rate has been high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, our financial condition and recent delays in our late- stage programs have made it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.~~ Insertional oncogenesis is a **significant** risk of gene therapies using viral vectors that can integrate into the genome ~~, and several patients with CALD treated with eli- cel in our clinical studies have been diagnosed with MDS likely mediated by Lenti- D LVV insertion~~ . ~~These~~ **Any such adverse** events may require us to halt or delay further clinical development of our product candidates ~~, such as eli- cel,~~ or to suspend or cease commercialization following marketing approval, and the commercial potential of our **products and** product candidates may be materially and negatively impacted **. Adverse events or other undesirable side effects caused by our product or product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay, denial or withdrawal of regulatory approval by the FDA or other comparable foreign regulatory authorities** . A potentially significant risk in any gene therapy product using viral vectors that can integrate into the genome is that the vector will insert in or near cancer- causing genes, leading to the proliferation of certain cellular clones that ~~can~~ **could** cause cancer in the patient, known as insertional oncogenesis. ~~Several~~ **For instance, three** patients with CALD treated with eli- cel **(now SKYSONA)** in our clinical studies have been diagnosed with **myelodysplastic syndrome (“** MDS **”)** likely mediated by Lenti- D LVV insertion ~~, and as a result, the FDA placed our clinical studies of eli- cel on clinical hold. On February 23, 2022, the FDA notified us that the clinical hold on the eli- cel program would remain in place, and requested additional information about safety events and monitoring in the eli- cel clinical program~~ . We ~~have no assurances as to whether we will successfully resolve the clinical hold. In addition, we~~ cannot make assurances that additional patients treated with **SKYSONA** ~~eli- cel~~ , **ZYNTEGLO** ~~beti- cel~~ or lovo- cel in the clinical or commercial setting ~~will not exhibit clonal predominance in the future, or that additional patients~~ will not be diagnosed with MDS, leukemia or lymphoma. **Moreover, in December 2021, the FDA placed the lovo- cel clinical development program under a partial clinical hold for patients under the age of 18.** ~~There~~ -- **The** ~~is~~ **hold related to a case persistent anemia in an adolescent patient with two α- globin gene deletions (− α3. 7 / − α3. 7),** also **known as alpha- thalassemia trait, who was treated with lovo- cel. In December 2022,** the ~~potential risk~~ **FDA lifted its partial clinical hold for patients under the age** of ~~delayed~~ **18 in studies evaluating lovo- cel for SCD. Notwithstanding the lifting of this partial clinical hold, additional** adverse events **or new data or analyses regarding previously reported events may indicate significant safety issues, and the FDA could potentially impose or reimpose a clinical hold in the future on studies evaluating lovo- cel. Moreover, laboratory results** following ~~exposure to~~ gene therapy ~~products due~~ **can be difficult** to ~~persistent biological activity of the genetic material~~ **interpret resulting in different or changing diagnoses by treating physicians.** ~~or~~ **For instance, on January 31, 2023, we received a physician diagnosis of MDS in a patient treated with lovo- cel, in response to lab results obtained through routine monitoring of** ~~other~~ -- **the** ~~components of products used~~ **same adolescent patient with** ~~to~~ **two** ~~carry~~ **α- globin gene deletions subject to** the ~~genetic material~~ **partial clinical hold noted above** . ~~The~~ **Consistent with established safety protocols, the information was reviewed by an independent Data Monitoring Committee which concluded that available evidence did not support a diagnosis of MDS and additional data would be needed to confirm such diagnosis, and that lovo- cel clinical studies should continue. Test results received since the investigator' s initial report (including integration site**

analysis) demonstrated no evidence of insertional oncogenesis and the patient continues to be clinically stable and is not undergoing treatment for an MDS diagnosis. Study investigators and the FDA **have been informed and we will continue to monitor additional analyses** ~~has~~ **as** ~~stated that LVV possess characteristics that may pose high risks of delayed~~ **further test results are received. We maintain dialogue with the FDA and, from time to time, as required or requested by the FDA, update the FDA on additional** adverse events ~~. If any such adverse~~ **or new data or analyses regarding previously reported** events ~~occur~~ **. Furthermore** , **treatment with** ~~further advancement of our clinical studies could be halted or~~ **our products and** ~~delayed, we may not receive marketing approval for our~~ product candidates ~~, and we may be unable to commercialize any approved product. It is possible that upon occurrence or recurrence of any of these events, the FDA may place one or more of our programs on hold, impose requirements that result in delays for regulatory approval for one or more of our programs, require risk evaluation or mitigation strategies as a condition for regulatory approval, or may cause us to cease commercialization following the receipt of any marketing approval. If any of these were to occur, the commercial potential of our programs may be materially and negatively impacted. Furthermore, treatment with our potential products~~ involve chemotherapy or myeloablative treatments which can cause side effects or adverse events that may impact the perception of the potential benefits of our ~~potential~~ products **and product candidates** . For instance, MDS leading to acute myeloid leukemia is a known risk of certain myeloablative regimens. ~~Additionally~~ **Accordingly** , ~~beti~~ **it is possible that the events of MDS and acute myeloid leukemia previously reported in our HGB** - ~~cel~~ **206 clinical study were caused by underlying SCD** , **transplant procedure** ~~eli- cel~~ , ~~or~~ **and stress on the bone marrow following drug product infusion in connection with the** lovo- cel **treatment. Additionally** , the procedures associated with ~~their~~ -- **the** administration ~~,~~ or ~~with the~~ collection of ~~patients'~~ cells **for ZYNTEGLO, SKYSONA, or lovo- cel** , could potentially cause other adverse events that have not yet been predicted. The inclusion of patients with significant underlying medical problems in our clinical studies may result in deaths, or other adverse medical events, due to other therapies or medications that such patients may be using, or the progression of their disease. ~~For~~ **Moreover, patients treated with our therapies, including lovo- cel, have exhibited persistent oligoclonality, which we define as two consecutive** ~~instance~~ **instances of (i) any LVV insertion site observed at > = 10 % relative frequency** , **or (ii) two or more insertion sites observed at > = to 5 % relative frequency, as measured by integration site analysis. Based on our clinical protocols, we increase monitoring of patients who exhibit persistent oligoclonality. It is not clear at this time whether persistent oligoclonality represents an increased risk of developing MDS, leukemia, or lymphoma in the future, but** it **is a criterion used by the FDA to evaluate the safety of gene therapies over time. Additionally, there is the potential risk of other delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. The FDA has stated that LVVs possess characteristics that may pose high risks of delayed adverse events. If any such adverse events occur, including insertional oncogenesis, further advancement of our clinical studies could be halted or delayed, we may not receive marketing approval for our product candidates, and we may be unable to commercialize our approved products in the manner we expect, or at all. It** is possible that **upon occurrence or recurrence of any of** ~~the~~ **these** events **, the FDA may place one** ~~of MDS and acute myeloid leukemia previously reported in our~~ - **or** ~~HGB- 206 clinical study~~ **more of our programs on hold, impose requirements that result in delays for regulatory approval for one or more of our programs, require risk evaluation or mitigation strategies as a condition for regulatory approval, or may cause us to cease commercialization of our approved products. If any of these** were **to occur** ~~caused by lovo- cel~~ , ~~in combination with underlying SCD, transplant procedure, and stress on~~ the ~~bone marrow following drug product infusion~~ **commercial potential of our programs may be materially and negatively impacted** . Even if a product **candidate** such as lovo- cel ~~, eli- cel or beti- cel~~ is ultimately approved **and** , ~~such~~ **although ZYNTEGLO and SKYSONA have been approved by the FDA, serious** safety events may result in the product being removed from the market or its market opportunity being significantly reduced. **For instance, it is possible that as we commercialize our products or test our product candidates in larger, longer and more extensive clinical trials, or as use of these products and product candidates (if approved) becomes more widespread, illnesses, injuries, discomforts and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects (that may or may not be related to our products or product candidates) are only detectable after investigational products are tested in large- scale clinical trials or, in some cases, after they are made available to patients on a commercial scale following approval.** Other patients receiving our **products and** product candidates may develop **cancers, including** leukemia, lymphoma, or MDS in the future, which may negatively impact the commercial prospects of our **products and** product candidates **. We or others may later identify undesirable side effects or adverse events caused by such products, and a number of potentially significant negative consequences could result, including but not limited to: • regulatory authorities may suspend, limit or withdraw approvals of such product, or seek an injunction against its manufacture or distribution; • regulatory authorities may require additional warnings on the label, including " boxed " warnings, or issue safety alerts," Dear Healthcare Provider" or" Dear Doctor" letters, press releases or other communications containing warnings or other safety information about the product; • we may be required to change the way the product is administered or conduct additional clinical trials or post- marketing studies; • we may be required to create a risk evaluation and mitigation strategy, or REMS which could include elements to assure safe use, or a medication guide outlining the risks of such side effects for distribution to patients; • we may be subject to fines, injunctions or the imposition of criminal penalties; • we could be sued and held liable for harm caused to patients; and • our reputation may suffer** . Any of these events could impair our ability to develop or commercialize our **products and** product candidates, and their commercial potential may be materially and negatively impacted. ~~Risks related to commercialization~~ We **rely on** ~~have limited experience as~~ a **complex supply chain for SKYSONA** ~~commercial company and the marketing and sale of beti- cel~~ , **ZYNTEGLO** ~~eli- cel~~ , and lovo- cel following marketing approval, if and when.....- cel, and lovo- cel . The manufacture **, testing** and delivery of LVV and drug

products present significant challenges for us, and we may not be able to produce our vector and drug products at the quality, quantities, ~~locations~~ or timing needed to support our clinical programs and commercialization ~~following marketing approval if and when obtained. In addition, we may encounter challenges with engaging or coordinating with qualified treatment centers needed to support commercialization following marketing approval if and when obtained~~. We rely on third parties to manufacture the LVV and the drug product for ~~any~~ **ZYNTEGLO and SKYSONA, our two commercial products, and for our** clinical trials ~~that we conduct~~, **including the ongoing phase 3 clinical study evaluating the efficacy** and ~~we intend to rely on third~~ **safety of lovo- cel in the treatment of** ~~parties~~ **patients with SCD** ~~for the supply of LVV and drug product for commercialization following any marketing approval, if and when obtained~~. ~~We~~ **Although we continue to advance plans to make additional investment in manufacturing to expand capacity, we, to date,** have not secured all of the commercial- scale manufacturing capacity that we anticipate requiring for the commercialization of our therapies to meet our forecasts beyond the **first year of anticipated sales** ~~potential launch, if they should receive marketing approval~~. If we fail to secure adequate capacity to manufacture our drug products or LVV used in the manufacture of our drug products in accordance with our forecasts ~~beyond the potential launch of our therapies~~, we may be unable to execute on our ~~development and~~ commercialization plans on the timing that we expect, or at all. The manufacture of LVV and drug products is complex and requires significant expertise. Even with the relevant experience and expertise, manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling out and validating initial production, managing the transition from clinical manufacturing to manufacturing in the commercial setting, and ensuring that the product meets required specifications. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, ~~shortages~~ **scarcity** of qualified personnel, **shortages of any production raw materials** as well as compliance with strictly enforced federal, state and foreign regulations. We cannot make any assurances that these problems will not occur in the future, or that we will be able to resolve or address in a timely manner or with available funds problems that occur. Because of this complexity, transitioning production of either LVV or drug products to backup or second source manufacturing ~~, or to internal manufacturing capacity,~~ requires a lengthy technology transfer process **and regulatory review and approval, which often takes significant time** and may require additional significant financial expenditures. Furthermore, our cost of goods development is at an early stage. The actual cost to manufacture our LVV and drug products could be greater than we expect and could materially and adversely affect the commercial viability of **SKYSONA** ~~beti- cel~~, **ZYNTEGLO** ~~eli- cel~~, or lovo- cel. If we or such third- party manufacturers are unable to produce the necessary quantities of LVV and our drug products, or in compliance with GMP or other pertinent regulatory requirements, and within our planned time frame and cost parameters, the development and commercialization of our ~~potential~~ products **and product candidates** may be materially harmed, result in delays in our plans or increased capital expenditures. In addition **, we currently have only one drug product supplier for ZYNTEGLO and SKYSONA and one drug product supplier anticipated for commercial distribution for lovo- cel and, accordingly** , any significant disruption in our supplier relationships could harm our business. We source key materials from third parties, either directly through agreements with suppliers or indirectly through our manufacturers who have agreements with suppliers. There are a small number of suppliers for certain key materials that are used to manufacture **SKYSONA** ~~beti- cel~~ , **ZYNTEGLO** ~~eli- cel~~, and lovo- cel. Such suppliers may not sell these key materials to us or to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these key materials by our manufacturers, and we currently do not have agreements for the commercial supply for all of these key materials. Additionally, since the HSCs used as starting material for drug products have a limited window of stability following procurement from a patient, we ~~must~~ **have initially** ~~establish~~ **established** transduction facilities in ~~the~~ **areas which we believe can adequately service patients from** regions where we **are** ~~wish to commercialize~~ **commercializing SKYSONA** ~~beti- cel~~, **ZYNTEGLO** ~~eli- cel~~, and **where we anticipate commercializing** lovo- cel ~~following marketing approval~~, if and when ~~obtained~~ **approved** . ~~Establishment of~~ **However, we cannot ensure that** such facilities **will enable us to produce and deliver drug product in a timely manner; any issues with production and delivery of drug product could have a material adverse effect on our successful commercialization of our product and product candidates. Moreover, establishing additional facilities in appropriate regions** may be financially impractical or impeded by technical, quality, or regulatory issues related to these new sites and we may also run into technical or scientific issues related to transfer of our transduction process or other developmental issues that we may be unable to resolve in a timely manner or with available funds. **Changes in our manufacturing processes may cause delays in our clinical development and commercialization plans. The manufacturing processes for our LVV and our drug products are complex.** We **explore improvements to our manufacturing processes on a continual basis, as we evaluate clinical and manufacturing data and based on discussions with regulatory authorities. In some circumstances, changes in the manufacturing process may require us to perform additional comparability studies, collect additional data from patients, submit additional regulatory filings, or comply with additional requirements, which may lead to delays in our clinical development and commercialization plans. For instance, in our lovo- cel program, we plan to seek regulatory approval for drug product utilizing LVV manufactured using a scalable suspension manufacturing process using bioreactors, rather than an adherent cell tray manufacturing process, and drug product manufactured a commercial, rather than a clinical, manufacturing facility. Such transitions require regulatory review and approval including reaching agreement with the FDA on an acceptable comparability data package. Based on feedback recently received from the FDA and related questions regarding the sufficiency of such comparability data, we** have ~~no assurance as~~ **submitted a comprehensive data package to the FDA in effort to demonstrate comparability between the** ~~to~~ **two** ~~when~~ **processes, which the FDA is reviewing prior to the submission of the BLA. The FDA may require us to conduct additional clinical studies, collect additional data, develop additional assays, or modify product specifications relating to such comparability analysis prior to the FDA accepting BLA for filing or potentially approving the application which may delay or prevent our plans for commercialization. Any such requests or delays may**

have a material adverse effect on our forecasted timelines for approval of lovo- cel and may require substantial additional funds. We are evaluating plans to transition our drug product manufacturing ~~using cryopreserved apheresis starting material will be available, if ever. Our commercial strategy is to engage apheresis and transplant centers as qualified treatment centers for the collection of patient HSCs and infusion of the drug product once manufactured. To ensure that the qualified treatment centers are prepared to collect patient HSCs and to ship them to our transduction facilities in accordance with our specifications and regulatory requirements, we train and conduct quality assessments of each center as part of engagement. These qualified treatment centers are the first and last points on our complex supply chain to reach patients in the commercial setting. We may not be able to engage qualified treatment centers in all of the regions in our commercial launch strategy, or we may encounter other challenges or delays in engaging qualified treatment centers. We may fail to manage the logistics of collecting and shipping patient material to the manufacturing site and shipping the drug product back to the patient. Logistical and shipment delays and problems caused by us, our third- party vendors, and other factors not in our control, such as weather, could prevent or delay the manufacture of or delivery of drug product to patients. If our qualified treatment centers fail to perform satisfactorily, we may suffer reputational, operational, and business harm. We are required to maintain a complex chain of identity and chain of custody with respect to patient material as it moves through the manufacturing~~ process ~~, from the qualified treatment center to the transduction facility, and back to the patient. Failure to maintain chain of identity and chain of custody could result in adverse patient outcomes, loss of product or~~ **for** ~~regulatory action. We have limited sales and distribution experience and limited capabilities for marketing and market access. We expect to invest significant financial and management resources to establish these capabilities and infrastructure to support commercial operations following marketing approval if and when obtained. If we are unable to establish these commercial capabilities and infrastructure or to enter into agreements with third parties to market and sell our potential products, we may be unable to generate sufficient revenue to sustain our business. We have limited prior sales or distribution experience and limited capabilities for marketing and market access, and we did not generate meaningful product sales following the commercial launch of beti- cel following marketing approval in Europe. To successfully commercialize beti- cel, eli- cel, and~~ lovo- cel ~~following marketing~~ **, if** approval **is** ~~in the United States, if and when~~ obtained, ~~we~~ **to utilize cryopreserved apheresis patient starting material in order to expand the potential reach of our therapy and to provide manufacturing flexibility. Such changes to our drug manufacturing process** will **similarly require comparability and process validation data** ~~need to further develop these capabilities. We may need to expand our infrastructure~~ to support **such transition** ~~commercial operations in the United States, either on our own or with others. Commercializing an~~ **and** ~~autologous gene therapy is resource- intensive and has required~~ , **therefore** ~~and will continue to require , substantial investment in commercial capabilities. We are competing with companies that currently have extensive and well- funded marketing and sales operations. Without significant commercial experience as a company or the support of a third- party to perform these functions, including marketing and sales functions, we~~ may **not** be **approved** ~~unable to compete successfully against these more established companies. Furthermore, a significant proportion of the patient populations for beti- cel, eli- cel, and lovo- cel lies outside of the United States. We currently expect to focus our operations and efforts on markets~~ in **a timely manner** ~~the United States and intend to rely heavily on third parties for geographies outside of the United States. We may enter into collaborations with third parties to utilize their mature marketing and distribution capabilities, but we may be unable to enter into agreements on favorable terms~~ , if at all. ~~If we do not enter into collaboration arrangements with third parties to pursue regulatory authorization or commercialization of our programs for markets outside of the United States, or if our future collaborative partners do not commit sufficient resources to such efforts, we may be unable to generate sufficient revenue to sustain our business. The insurance coverage and reimbursement status of newly- approved products in the United States is uncertain. Due to the novel nature of our technology and the potential for our product to offer lifetime therapeutic benefit in a single administration, we face additional challenges in obtaining adequate pricing and reimbursement for our product. Failure to obtain or maintain adequate coverage and reimbursement for any new or current product could limit our ability to market those products and decrease our ability to generate revenue. The availability and extent of reimbursement by governmental and private payers is essential for most patients to be able to afford expensive treatments, such as gene therapy products. Sales of our potential products will depend substantially, both domestically and abroad, on the extent to which the costs of our potential products will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other payers. There is no assurance that the approved prices or reimbursement levels that payers will be willing to pay will be acceptable to us. In addition, because our therapies represent new treatment approaches, the estimation of potential revenues will be complex. For products administered under the supervision of a physician, obtaining reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products, including gene therapies that are potential one- time treatments. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services (" CMS") an agency within the U. S. Department of Health and Human Services (" HHS"), as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payers tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Moreover, increasing efforts by governmental and third- party payers to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for beti- cel, eli- cel, or lovo- cel following marketing approval, if and when obtained. We expect to experience pricing pressures in connection with the sale of our potential products, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional**

~~legislative changes. Net prices for drugs may be reduced by mandatory discounts or rebates required by government or private payers and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. Furthermore, because our target patient populations are relatively small, the pricing and reimbursement of our potential products must be adequate to cover the costs to treat and support the treatment of patients. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our potential products will be adversely affected. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. In addition, the administration of autologous drug products requires procedures for the collection of HSCs from the patient, followed by chemotherapy and myeloablative treatments, before infusion of the engineered cell therapy product. The manner and level at which reimbursement is provided for these services is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our product. Although we have proposed novel payment models, including outcomes- based arrangements with payments over time, to assist with realizing the value and sharing the risk of a potential one-time treatment, we did not reach agreement with payers on an acceptable price for reimbursement in our priority markets in Europe. In addition, to the extent reimbursement for our product is subject to outcomes- based arrangements, the total payments received from product sales may vary, our cash collection of future payments and revenue assumptions from product sales will be at risk, and the timing of revenue recognition may not correspond to the timing of cash collection. We plan on commercializing our product candidates in the United States once approved, and will be subject to price reporting obligations set forth by CMS. To the extent reimbursement for our potential products in the United States by U. S. governmental payers is subject to outcomes- based arrangements, the increased complexity increases the risk that CMS may disagree with the assumptions and judgments that we use in our price reporting calculations, which may result in significant fines and liability. Collectively, these factors could affect our ability to successfully commercialize our potential products and generate or recognize revenues, which would adversely impact our business, financial condition, results of operations and prospects. Risks related to the research and development of our product candidates~~ We cannot predict when or if we will obtain marketing approval to commercialize ~~beti- cel, eli- cel, or~~ lovo- cel, and the marketing approval of our product candidates may ultimately be for more narrow indications than we expect. If **lovo- cel** ~~our~~ **or other** product candidates are not approved in a timely manner or at all for any reason, our business prospects, results of operations, and financial condition would be adversely affected. ~~Before obtaining marketing approval from regulatory authorities for the commercialization of our product candidates, we must conduct extensive clinical studies to demonstrate the safety, purity and potency, and efficacy, of the product candidates in humans. Clinical testing is expensive, time- consuming and uncertain as to outcome. There~~ **The** ~~is a high failure rate for therapies proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical studies even after achieving promising~~ results ~~in earlier stage clinical studies. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include: • delays in reaching a consensus with regulatory agencies on study design; • imposition of a clinical hold by regulatory agencies, after an inspection of our clinical study operations or study sites or due to unforeseen safety issues; • delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites; • failure to obtain sufficient cells from patients to manufacture enough drug product or achieve target cell doses; • delays patient enrollment, or in having patients complete participation in a study or return for post- treatment follow- up; • occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols. We have experienced delays in some of our clinical studies in the past, and we may experience similar delays in the future. Results~~ from previous or ongoing studies are not necessarily predictive of our future clinical study results, and initial or interim results may not continue or be confirmed upon completion of the study. There ~~is~~ **are** limited data concerning long- term safety and efficacy following treatment with our product candidates. These data, or other positive data, may not continue ~~or~~ **to** occur for these patients or for any future patients in our ongoing or future clinical studies, and may not be repeated or observed in ongoing or future studies involving our product candidates. Furthermore, our **marketed products or** product candidates may also fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. There can be no assurance that any of these studies will ultimately be successful or support further clinical advancement or marketing approval of our product candidates. For instance, while patients with SCD who have been treated with lovo- cel may experience a reduction of vaso- occlusive events following successful engraftment, there can be no assurance that they will not experience vaso- occlusive events in the future. We have experienced unexpected results in the past, and we may experience unexpected results in the future. Even if our product candidates demonstrate safety and efficacy in clinical studies, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development. We may experience delays or rejections based upon additional government regulation from future legislation or administrative action, changes in regulatory agency policy, or additional regulatory feedback or guidance during the period of product development, clinical studies and the review process. The field of cell and gene therapy is evolving, and as more products are reviewed by regulatory authorities, they may impose additional requirements that were not previously anticipated. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post- marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our treatment candidates. For example, the development of our product candidates for pediatric use is an important part of our current business strategy, and if we are

unable to obtain marketing approval for the desired age ranges, **such as using lovo** ~~our business may suffer. The BLA submission for beti-~~ cel **for** ~~is based on data from patients treated~~ **treatment** ~~in our studies, including the Phase 3 HGB- 207 (Northstar- 2) and HGB- 212 (Northstar- 3) studies, and the Phase 1 / 2 HGB- 204 (Northstar) and HGB- 205 studies, and has been accepted~~ for ~~filing by~~ **children under** the **age** ~~FDA with priority review and a PDUFA goal date~~ of **18** ~~August 19~~ , ~~2022. However, it should be noted that~~ our **business may suffer. Our** ability to obtain approval of a BLA is ultimately an FDA review decision, which will be dependent upon the data and information submitted in the original BLA and during review, and the data submitted may not be sufficiently robust from a safety and / or efficacy perspective, or from a manufacturing **, comparability** and / or quality perspective, to support the approval of the BLA. Based on ~~the available data from these clinical studies and the information submitted, the FDA may require that we conduct additional or larger pivotal trials before we can obtain approval of the BLA for beti- cel for the treatment of patients with β- thalassemia who require regular transfusions. The BLA submission for eli- cel is based on the safety and efficacy data from our completed Starbeam study, our ongoing ALD- 104 study, and the completed ALD- 103 observational study, and has been accepted for filing by the FDA for filing and and granted priority review, with a PDUFA goal date of September 16, 2022. Whether eli- cel is eligible for approval will ultimately be determined at the discretion of the FDA, and is dependent upon the data and information submitted in the BLA and during review, and the data submitted may not be sufficiently robust from a safety and / or efficacy perspective, or from a manufacturing and / or quality perspective, to support approval of the BLA. Moreover, several patients with CALD treated with eli- cel in our clinical studies have been diagnosed with MDS likely mediated by Lenti- D LVV insertion, and as a result, our clinical studies of eli- cel have been subject to a clinical hold. On February 23, 2022, the FDA notified us that the clinical hold on the eli- cel program would remain in place, and requested additional information about safety events and monitoring in the eli- cel clinical program. We have no assurances as to whether we will successfully resolve the clinical hold. Based on the available data submitted from our clinical studies, and pending the resolution of the clinical hold, the FDA may determine that eli- cel cannot be approved or it may require that we conduct additional follow- up or larger clinical trials before we can obtain approval of the BLA for eli- cel for the treatment of patients with CALD, if ever. Based on~~ our discussions with the FDA, we **are seeking** ~~believe that we may be able to seek~~ approval for lovo- cel in the United States on the basis of clinical data from Group C of our ongoing HGB- 206 clinical study ~~,~~ and supporting data from our ongoing HGB- 210 clinical study. However, **the FDA may require** ~~in December 2021, we announced~~ that **we conduct additional** ~~the FDA has placed our~~ **or** ~~clinical program~~ **larger pivotal trials before we can obtain approval of a BLA** for lovo- cel ~~on partial~~ **, if ever. Please also see risk factor above —" Changes in our manufacturing processes may cause delays in our** clinical **development** ~~hold for patients under the age of 18, which relates to our ongoing investigation into an~~ **and commercialization plans ". If** ~~adolescent patient with persistent, non- transfusion- dependent anemia following treatment with~~ lovo- cel ~~, who was 18 months post- treatment. We do not have any assurance as to when, if ever, we may resume enrolling patients under the age of 18 in our~~ **or** ~~lovo- cel studies. The partial clinical hold has the~~ **other** ~~potential to negatively impact our ability to generate the analytical comparability and validation data for our commercial manufacturing process needed to support our planned BLA submission for lovo- cel. If our~~ product candidates are ultimately not approved for any reason, our business, prospects, results of operations and financial condition would be adversely affected. ~~Changes in~~ **Risks related to commercialization We have limited experience as a commercial company and the marketing and sale of ZYNTEGLO, SKYSONA and of lovo- cel following marketing approval (if and when obtained), may be unsuccessful** ~~our~~ ~~2021,we announced that we are focusing our~~ **or less successful than anticipated** ~~efforts in the near- term on the U~~ . ~~S.~~ **We have limited experience as a commercial company as we have only recently launched ZYNTEGLO and SKYSONA in the US,our first two commercial products** ~~market~~ **marketed in the US** ~~and plan to execute an orderly wind down of our European operations~~ .Consequently,there is limited information about our ability to overcome many of the risks and uncertainties encountered by companies commercializing products in the biopharmaceutical industry **in the U.S** .To execute our business plan,we will need to successfully:• gain regulatory approval to commercialize ~~beti- cel,eli- cel,and~~ lovo- cel in the United States;• ~~obtain~~ **sustain** adequate pricing and reimbursement for **ZYNTEGLO** ~~beti- cel,eli- cel,~~ and **SKYSONA,across all U.S.payer segments,and obtain pricing and reimbursement for** lovo- cel across payers in the ~~United States~~ **US,when and if approved** ;• establish and maintain,in the regions where we hope to treat patients,relationships with qualified treatment centers who will be treating the patients who receive **ZYNTEGLO** ~~beti- cel~~ , **SKYSONA** ~~eli- cel~~ ,and lovo- cel **,when and if approved** ;• manage our spending **as we** ~~in the conduct of our clinical trials,~~ seek marketing approvals,and engage in commercialization efforts ~~,including for any extension of marketing approval of beti- cel,eli- cel,and lovo- cel~~ ;and • initiate,develop and maintain successful strategic alliances.If we are not successful in accomplishing these objectives,we may not be able to **effectively commercialize ZYNTEGLO or SKYSONA,** develop ~~and~~ **or** commercialize ~~beti- cel,eli- cel,or~~ lovo- cel,raise capital,expand our business,or continue our operations.The commercial success of **ZYNTEGLO** ~~beti- cel~~ , **SKYSONA** ~~eli- cel,~~ and **of** lovo- cel following marketing approval ~~,~~ **(** if and when obtained **)** ,will depend upon the degree of market acceptance by physicians,patients,payers and ~~others~~ **other stakeholders** ~~in the medical community~~ .The commercial success of **ZYNTEGLO** ~~beti- cel~~ , **SKYSONA** ~~eli- cel~~ ,and **of** lovo- cel following marketing approval,if and when obtained,will depend in part on the medical community,patients,and third- party or governmental payers accepting gene therapy products in general,and **ZYNTEGLO** ~~beti- cel~~ , **SKYSONA** ~~eli- cel~~ ,and lovo- cel,in particular,as medically useful,cost- effective,and safe. **ZYNTEGLO** ~~Beti- cel~~ , **SKYSONA** ~~eli- cel~~ ,and lovo- cel ~~that~~ **,which** we may bring to the market **if approved,** may not gain market acceptance by physicians,patients,payers and ~~others~~ **other stakeholders** ~~in the medical community~~ .If these products do not achieve an adequate level of acceptance,we may not generate significant product revenue and may not become profitable.The degree of market acceptance of **ZYNTEGLO** ~~beti- cel~~ , **SKYSONA** ~~eli- cel~~ ,and **of** lovo- cel ~~following marketing approval~~ ,if and when ~~obtained~~ **approved** ,will depend on a number of factors,including:• the potential **and perceived** efficacy and potential advantages over alternative treatments;• the prevalence and severity of any side effects,including any limitations or warnings contained in a product' s approved labeling; **for instance,the SKYSONA product**

label includes a boxed warning for the risk of hematologic malignancy; • the prevalence and severity of any side effects resulting from the chemotherapy and myeloablative treatments associated with the procedure by which our ~~potential~~ products are administered **,including the possible prejudicial effects that chemotherapy can have on fertility** ;• relative convenience and ease **of administration;• given the complexity of** manufacturing **product,** the ~~prevalence and severity~~ **perception that issues may arise in the supply** of **product** ~~any side effects resulting from the chemotherapy and myeloablative treatments associated with the procedure by~~ which **could delay treatment** ~~our potential products are administered;• relative convenience and ease of administration~~ ;• the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;• the strength of marketing and distribution support and timing of market introduction of competitive products;• the pricing of our ~~potential~~ products;• publicity concerning our ~~potential~~ products,or competing products and treatments; ~~and~~ • sufficient insurance coverage or reimbursement ~~.Even~~ **;• the possible occurrence of adverse clinical findings or decreased effectiveness of a product or product candidate over time identified during continued monitoring and evaluation of patients;and • the mix of private and governmental payers coverage,particularly** if **the percentage** ~~a potential product displays a favorable efficacy and safety profile in preclinical and clinical studies,market acceptance~~ of **patients receiving reimbursement from state Medicaid** ~~the product will not be known until after it~~ is ~~launched.Our~~ **high since such** ~~processes~~ **-- process can be slower to** ~~reimbursement~~ **---- reimburse** .Even if a ~~potential~~ product displays a favorable efficacy and safety profile in ~~preclinical and~~ clinical studies,market acceptance of the product will not be known until **some period** after it is launched.Our efforts to educate the medical community and payers on the benefits of our ~~potential~~ products may require significant resources and may never be successful.For instance,following marketing approval of **ZYNTEGLO** ~~beti- cel~~ in the European Union,we did not reach agreement with payers on an acceptable price for reimbursement in our priority markets in Europe,and we are no longer seeking to commercialize our **products and** product candidates in Europe for the foreseeable future.Our efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors.Any of these factors ~~may cause beti~~ may cause ~~delays in~~ **ZYNTEGLO, SKYSONA,** ~~our~~ **or lovo- cel, to be unsuccessful or less successful than anticipated. Our ability to successfully commercialize our products or product candidates, if approved, including our ability to achieve their widespread market acceptance, is** ~~clinical~~ **critical** ~~development~~ **to the success of our business. We dedicate a substantial amount of our resources to the commercialization of ZYNTEGLO** and **SKYSONA. Our ability to generate revenue in the near- term will depend almost entirely on our ability to execute on our** commercialization plans ~~. The manufacturing processes~~ **and the level of market adoption for, and the continued use of, ZYNTEGLO and SKYSONA and, if approved, lovo- cel, by physicians, hospitals, patients, and /** ~~for -~~ **or** ~~our LVV~~ **healthcare payers, including government payers, consumers, managed care organizations,** and **retail and specialty pharmacies. If we are not successful in commercializing** our ~~drug~~ products **, including achieving and maintaining an adequate level of market adoption, our profitability and our future business prospects will be adversely impacted. Future expansion of commercial opportunity is dependent upon lifecycle management and access to complementary therapies. Our efforts to reduce cost of goods through efficiencies of scale or new technologies, such as improved mobilization, may not be successful and / or we may not have access to the complementary technologies we need to succeed, which could impact the level of future profitability. For instance, improvements in conditioning regimens (which could increase the patient population who has access to our products), may not be successfully developed and approved, and if they** are ~~complex~~ **, we may not have access to those improvements which, in most instances, are technology owned by third- parties. Additionally, the future opportunity to market our therapies in geographies outside the US through partnership or our internal efforts may not materialize. If the market opportunities for our product candidates are smaller than we believe they are, and if we are not able to successfully identify patients and achieve significant market share, our revenues may be adversely affected and our business may suffer** . We **focus** ~~explore improvements to~~ our ~~manufacturing processes~~ **research and product development** on ~~a continual basis~~ **treatments for severe genetic diseases. Our projections of both the number of people who have these diseases** , as ~~we evaluate clinical and manufacturing data and~~ **well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are** based on ~~discussions~~ **estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower or more difficult to identify than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment** with ~~regulatory authorities. In some circumstances, changes in the manufacturing process may require us to perform additional comparability studies, collect additional data from patients, submit additional regulatory filings, or~~ **our product candidates** ~~comply with additional requirements, which may lead to delays in our clinical development and commercialization plans~~ . For instance, ~~These estimates have been derived from a variety of sources,including scientific literature,surveys of clinics,patient foundations,or market research,and may prove to be incorrect.Further,new studies may change the estimated incidence or prevalence of these diseases.The number of patients may turn out to be lower or more difficult to identify than expected.Additionally,the potentially addressable patient population for our potential products may be limited or may not be amenable to treatment with our potential products.For instance,~~ in our lovo- cel and **SKYSONA** ~~eli- cel~~ programs,we have received notice of safety events of acute myeloid leukemia or myelodysplastic syndrome,and additional such events may be reported in the future.The market opportunity for our gene therapies may be negatively impacted even if our gene therapies ultimately receive marketing approval.Even if we obtain significant market share for a product within an approved indication,because the potential target populations for our ~~potential~~ products **and product candidates** are small,we may never achieve profitability without obtaining marketing approval for additional indications.Any of these factors may negatively affect our ability to generate revenues from sales of our ~~potential products~~ **product candidates** and our ability to achieve and

maintain profitability and,as a consequence,our business may suffer.We ~~rely on a~~ **have limited sales and distribution experience and limited capabilities for marketing and market access.Although we have invested and expect to continue to invest significant financial and management resources,if we are unable to establish and maintain these commercial capabilities and infrastructure,or to enter into agreements with third parties to market and sell our products,we may be unable to generate sufficient revenue to sustain our business.We have limited prior sales or distribution experience and limited capabilities for marketing and market access,and we did not generate meaningful product sales** following the ~~conditional approval~~ **commercial launch** of beti- cel **following marketing approval** ~~by the European Commission, we continued to refine our commercial drug product manufacturing process to narrow some of the manufacturing process parameters and to tighten the range of commercial drug product release specifications, based on discussions with the European Medicines Agency and evolving clinical data. Implementing these changes to the beti- cel commercial manufacturing process had the effect of delaying our ability to treat the first patient in the commercial context~~ in Europe. ~~In~~ **To successfully commercialize ZYNTEGLO, SKYSONA, and** lovo- cel **(following marketing** ~~, we plan to seek regulatory~~ approval **in the United States** ~~for drug product utilizing LVV manufactured using a scalable suspension manufacturing process using bioreactors~~ , **if** ~~rather than an~~ **and when obtained)** ~~adherent cell tray manufacturing process~~ , ~~and~~ we will need to **further develop** ~~generate analytical comparability and validation data that is acceptable to the~~ **these** ~~FDA in~~ **capabilities. We may need to expand our infrastructure to further** support **commercial operations** ~~of such process change. Over time, we also intend to transition the LVV manufacturing process for beti- cel~~ in the United States ~~to the suspension manufacturing process~~ , **either on our own or with others. Commercializing** ~~and~~ **an** ~~the timing~~ **autologous gene therapy is resource- intensive and has required, and will continue to require, substantial investment** in ~~which we~~ **commercial capabilities. We** are ~~able to make the transition~~ **competing with companies that currently have extensive and** ~~will~~ **well - funded marketing and sales operations. Without significant commercial experience as a company or the support of a third- party to perform these functions, including marketing and sales functions, we may** be ~~dependent upon reaching agreement with~~ **unable to compete successfully against** ~~the~~ **these** ~~FDA~~ **more established companies. Furthermore** , **a significant proportion of the patient populations** ~~which may require us to conduct additional studies, collect additional data, develop additional assays, or~~ **for ZYNTEGLO** ~~modify release specifications. Following potential marketing approval if and when received~~ , **SKYSONA, and** ~~we also intend to transition our drug product manufacturing process in~~ lovo- cel **lies outside of the United States. We currently expect to focus our operations and efforts on markets in the United States and will need to rely heavily on third parties for commercializing any products in geographies outside of the United States. We may enter into collaborations with third parties** to utilize ~~cryopreserved apheresis patient starting material in order~~ **their mature marketing and distribution capabilities, but we may be unable** to ~~expand~~ **enter into agreements on favorable terms, if at all. If we do not enter into collaboration arrangements with third parties to pursue regulatory authorization or commercialization of our programs for markets outside of the United States, or if our future collaborative partners do not commit sufficient resources to such efforts, we may be unable to generate sufficient revenue to sustain our business. We may encounter challenges with engaging or coordinating with qualified treatment centers needed for the ongoing commercialization of ZYNTEGLO and SKYSONA and** the potential ~~reach of our therapy, which would similarly require comparability and process validation data to support such transition. We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are more advanced, safer or more effective than ours, which may adversely affect our financial condition and our ability to successfully develop and commercialize~~ **commercialization of** ~~beti- cel, eli- cel, and~~ lovo- cel. ~~If our competitors obtain orphan~~ **Our commercial strategy is to engage apheresis and transplant centers as qualified treatment centers for the collection of patient hematopoietic stem cells (" HSCs") and infusion of the** drug ~~exclusivity for products~~ **product once manufactured. To ensure** that **the qualified treatment centers are prepared to collect patient HSCs and to ship them to our transduction facilities in accordance with our specifications and** regulatory **requirements, we train** ~~authorities determine constitute the same drug~~ and ~~treat the same indications~~ **conduct quality assessments of each center** as ~~our product candidates, and~~ **part of engagement. These qualified treatment centers are** ~~they~~ **the** ~~obtain marketing authorization, we~~ **first and last points on our complex supply chain to reach patients in the commercial setting. We** may not be able to **engage qualified treatment centers in all of the regions in our commercial launch strategy, or we may encounter other challenges or delays in engaging qualified treatment centers. For instance, we** have ~~competing~~ **currently signed agreements with twelve such treatment centers and our corporate strategy is to contract with at least 40 such centers by the end of 2023. Any delay or failure to meet these goals may limit patient access to our therapies and, accordingly, have a material adverse effect on our commercial forecasts and business. Furthermore, we may fail to manage the logistics of collecting and shipping patient material to the manufacturing site and shipping the drug product back to the patient. Logistical and shipment delays and problems caused by us, our third- party vendors, and other factors not in our control, such as weather, could prevent or delay the manufacture of or delivery of drug product to patients. If our qualified treatment centers fail to perform satisfactorily, we may suffer reputational, operational, and business harm. Additionally, delays with infusion at the qualified treatment centers, due to, for instance, the patient' s schedule or health condition or such center' s capacity, could result in a patient becoming medically ineligible for our treatment, the drug product becoming unusable and loss of medical coverage, which would have a material adverse effect on commercial sales. We are required to maintain a complex chain of identity and chain of custody with respect to patient material as it moves through the manufacturing process, from the qualified treatment center to the transduction facility, and back to the patient. Failure to maintain chain of identity and chain of custody could result in adverse patient outcomes, loss of product or regulatory action. The insurance coverage and reimbursement status of newly- approved products in the United States is uncertain. Due to the novel nature of our technology and the potential for our product to offer lifetime therapeutic benefit in a single administration, we face**

unique and additional challenges in obtaining adequate pricing and reimbursement for our products. Failure to obtain or maintain adequate coverage and reimbursement for any new or current product could limit our ability to market those products and decrease our ability to generate revenue. The availability and extent of reimbursement by governmental and private payers is essential for most patients to be able to afford healthcare, and especially expensive medicines, such as gene therapy products. Sales of our products will depend substantially on the extent to which the costs of our products will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other payers. There is no assurance that payers will be willing to reimburse providers at the company-established list price or reimbursement levels that payers will be willing to pay will be acceptable to us. Moreover, given that our therapies are likely to be administered in the inpatient care setting, it will be important that our products are reimbursed as a separate item from the underlying services incurred during the patient' s hospitalization; however, such " separate reimbursement " is not guaranteed by all payers. Accordingly, the estimation of potential revenues will be complex and it is difficult to predict what payers will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. In the U. S., regional Medicare Administrative Contractors (" MACs ") are responsible for making a determination with regard to whether a new therapy meets the Centers for Medicare and Medicaid Services' (" CMS") standard of " reasonable and necessary " such that it is covered and reimbursed by Medicare and Medicaid. Reimbursement methodologies in Medicare and Medicaid vary based on the type of therapeutic agent and setting of care, and in Medicaid, the reimbursement methodologies also vary by state. We anticipate that coverage determinations for our marketed therapies and for lovo- cel, if granted FDA approval in the future, will be made by MAC. While there is uncertainty with this process both in terms of the timing of the decision making process and the decision to cover itself, our exposure to the Medicare program is limited given that only a small percentage of our patient population may be Medicare eligible (i. e., a small percentage of patients may be dually eligible for Medicare and Medicaid, in which case Medicare services as the primary payer and Medicaid as the secondary payer for any service not otherwise covered by Medicare). Moreover, increasing efforts by governmental and third- party payers to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved **and, as a result, they may not cover or provide adequate payment for ZYNTEGLO, SKYSONA, or for lovo- cel following marketing approval, if and when obtained. We expect to experience pricing pressures in connection with the sale of our products due to greater scrutiny on list prices and total prescription drug spending across all payer channels as well additional legislative changes. Net prices for drugs may be reduced** by **mandatory discounts or rebates required by government or private payers. As a result, increasingly high barriers are being erected to the entry of new products often in the form of limiting the patient population for whom a new therapy is deemed " medically necessary. " Even if coverage is provided, the amount payers are willing to reimburse may not be a sufficient return on our investment. Furthermore, because a provider is responsible for costs associated not just with obtaining our medicines but also with the underlying hospital stay in which the administration of our therapies occur, the pricing and reimbursement dynamics that impact patient access are not entirely within our control as providers and payers negotiate separately for the cost of the associated items and services, decisions in which we cannot and do not play a role. These services include the collection of HSCs from the patient, followed by chemotherapy and myeloablative treatments, and inpatient hospital stay following drug product infusion. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our products will be adversely affected. We have entered into and continue to engage with payers across all channels around outcomes- based contracts for ZYNTEGLO. We also offer the option to pay for the therapy in installments over time. In the event that a payer opts for the outcomes- based contract, we will need to reserve a certain portion of revenue from each sale to account for the potential that a rebate will be owed if the patient fails to meet the pre- established outcome metric over a one or two year evaluation period following drug product administration. These contracts also may result in the timing of revenue recognition not corresponding to the timing of cash collection. Despite our efforts to engage with CMS and work with experts to ensure all of our payer contracting efforts comply with relevant federal and state regulations, including government price reporting obligations, given the complexity of ~~the~~ these arrangements, we may not be able to satisfy the compliance requirements, which may result in significant fines and liability. Collectively, these factors could affect our ability to successfully commercialize our products and generate or recognize revenues, which would adversely impact our business, financial condition, results of operations and prospects. Risks related to the research and development of our product candidates Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of lovo- cel or other product candidates. Before obtaining marketing approval from regulatory authorities for the commercialization of our product candidates, we must conduct extensive clinical studies to demonstrate the safety, purity and potency, and efficacy, of the product candidates in humans. Clinical testing is expensive, time- consuming and uncertain as to outcome. There is a high failure rate for therapies proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical studies even after achieving promising results in earlier stage clinical studies. We cannot guarantee that any clinical studies will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical studies can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development of lovo- cel or any other product candidate include: • inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials; • delays or failure in obtaining regulatory authorization to commence a trial; • delays in reaching**

agreement on acceptable terms with prospective contract research organizations (“ CROs ”), and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites; • delays in identifying, recruiting and training suitable clinical investigators; • delays in obtaining required IRB or ethics committee approvals at each clinical trial site; • delays in manufacturing, testing, releasing, validating or importing / exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing; • insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials; • imposition of a clinical hold by regulatory agencies, including after review of an IND or amendment or equivalent foreign application or amendment, as a result of a new safety finding that presents unreasonable risk to clinical trial participants or after an inspection of our clinical study operations or study sites or due to unforeseen safety issues; • failure by our CROs, other third parties or us to adhere to clinical trial protocols or failure to perform in accordance with the FDA’ s or any other regulatory authority’ s good clinical practice requirements (“ GCPs ”) or applicable regulatory **guidelines** ~~authority for a significant period of time. We are engaged~~ in ~~the development of gene therapies for severe genetic diseases, which is a competitive and rapidly- changing field. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and~~ other ~~research institutions. Many~~ **countries; • occurrence** of **adverse events associated with** ~~our competitors have substantially greater financial, technical and other~~ **the** ~~resources, such as larger research and development staff, more experienced manufacturing capabilities, or more established commercial infrastructure. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products~~ **product candidate** that are ~~more effective~~ **viewed to outweigh its potential benefits** , ~~safer,~~ or ~~less costly than any products~~ **occurrence of adverse events in trial of the same class of agents conducted by other companies, particularly due to the fact** that we **are required to follow** ~~may develop, or achieve patent~~ **patients in our clinical studies for** ~~protection, marketing approval, product commercialization and~~ **an** ~~market penetration earlier than us.~~ **extended period of time (up to 15 years); • changes to the clinical trial protocols; • clinical sites deviating from trial protocol or dropping out of a trial; • changes in the standard of care on which a clinical development plan was based, which may require new or** ~~Additionally~~ **additional** ~~, technologies developed by~~ **trials; • selection of clinical endpoints that require prolonged periods of observation** ~~our~~ **or analyses of resulting data; • the cost of clinical trials of** ~~competitors may render our potential products uneconomical or obsolete, and we may not be successful in marketing~~ our product candidates ~~against competitors.~~ **being greater than we anticipate; • clinical trials of our product candidates producing negative** ~~For~~ **or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct** additional ~~information regarding~~ **clinical trials** ~~our~~ **or** ~~competition,~~ **abandon development of such product candidates; • transfer of manufacturing processes to larger- scale facilities operated by a contract manufacturing organization (“ CMO ”) and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process (please** see **" Risk Factors** ~~“ Item 1. Business~~ **Changes** ~~Competition ”~~ in our **manufacturing processes may cause delays in our clinical development and commercialization plans" of this** Annual Report on Form 10- K **for further information); or • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols. Clinical trials must be conducted in accordance with the FDA and other applicable regulatory authorities’ legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where the clinical trials are conducted. Further, conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly. We depend on enrollment of patients in our clinical trials for our product candidates. If we experience delays or difficulties enrolling in our clinical trials, our research and development efforts and business, financial condition, and results of operations could be materially adversely affected. Successful and timely completion of clinical trials, including additional trials which the FDA may require we complete**

prior to or as part of approval of our product and product candidates, will require that we enroll a sufficient number of patient candidates. These trials and other trials we conduct may be subject to delays for a variety of reasons, including as a result of patient enrollment taking longer than anticipated, patient withdrawal or adverse events. These types of developments could cause us to delay the trial or halt further development. Our clinical trials will compete with other clinical trials that are in the same therapeutic areas as our product candidates, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators and clinical trial sites is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites. In addition, there may be limited patient pools from which to draw for clinical studies. In addition to the rarity of some diseases, the eligibility criteria of our clinical studies will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure or to assure their disease is either severe enough or not too advanced to include them in a study. Patient enrollment depends on many factors, including: • the size and nature of the patient population; • the severity of the disease under investigation; • eligibility criteria for the trial; • the proximity of patients to clinical sites; • the design of the clinical protocol; • the ability to obtain and maintain patient consents; • the ability to recruit clinical trial investigators with the appropriate competencies and experience; • the risk that patients enrolled in clinical trials will drop out of the trials before the administration of our product candidates or trial completion; • the availability of competing clinical trials; • the availability of new drugs approved for the indication the clinical trial is investigating; and • clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies. These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost- effective manner. Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, some of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Data from our clinical trials that we announce or publish from time to time may change as more patient data become available either through long- term patient follow- up and / or as such data is audited and verified which could result in material changes to clinical and safety profiles for our products. From time to time, we may disclose data from our preclinical studies and clinical trials. Such data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. In addition, the clinical trials evaluating our products and product candidates generally require that we continue to monitor and evaluate safety and efficacy in patients over an extended period of time following treatment, including for up to fifteen years for some studies, which may result in the safety or efficacy profile to change over time. Changes in the efficacy and safety profile of our product or product candidates over time could significantly harm our business prospects including resulting in volatility in the price of our common stock. Additionally, from time to time, we may publicly disclose preliminary or top- line data from our preclinical studies and clinical trials, which are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top- line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top- line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top- line data should be viewed with caution until the final data are available. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If others, including regulatory authorities, disagree with the conclusions reached with respect to such information and assessments, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition . Even if we **have received or will receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post- marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained. In September 2022, SKYSONA received accelerated approval from the FDA, and we may in the future receive accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life- threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not**

itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor' s agreement to conduct, in a diligent manner, one or more additional confirmatory studies to verify and describe the drug' s clinical benefit. If such post- approval studies fail to confirm the drug' s clinical benefit or are ~~successful~~ **not completed** in ~~achieving~~ **a timely manner, the FDA may withdraw its approval of the drug on an expedited basis. For example, we agreed to provide confirmatory long- term clinical data to the FDA as a condition of the SKYSONA accelerated approval, and continued approval for the approved indication will be contingent upon verification and description of clinical benefit in a confirmatory trial. Moreover, certain payers, including state medicaid agencies, may scrutinize therapies that reach the market through accelerated approval, which can lead to delays in broader access after approval and require additional company resources to address any concerns. In addition, in December 2022, President Biden signed an omnibus appropriations bill to fund the U. S. government through fiscal year 2023. Included in the omnibus bill is the Food and Drug Omnibus Reform Act of 2022, which among other things, introduced reforms intended to expand the FDA' s ability to regulate products receiving accelerated approval, including by increasing the FDA' s oversight over the conduct of confirmatory trials; however, the ultimate impact of these reforms remains unclear. A Regenerative Medicine Advanced Therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive** marketing approval ~~to commercialize a~~ **. We have obtained Regenerative Medicine Advanced Therapy (" RMAT ") designation for lovo- cel for the treatment of SCD, and we may seek additional RMAT designations for our product candidates. A biological** product candidate ~~faster~~ **is eligible for RMAT designation if: (1) it meets the definition of a regenerative medicine therapy, which the FDA defines as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) the candidate is intended to treat, modify, reverse, or cure a serious disease or condition; and (3) preliminary clinical evidence indicates that the candidate has the potential to address unmet medical needs for such disease or condition. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and eligibility for rolling review o and priority review of BLAs. Product candidates granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long- term clinical benefit, or through reliance upon data obtained from a meaningful number of sites, including through expansion to a sufficient number of sites, as appropriate. RMAT- designated product candidates that receive accelerated approval may, as appropriate, be able to fulfill their post- approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real- world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post- approval monitoring of all patients treated with such therapy prior to approval of the therapy. RMAT designation is within the sole discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for RMAT designation, the FDA may disagree and instead determine not to make such designation. RMAT designation does not change the standards for product approval, and there is no assurance that such designation or eligibility for such designation will result in expedited review or approval or that the approved indication will not be narrower** than **the indication covered by the RMAT designation. Additionally, RMAT designation can be revoked if the product candidate fails to meet the qualifications as clinical data continue to emerge. We have obtained and may seek orphan drug designation for our product candidates, but we may be unable to obtain such designation** ~~our~~ - **or to obtain or maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our product revenue, if any, to be reduced. We have obtained orphan drug designations for certain diseases or conditions for beti- cel, lovo- cel and eli- cel. Under the Orphan Drug Act, the FDA may designate a biological product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200, 000 in the United States, or a patient population greater than 200, 000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Orphan drug designation must be requested before submitting a BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, waivers from certain pediatric clinical trial requirements, and application fee waivers. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. In addition, if a product candidate receives the first FDA approval for the disease or condition for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same disease or condition for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity for the orphan patient population. Exclusive marketing rights in the United States may also be unavailable if we or our collaborators seek approval for a disease or condition broader than the orphan designated disease or condition and may be lost if the FDA later determines that the request for designation was materially defective. Even if we obtain orphan drug designation, we may not be the first to obtain marketing approval for any particular orphan disease or condition due to the uncertainties associated with developing pharmaceutical products. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from ~~competitors~~ competition because different drugs can be approved for the same disease**

condition. Even after an orphan drug is approved , the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is safer, more effective, or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. We have obtained a rare pediatric disease designation for lovo- cel for the treatment of SCD; however, there is no guarantee that FDA approval will result in issuance of a priority review voucher. In 2012, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications. This program is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a " rare pediatric disease " that meets certain criteria may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. The FDA may also revoke any priority review voucher if the rare pediatric disease drug for which the voucher was awarded is not marketed in the U. S. within one year following the date of approval. We have obtained a rare pediatric disease designation for lovo- cel for the treatment of SCD. However, there is no guarantee that we **will be able to obtain a priority review voucher, even if lovo- cel is approved by the FDA. For example, even though we received priority review vouchers in connection with the approvals of SKYSONA and ZYNTEGLO, the FDA may determine that a BLA for lovo- cel, even if ultimately approved, does not meet the eligibility criteria for a priority review voucher, such as where the FDA limits approval, if ultimately received, to a patient population over 18 years of age. Moreover, Congress included a sunset provision in the statute authorizing the rare pediatric disease priority review voucher program. Under the current statutory sunset provisions, after September 30, 2024, FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the product candidate, and that designation was granted by September 30, 2024. After September 30, 2026, FDA may not award any rare pediatric disease priority review vouchers. Our biological products and product candidates** may face competition **sooner than anticipated** ~~from biosimilars due to the changing regulatory environment .~~ ~~In the United States,~~ **The Affordable Care Act includes a subtitle called** the Biologics Price Competition and Innovation Act of 2009 **(" BPCIA "), which** created an abbreviated approval pathway for biological products that are ~~demonstrated to be " highly similar, " or~~ biosimilar ~~,~~ to or ~~"~~ interchangeable ~~"~~ with an FDA- ~~approved~~ **licensed reference** biological product. ~~This pathway could allow competitors~~ **Under the BPCIA, an application for a highly similar or " biosimilar " product may not be submitted** to **the FDA until four years following the date that the** reference ~~data from biological products~~ **product** ~~already~~ **was first** approved ~~after~~ **by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until** 12 years from the **date on which** ~~time of approval. In Europe,~~ the **reference** ~~European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and~~ product **was first** ~~class- specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data from biological products already~~ approved ~~, but will not be able to get on the market until 10 years after the time of approval .~~ **During** ~~This~~ **this** ~~10~~ **12** - year period **of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor' s own preclinical data and data from adequate and well- controlled clinical trials to demonstrate the safety, purity and potency of their product. We believe that any of our product candidates approved 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 our product candidates to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved,** will be **substituted for** ~~extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an~~ **any** ~~approval for~~ one **of** ~~or~~ **our reference products in a way that is similar to traditional generic substitution for non- biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are** more ~~new therapeutic indications~~ **advanced, safer or more effective** ~~that~~ **than** ~~bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our~~ **ours** ~~potential products. If competitors are able to obtain marketing approval for biosimilars referencing our potential products~~ , **which** ~~our potential products~~ may **adversely affect** ~~become subject to competition from such biosimilars, with the attendant competitive pressure and consequences. Expiration or~~ **our financial condition and our ability to** ~~successful~~ **successfully develop and commercialize ZYNTEGLO** ~~challenge of our applicable patent rights could also trigger competition from other products~~ , **SKYSONA** ~~assuming any relevant exclusivity period has expired. In addition, although beti- cel, eli- cel,~~ and lovo- cel **. We are engaged in the development of gene therapies for severe genetic diseases, which is a competitive and rapidly- changing field. We** have **competitors both in** ~~been granted orphan drug status by the FDA there are limitations to the exclusivity. In~~ the United States **and internationally , including major multinational pharmaceutical companies, biotechnology companies and universities and** ~~the~~ **other** ~~exclusivity period~~ **research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff, more experienced manufacturing capabilities,** ~~for -~~ **or** ~~orphan drugs is seven years~~ **more established commercial infrastructure. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing , while pediatric acquiring or licensing on an** ~~exclusivity~~ **exclusive** ~~adds six months to~~ **basis, products that are more effective, safer, or less**

costly than any ~~existing patents or exclusivity periods. Generally, if a product~~ **products** ~~with an orphan drug designation receives the first~~ **that we may develop, or achieve patent protection,** marketing approval ~~for the indication for which it has such designation~~ , ~~the~~ product ~~is entitled to a period of~~ **commercialization and market penetration earlier than us. Additionally, technologies developed by our competitors may render our products or product candidates uneconomical or obsolete, and we may not be successful in** marketing **our** ~~exclusivity, which precludes the FDA from approving another marketing application for a~~ product **candidates against competitors** ~~that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances~~ . **For additional information regarding** ~~If another sponsor receives such approval before we do (regardless of~~ our **competition** ~~orphan drug designation)~~ , **see " Part I, Item 1. Business — Competition "** ~~we will be precluded from receiving marketing approval for our potential products for the exclusivity period for the applicable indication~~ . Finally, 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. We may not be successful in our efforts to expand applications of our platform technologies through the discovery of additional product candidates or complementary technologies such as reduced toxicity conditioning. The success of our business depends ~~primarily~~ **, in part,** upon our ability to identify, develop and commercialize products based on our platform technologies ~~, such as in vivo product candidates~~ . Our growth strategy also depends upon our ability to leverage advancements in complementary technologies such as in reduced toxicity conditioning or in stem cell mobilization. Our research programs may fail to identify other potential product candidates for clinical development or advance such complementary technologies for a number of reasons. We may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. Research programs to identify new product candidates and new technologies 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. If any of these events occur, we may be forced to abandon ~~our~~ **any** research, development or commercialization efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our ~~potential~~ products **and product candidates** or adversely affect our ability to conduct our business or obtain and maintain marketing approvals for our **products and** product candidates. Public perception may be influenced by claims that gene therapy, including gene editing technologies, is unsafe or unethical, and research activities and adverse events in the field, even if not ultimately attributable to us or our **products and** product candidates, could result in increased governmental regulation, unfavorable public perception, challenges in recruiting patients to participate in our clinical studies, potential regulatory delays in the testing or approval of our ~~potential products~~ **product candidates** , stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any approved products **. Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, prevent new or modified products from being developed, reviewed, approved or commercialized in a timely manner or at all, which could negatively impact our business. The ability of the FDA and foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA' s or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA may also slow the time necessary for new drugs, medical devices and biologics or modifications to approved drugs and biologics 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, have had to furlough critical FDA employees and stop critical activities. Separately, in response to the global COVID- 19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to the evolving COVID- 19 pandemic, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the United States have adopted similar policy measures in response to the COVID- 19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business** . Risks related to our reliance on third parties We rely on third parties to conduct some or all aspects of our LVV production, drug product manufacturing, and testing, and these third parties may not perform satisfactorily. We do not independently conduct all aspects of our LVV production, drug product manufacturing, and testing. We currently rely, and expect to continue to rely, on third parties with respect to these items, including manufacturing and testing in the commercial context. Our reliance on these third parties for manufacturing, testing, research and development activities reduce our control over these activities but will not relieve us of our

responsibility to ensure compliance with all required regulations and study protocols. For example, for products that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND- enabling studies and clinical studies are conducted in accordance with the study plan and protocols, and that our LVV and drug products are manufactured in accordance with GMP as applied in the relevant jurisdictions. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, or manufacture our LVV and drug products in accordance with GMP, whether due to the impacts of COVID- 19 or otherwise, we will not be able to **support commercialization of SKYSONA and ZYNTEGLO and** complete, or may be delayed in completing, the preclinical and clinical studies and manufacturing process validation activities required to support future IND and BLA submissions ~~and approval of our product candidates~~ , **including** ~~or~~ **for lovo- cel** ~~to support commercialization of our products, if approved~~ . Many of our agreements with these third parties contain termination provisions that allow these third parties to terminate their relationships with us at any time. If we need to enter into alternative arrangements, our product development and commercialization activities could be delayed. Reliance on third- party manufacturers entails risks to which we would not be subject if we manufactured the products ourselves, including: • the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms **, including the inability to negotiate favorable terms to increase capacity to meet future forecasted demand** ; • reduced control as a result of using third- party manufacturers for all aspects of manufacturing activities; • the risk that these activities are not conducted in accordance with our study plans and protocols; • termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and • disruptions to the operations of our third- party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier. We may be forced to manufacture LVV and drug product ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different manufacturer, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills required to manufacture our LVV or drug product candidates may be unique or proprietary to the original manufacturer, and we may have difficulty or there may be contractual restrictions prohibiting us from, transferring such skills to a back- up or alternate supplier, or we may be unable to transfer such skills at all. Any of these events could lead to clinical study delays or failure to obtain marketing approval, or impact our ability to successfully commercialize our ~~potential~~ products **or product candidates** . Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production. We and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity. All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates, are subject to extensive regulation. Some components of a finished therapeutic product approved for commercial sale or used in late- stage clinical studies must be manufactured in accordance with GMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and where required, must adhere to the FDA' s or other regulator' s good laboratory practices (" GLP"), and GMP regulations enforced by the FDA or other regulator through facilities inspection programs. Some of our contract manufacturers **, particularly those we anticipate using for production of lovo- cel (when and if approved)** have not produced a commercially- approved product and therefore have not obtained the requisite FDA or other marketing approvals to do so. Our facilities and quality systems and the facilities and quality systems of some or all of our third- party contractors ~~must pass~~ **may be required to successfully complete** a pre- approval inspection for compliance with **GMPs and** ~~the~~ **other** applicable regulations as a condition of marketing approval of our ~~potential products~~ **product candidates** . In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our ~~potential~~ products **or product candidates** or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not ~~pass~~ **successfully complete** a pre- approval plant inspection, **it is possible** FDA or other marketing approval of the ~~products~~ **product** ~~will not~~ **candidates may** be ~~granted~~ **delayed or prevented** . The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third- party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and / or time- consuming for us or a third- party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business. If we or any of our third- party manufacturers fail to maintain regulatory compliance, the FDA or other regulators can impose regulatory sanctions including, among other things, refusal to approve a pending application for a biologic product, or revocation of a pre- existing approval. As a result, our business, financial condition and results of operations may be materially harmed. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in commercial supply. The number of manufacturers with the necessary manufacturing capabilities is limited. In addition, an alternative manufacturer would need to be qualified through a BLA supplement or similar regulatory submission which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our ~~potential~~ products **or product candidates** , cause us to incur higher costs and

prevent us from **successfully** commercializing our ~~potential~~ products ~~successfully~~ **or product candidates** . Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenues. We ~~expect to~~ rely on third parties to conduct, supervise and monitor our clinical studies, and if these third parties perform in an unsatisfactory manner, it may harm our business. We ~~expect to~~ rely on **contract research organizations ("** CROs **")** and clinical study sites to ensure our clinical studies are conducted properly and on time. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical studies is conducted in accordance with the applicable protocol **and in accordance with applicable GCPs** , **GLPs and other** legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with the FDA' s and other regulatory authorities' GCPs for conducting, recording and reporting the results of clinical studies to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical study participants are protected **. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations** . If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical studies may be deemed unreliable and the FDA and other regulatory authorities may require us to perform additional clinical studies before approving any marketing applications. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical studies may be extended, delayed or terminated, and we may not be able to obtain marketing approval for, or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed. Because we rely on third parties to manufacture our vectors and our drug products, and because we collaborate with various organizations and academic institutions on the advancement of our gene therapy platform, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business. In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor' s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business. Risks related to our financial condition and capital requirements We have not generated material revenue from product sales and may never be profitable. Our ability to generate revenues and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully **commercialize ZYNTEGLO and SKYSONA and** complete the development of, and obtain the regulatory, pricing and reimbursement approvals necessary to commercialize ~~beti- cel, eli- cel, or~~ lovo- cel **(if and when approved)** . Our ability to generate revenues from product sales depends heavily on our success in: • completing research and preclinical and clinical development of our product candidates; • seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies; • developing a sustainable, commercial- scale, reproducible, and transferable manufacturing process for our vectors and drug products; • establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development for our product candidates and commercial demand for ~~any~~ **our** approved ~~product~~ **products** ; • launching and commercializing ~~any~~ **our** approved ~~product~~ **products** ~~, either by collaborating~~ with a **sustainable** ~~partner or, if launched independently, by establishing a~~ field- based team ~~,~~ **and** marketing and distribution infrastructure; • obtaining sufficient pricing and reimbursement for ~~any~~ **our** approved ~~product~~ **products** from private and governmental payers; • obtaining market acceptance and adoption of ~~any~~ **our** approved ~~product~~ **products** and gene therapy as a viable treatment option; • addressing any competing technological and market developments; • negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter; and • maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know- how. We expect to continue to incur significant expenditures for the foreseeable future, and we expect these expenditures to increase, which costs may increase further as competitors enter the market. Our expenses could increase beyond expectations if we are required by the FDA or other

regulatory agencies, domestic or foreign, to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate material product revenues, we may not become profitable and may need to obtain additional funding to continue operations. If the estimates we make, or the assumptions on which we rely, in preparing our consolidated financial statements are incorrect, our actual results may vary from those reflected in our projections and accruals. Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (" GAAP"). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct. We may be incorrect in our assumptions regarding the applicability of drug pricing programs and rebates that may be applicable to our ~~potential~~ products **and product candidates** , which may result in our under- or over- estimating our anticipated product revenues especially as applicable laws and regulations governing pricing evolve over time. In addition, to the extent payment for our ~~potential~~ products **and product candidates** is subject to outcomes- based arrangements over time **, as it is for ZYNTEGLO** , the total payments received from product sales may vary, our cash collection of future payments and revenue assumptions from product sales will be at risk, and the timing of revenue recognition may not correspond to the timing of cash collection. Further, from time to time we issue financial guidance relating to our expectations for our cash, cash equivalents, and marketable securities available for operations, which guidance is based on estimates and the judgment of management. **For instance, a portion of our financial runway guidance includes $ 45. 4 million of restricted cash which is currently unavailable for use and there is no assurance as to when or if our restricted cash will become available. Moreover, our future net product revenues will depend upon the size of the markets which the products have received approval, its ability to achieve sufficient market acceptance, reimbursement from third- party payers, adequate market share in those markets and performance of the drug product subject to outcome- based programs.** If, for any reason, our expenses differ materially from our guidance or we utilize our cash more quickly than anticipated, we may have to adjust our publicly announced financial guidance. If we fail to meet, or if we are required to change or update any element of, our publicly disclosed financial guidance or other expectations about our business, our stock price could decline. Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance. Our operating results are difficult to predict and will likely fluctuate from quarter to quarter and year to year. We expect that ~~following marketing approval, if and when obtained,~~ revenues from product sales will be difficult to predict from period to period, given the absence of historical sales data for **ZYNTEGLO** ~~beti- cel~~ , **SKYSONA,** ~~eli- cel~~ and lovo- cel **, if approved** . Further, changes in our operations, such as increased development, manufacturing and clinical trial expenses in connection with expanding our pipeline programs, or our undertaking of additional programs, or business activities, or entry into strategic transactions, including potential future acquisitions of products, technologies or businesses may also cause significant fluctuations in our expenses. The cumulative effects of these factors, further exacerbated by the impacts of the ongoing COVID- 19 pandemic on healthcare systems and economic conditions, will likely result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period- to- period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide. Risks related to our business operations Our **future success depends on our ability to retain key employees and to attract, retain and motivate qualified personnel. We are highly dependent on our executive team and key employees, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are " at will " employees. Recruiting and retaining other qualified employees, consultants and advisors for our** business ~~may~~ **, including scientific and technical personnel, will also** be ~~materially~~ **critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense** and ~~adversely affected by~~ **our turnover rate has been high. We may not be able to attract and retain personnel on acceptable terms given** the ~~ongoing COVID- 19 pandemic~~ **competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, our financial condition has made it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives** . The COVID- 19 pandemic has had, and may continue to have, an impact on various aspects of our business and that of third parties on which we rely. The extent to which the COVID- 19 pandemic impacts our business will depend in part on future developments, which are uncertain and unpredictable in nature. ~~Since March 2020, when the World Health Organization characterized COVID- 19 as a pandemic, the related adverse public health developments, including orders to shelter- in- place, travel restrictions, and the imposition of additional requirements on businesses, have adversely affected workforces, organizations, healthcare communities, economies, and financial markets globally, leading to economic uncertainty and increased market volatility. It has also disrupted the normal operations of businesses across industries, including ours.~~ As a result of the COVID- 19 pandemic, we have experienced and ~~expect to~~ **may in the future** experience disruptions in our operations and business, and those of third parties upon whom we rely. For instance, we have experienced disruptions in the conduct of our clinical trials, manufacturing and commercialization efforts, ~~including the commercial launch of beti- cel in Germany~~ and the treatment of patients in the commercial context ~~. We~~

~~cannot reasonably assess or predict at this time the full extent of the negative impact that the COVID- 19 pandemic and related effects may have on our business, financial condition, results of operations and cash flows. We expect to continue experiencing these disruptions in our operations and those of our third parties for an unknown period of time, as the trajectory of the COVID- 19 pandemic remains uncertain and continues to evolve in the United States. These impacts, which may materially and adversely affect our business, include the following: • We are conducting a number of clinical studies across our programs in geographies which are affected by the COVID- 19 pandemic~~ . The COVID- 19 pandemic has **also** ~~had, and will likely continue to have, an impact on various aspects of our clinical studies. Policies at various clinical sites and federal, state, local and foreign laws, rules and regulations are continuing to evolve, including through the implementation of quarantines and travel restrictions, and direction of healthcare resources toward pandemic response efforts. For instance, the availability of intensive care unit beds and related healthcare resources available to support activities unrelated to COVID- 19 response have fluctuated with the incidence of severe cases of COVID- 19 in the surrounding communities, and we anticipate that the availability of healthcare resources will continue to fluctuate and may become significantly constrained, with variability across geographies. The COVID- 19 pandemic has~~ disrupted the conduct of our ongoing clinical studies, with the result of slower patient enrollment and treatment as well as delays in post- treatment patient follow- up visits. These impacts have varied by clinical study, with the most significant impacts being on our ongoing HGB- 210 study for lovo- cel. It is possible that these delays may impact the timing of our regulatory submissions. **Furthermore, certain** ~~It is unknown how long these disruptions could continue. • We currently rely on~~ third parties ~~to manufacture, perform quality testing, and ship LVV and drug product for our clinical studies and, if and when we receive marketing approval for our therapies, expect to rely on such third parties to support commercialization efforts. The third parties~~ in our supply chain ~~have been and may continue to be subject to restrictions in operations arising from the COVID- 19 pandemic, and in addition, a number of these third parties~~ have experienced operational disruptions, which have affected activities necessary for our research and development efforts, as well as our commercialization efforts in the United States. **We cannot reasonably assess** ~~These restrictions and disruptions in operations have also given rise to staffing shortages from time to time, which may result in production slowdowns and / or disruptions in delivery systems, potentially interrupting our~~ -- **or predict at** ~~supply chain and limiting our ability to manufacture LVV and drug product for our clinical studies and for commercial use. At~~ this time ~~, it is unknown how long these disruptions may continue, or~~ the full extent of ~~their~~ -- **the negative impacts** -- **impact that** ~~. • The operations of health regulatory agencies globally have been impacted as a result of~~ the COVID- 19 pandemic ~~. They~~ **and related effects may** have **on our business** ~~communicated slower response times to regulatory interactions and submissions and~~ , **financial condition** ~~in the future~~ , **results of operations and cash flows. We expect we** may ~~lack resources to~~ continue to ~~monitor our clinical studies or to engage in other activities related to review of regulatory submissions in drug development. As a result, timelines for the review of regulatory submissions for our programs have been impacted, and we may~~ experience ~~other delays~~ **these disruptions in our operations and those** of **our third parties for an** unknown **period** ~~duration in the review, inspection, and other regulatory interactions. Any de- prioritization~~ of **time** ~~our clinical studies or delay in regulatory review or interaction resulting from such disruptions could materially affect the development of our product candidates. In addition~~ , ~~we have been engaging in reimbursement discussions with governmental health programs~~ as ~~part of our commercial preparation activities. • The trading prices for our shares of common stock and other~~ -- **the trajectory** ~~biopharmaceutical companies have been highly volatile as a result~~ of ~~the economic volatility and uncertainty caused by~~ the COVID- 19 pandemic **remains** ~~. As a result, we may face difficulties raising capital through sales of shares of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of, or failure to manage or contain, the COVID- 19 pandemic will materially and adversely affect our business, the value of our common stock, and our ability to operate under our operating plan and execute our strategy. Our business and operating plan have already been impacted by the COVID- 19 pandemic, the associated governmental restrictions, and the resulting economic conditions, leading us to reduce and defer costs, adjust our priorities, timelines and expectations, and review and revise our operating plans with the intention that it would enable us to advance our corporate strategy and pipeline during an extended period of uncertainty~~ -- **uncertain** ~~. The extent of the impacts described above will depend on numerous evolving factors that we may not be able to accurately predict, including: • the duration, severity,~~ and **continues to evolve** ~~scope of the pandemic~~ in the United States ~~and globally; • the effectiveness of governmental, business and individuals' protocols and actions that have been and continue to be taken in response to the pandemic; • the impact of the pandemic on economic activity and actions taken in response; • the effect on patients, healthcare providers and business partners; • uncertainty as to when we will be able to resume normal clinical study enrollment and patient treatment or follow up activities, particularly at clinical study sites located in highly impacted geographies as a result of disruptions at these sites; • the ability to obtain or deliver sufficient and timely supplies, given the disruptions to the production capabilities of our manufacturers and suppliers, particularly with respect to the priority given to the development, regulatory approval, and manufacture of COVID- 19 vaccines and diagnostic tests; • our access to the debt and equity markets on satisfactory terms, or at all; • disruptions in regulatory oversight and actions, as a result of significant and unexpected resources expended to address the COVID- 19 by regulators and industry professionals; and • any impacts on our and our partners' offices, operations and facilities~~ . The ultimate impact of the COVID- 19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments which are difficult to predict, including the duration **and any potential resurgence** of the pandemic **and** ~~, the ultimate geographic spread of the disease,~~ additional or modified government ~~actions, new information that will emerge concerning the severity and impact of COVID- 19 and other~~ actions taken to contain or address its impact in the short and long term, among others. We do not yet know the full extent of potential delays or impacts on our business, our clinical studies, our research programs, our commercial ~~readiness~~ activities in the United States, healthcare systems or the global economy **. For instance, we continue to evaluate any impact of COVID- 19 on our QTC network, our supply chain, and any potential future clinical trials** . If the ultimate impact of the COVID- 19 pandemic and the resulting uncertain economic and healthcare

environment is more severe than we anticipated, we may not be able to execute on our current operating plan or on our strategy. ~~If the duration of the COVID- 19 pandemic and the associated period of business and social restrictions and economic uncertainty is longer than we anticipated, our cash, cash equivalents, and marketable securities may not be sufficient to fund the activities under our operating plan for the time period that we anticipated, and we may be required to revise our operating plan further.~~ To the extent the COVID- 19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this " Risk Factors " section. **Our products, whether FDA- approved or investigational, remain subject to regulatory scrutiny. For any regulatory approvals that we have or may receive, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our products and / or product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post- marketing information and reports, registration, as well as ongoing compliance with cGMPs and GCPs for any clinical trials that we may conduct. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards.** Even ~~if~~ **though** we ~~receive~~ **have obtained** marketing approval **in the U. S.** for ~~a product candidate~~ **ZYNTEGLO and SKYSONA and may obtain regulatory approval in the U. S. for lovo- cel** , any ~~approved product~~ **regulatory approvals we may receive** will ~~remain subject~~ **require the submission of reports** to ~~regulatory scrutiny. Even if we obtain marketing approval in a jurisdiction,~~ regulatory authorities **and surveillance to monitor the safety and efficacy of the product candidates, and such approvals** may **contain** ~~still impose~~ significant **limitations related to use** restrictions ~~on the indicated uses or~~ **for specified age groups** ~~marketing of any approved products~~ , **warnings, precautions** ~~or impose ongoing requirements for~~ **or** ~~potentially costly~~ **contraindications, and may include burdensome** post- approval **study** ~~studies, post- market surveillance~~ or ~~patient or drug restrictions~~ **risk management requirements.** . For example, the FDA typically advises that patients treated with gene therapy undergo follow- up observations for potential adverse events for a 15- year period. **Furthermore, we have agreed to provide confirmatory long- term clinical data to the FDA as a condition of the SKYSONA accelerated approval, and continued approval for the approved indication will be contingent upon verification and description of clinical benefit in a confirmatory trial. If our confirmatory trials fail to adequately verify or describe the anticipated clinical benefit of SKYSONA, or if we fail to conduct such trials in a timely manner, the FDA could withdraw its approval for SKYSONA on an expedited basis.** Additionally, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. We have experienced interruptions in **clinical programs** ~~our marketing of beti- cel in Europe~~ due to safety concerns arising from our **SKYSONA and** lovo- cel ~~program~~ **programs** , and we can make no assurance that we will not experience interruptions in any **clinical studies,** marketing or other commercialization activities in the future, whether due to safety concerns in any approved **or investigational** products, or due to events arising from programs that utilize technologies similar to or related to ours. In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with good manufacturing practices (" GMP") and adherence to commitments made in the BLA. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we fail to comply with applicable regulatory requirements following marketing approval for a product, a regulatory agency may: • issue a warning letter asserting that we are in violation of the law; • seek an injunction or impose civil or criminal penalties or monetary fines; • suspend or withdraw marketing approval; • suspend any ongoing clinical studies; • refuse to approve a pending marketing application, such as a BLA or supplements to a BLA submitted by us; • seize product; or • refuse to allow us to enter into supply contracts, including government contracts. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize any approved product and generate revenues. **The FDA' s and other regulatory authorities' policies may change and additional government regulations may be promulgated that could prevent, limit or delay marketing authorization of any product candidates we develop. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or 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 be subject to enforcement action and we may not achieve or sustain profitability. The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off- label uses. The FDA strictly regulates marketing, labeling, advertising and promotion of prescription drugs and biologics. These regulations include standards and restrictions for direct- to- consumer advertising, industry- sponsored scientific and educational activities, promotional activities involving the internet and off- label promotion. Any regulatory approval that the FDA grants is limited to those specific diseases and indications for which a product is deemed to be safe, pure and potent, or effective, by the FDA. For example, the current FDA- approved indication for ZYNTEGLO is limited to the treatment of adult and pediatric patients with β- thalassemia who require regular red blood cell transfusions, and the FDA- approved indication for SKYSONA is limited to slow the progression of neurologic dysfunction in boys 4- 17 years of age with early, active CALD, which is defined to include to asymptomatic or mildly symptomatic (neurologic function score, NFS ≤ 1) boys who have gadolinium enhancement on**

brain magnetic resonance imaging and Loes scores of 0. 5- 9. While physicians in the United States may choose, and are generally permitted, to prescribe drugs for uses that are not described in the product' s labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, our ability to manufacture and promote any products will be narrowly limited to those indications that are specifically approved by the FDA. If we are found to have manufactured and promoted such off- label uses, we may become subject to significant liability. The U. S. federal government has levied large civil and criminal fines against companies for alleged improper promotion of off- label use and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. If we cannot successfully manage the promotion any product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition. We are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws **and** , false claims ~~laws and health information privacy and security~~ laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties, reputational harm, and diminished profits and future earnings. In the United States, the research, manufacturing, distribution, sale, and promotion of drugs and biologic products are subject to regulation by various federal, state, and local authorities in addition to FDA, including CMS, other divisions of the HHS, (e. g., the Office of Inspector General), the United States Department of Justice offices of the United States Attorney, the Federal Trade Commission and state and local governments. Our operations are directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations described in more detail under" Item 1. Business-- Government regulation" in our Annual Report. These include the federal Anti- Kickback Statute, federal civil and criminal false claims laws and civil monetary penalty laws (including False Claims Laws), HIPAA, transparency requirements created under the Affordable Care Act, as well as analogous state and foreign laws. These laws apply to, among other things, our sales, marketing **, patient services** and educational programs. State and federal regulatory and enforcement agencies continue actively to investigate violations of health care laws and regulations, and the United States Congress continues to strengthen the arsenal of enforcement tools. Most recently, the Bipartisan Budget Act of 2018 increased the criminal and civil penalties that can be imposed for violating certain federal health care laws, including the Anti- Kickback Statute. Enforcement agencies also continue to pursue novel theories of liability under these laws. In particular, government agencies have recently increased regulatory scrutiny and enforcement activity with respect to programs supported or sponsored by pharmaceutical companies, including reimbursement and co- pay support, funding of independent charitable foundations and other programs that offer benefits for patients. Several investigations into these programs have resulted in significant civil and criminal settlements. 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 ability to operate our business and our results of operations. 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 financial condition and divert the attention of our management from operating our business. **Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition. The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal information, such as information that we may collect in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business, affect our ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulations, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our business, results of operation, and financial condition.** In ~~addition, we may be subject to patient privacy laws by both~~ the **U** ~~federal government and the states in which we conduct our business~~ . ~~For example~~ **S.** , HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (" HITECH") and their ~~respective~~ implementing regulations **(collectively," HIPAA")** , imposes requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions **. Certain states have also adopted comparable privacy** ~~In addition to HIPAA, as amended by HITECH,~~ and ~~their respective implementing~~ **security laws and** regulations, **which govern the privacy, processing and protection of health- related and other personal information. For example,** California ~~recently~~ enacted the California Consumer Privacy Act (" CCPA") which creates new individual privacy rights for California

consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt- out of certain sales or transfers of personal information. While there is currently an exception for protected health information that is subject to HIPAA, as currently written, the CCPA may impact our business activities. The **CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with data breach litigation. Further, the** California ~~Attorney~~ **Privacy Rights Act (“ CPRA ”)** ~~General~~ **generally** ~~has~~ **went into effect on January 1, 2023, and significantly amends the CCPA. It imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may also be required. Similar laws have passed in Virginia, Colorado, Connecticut and Utah, and have been** proposed ~~draft regulations~~ **in other states and at the federal level** , ~~which~~ **reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could** have **potentially conflicting requirements** ~~not been finalized to date,~~ that **would make compliance challenging. In** ~~may further impact our business activities if they~~ **the event that we** are ~~adopted. The uncertainty surrounding~~ **subject to or affected by HIPAA,** the ~~implementation of~~ CCPA ~~exemplifies~~ **,** the **CPRA** ~~vulnerability of our~~ **or** ~~business to the evolving regulatory environment related to personal data and protected health information. EU member states, Switzerland and~~ other **domestic privacy and** ~~countries have also adopted~~ data protection laws **, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition. Furthermore, the Federal Trade Commission (FTC) and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination and security practices that appear to be unfair or deceptive. For example, according to the FTC, failing to take appropriate steps to keep consumers’ personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5 (a) of the Federal Trade Commission Act. The FTC expects a company’ s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. We are also or may become subject to rapidly evolving data protection laws, rules** and regulations **in foreign jurisdictions** ~~, which impose significant compliance obligations~~ . ~~In~~ **For example, in Europe,** the European Union ~~, the collection and use of personal health data is currently governed by the provisions of the~~ General Data Protection Regulation (~~"~~ **“** GDPR ~~"~~ **”**) **went into effect in May 2018 and imposes strict requirements for** ~~. The GDPR, together with the national legislation of the individual EU member states governing the~~ processing ~~of~~ **the** personal data ~~, impose strict~~ **of individuals within the European Economic Area (“ EEA ”). Companies that must comply with the GDPR face increased compliance** obligations and ~~restrictions on~~ **risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant company, whichever is greater. Among** ~~the~~ **other requirements** ~~ability to collect~~ , ~~analyze and~~ **the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States; in July 2020, the Court of Justice of the EU (“ CJEU ”) limited how organizations could lawfully** transfer personal data **from the EU / EEA to the United States by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses (“ SCCs ”). In March 2022** , ~~including health~~ **the US and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU- US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 16, 2020 have taken a restrictive approach to international** data **transfers** ~~from clinical trials and adverse event reporting~~ . **As supervisory authorities issue further guidance on** ~~In particular, these obligations and restrictions concern the consent of the individuals to whom the~~ personal data ~~relates~~ **export mechanisms** , **including circumstances where** the **SCCs cannot** ~~information provided to the individuals for the consent to~~ be **used** ~~considered valid~~ , ~~the~~ **and / or start taking enforcement action, we could suffer additional costs, complaints and / or regulatory investigations or fines, and / or if we are otherwise unable to** transfer ~~of~~ personal data ~~out~~ **between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation** of **our relevant systems and operations, and could adversely affect our financial results. Since the beginning of 2021, after the end of the transition period following the United Kingdom’ s departure from** the European **Union** ~~Economic Area~~ , ~~security~~ **we are also subject to the United Kingdom data protection regime, which imposes separate but similar obligations to those under the GDPR and comparable penalties, including fines of up to £ 17. 5 million or 4 % of a noncompliant company’ s global annual revenue for the preceding financial year, whichever is greater. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business. If we fail to comply with reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. We participate in governmental programs that impose extensive drug price reporting and payment obligations on pharmaceutical manufacturers. Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. Under the Medicaid Drug Rebate Program (the “ MDRP ”), as a condition of federal funds being made available for our covered outpatient**

drugs under Medicaid and certain drugs or biologicals under Medicare Part B, we pay a rebate to state Medicaid programs for ~~breach --~~ each ~~notifications~~ unit of our covered outpatient drugs dispensed to a Medicaid beneficiary and paid for by the state Medicaid program. Medicaid rebates are based on pricing data that we report on a monthly and quarterly basis to CMS , the federal agency that administers the MDRP and Medicare programs. For the MDRP, ~~the~~ these ~~use of third- party processors~~ data include the Average Manufacturer Price (" AMP ") for each drug and, in the case of innovator products, best price. In connection with Medicare Part B ~~the processing of the personal data , confidentiality of the personal data~~ a pharmaceutical manufacturer must provide CMS with average sales price (" ASP ") information for certain drugs or biologicals on a quarterly basis. ASP is calculated based on a statutorily defined formula , as well as ~~substantial potential fines~~ regulations and interpretations of the statute by CMS. If we become aware that our MDRP price reporting submission for a prior period was incorrect ~~for -~~ or ~~breaches~~ has changed as a result of recalculation of the pricing data ~~protection obligations. Data protection authorities from the different EU member states may interpret the GDPR and national laws differently and impose additional requirements , which add to~~ we must resubmit the corrected ~~complexity of processing personal~~ data ~~in~~ for up to ~~the~~ three years after ~~European Union. The GDPR also imposes strict rules on the~~ those ~~transfer of personal~~ data originally were due ~~to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to € 20 million or 4 % of annual global revenues, whichever is greater .~~ If we fail ~~The GDPR also confers a private right of action on data subjects and consumer associations~~ to provide information ~~lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time~~ timely ~~- intensive process that may increase our -~~ or are found ~~cost of doing business or require us~~ to have knowingly submitted false information to ~~change our business practices, and despite those --~~ the ~~efforts~~ government , ~~there is a risk that~~ we may be subject to ~~fines and~~ civil monetary penalties and other sanctions , ~~litigation~~ including termination from the MDRP , in which case payment would not be available for our covered outpatient drugs under Medicaid or, if applicable, Medicare Part B. Federal law requires that any company that participates in the MDRP also participate in the 340B program in order for federal funds to be available for the manufacturer' s drugs under Medicaid and Medicare Part B. The 340B program is administered by HRSA and imposes a statutorily defined " ceiling price " for pharmaceutical products purchased by defined " covered entities " when administered in the outpatient setting. bluebird' s therapies are administered in the inpatient setting exclusively and thus, we do not anticipate any 340B claims and requires us, as a participating manufacturer, to agree to charge statutorily defined covered entities no more than the 340B " ceiling price " for our covered drugs used in ~~and -~~ an ~~reputational harm~~ outpatient setting. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low income patients. A drug that is designated for a rare disease or condition by the Secretary of Health and Human Services is not subject to the 340B ceiling price requirement with regard to the following types of covered entities: rural referral centers, sole community hospitals, critical access hospitals, and free standing cancer hospitals. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B covered entities. HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B eligible drugs. HRSA has also finalized an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B covered entities for engaging in ~~connection~~ unlawful diversion or duplicate discounting of 340B drugs. In addition, legislation may be introduced that, if passed, would further expand the 340B program, such as adding further covered entities or requiring participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting. In order to be eligible to have drug products paid for with federal funds under Medicaid and Medicare Part B and purchased by certain federal agencies and grantees, we must also participate in the VA / FSS pricing program. Under the VA / FSS program, we must report the Non- FAMP for our covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non FAMP using a statutory formula. These four agencies are the VA, the U. S. Department of Defense, the U. S. Coast Guard, and the U. S. Public Health Service (including the Indian Health Service). We must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. If we fail to provide timely information or are found to have knowingly submitted false information, we may be subject to civil monetary penalties. Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and states may impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements. If we are found to have violated state law requirements, we may become subject to penalties or other enforcement mechanisms, which could have a material adverse effect on our business. Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us,

governmental or regulatory agencies, and the courts, which can change and evolve over time. Such pricing calculations and reporting, along with any **necessary restatements and recalculations** ~~activities falling within the scope of the GDPR. Further~~ , ~~Brexit has created uncertainty~~ **could increase our costs for complying** with ~~regard~~ **the laws and regulations governing the MDRP and other governmental programs, and under the MDRP could result in an overage or undercharge in Medicaid rebate liability for past quarters. Price recalculations under the MDRP also may affect the ceiling price at which we are required** to **offer products under the 340B program. Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we fail to submit the required price** data **on a timely basis** ~~protection regulation in the United Kingdom. In particular~~ , **or if we are found** ~~it is unclear how data transfers~~ to ~~and from~~ **have charged 340B covered entities more than** the ~~United Kingdom~~ **statutorily mandated ceiling price. CMS could also terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B, if applicable, for our covered outpatient drugs. Pursuant to the Inflation Reduction Act of 2022 (the " IRA "), the AMP figures we report** will **also** be ~~regulated~~ **used to compute rebates under Medicare Part D triggered by price increases that outpace inflation. We cannot assure you that our submissions will not be found to be incomplete or incorrect** . We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our **products or** product candidates ~~harms~~ **harm** patients, or is perceived to harm patients even when such harm is unrelated to our **products or** product candidates, our marketing approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. The use of our product candidates in clinical studies and the sale of ~~any~~ products for which we **have** ~~obtain~~ **obtained** marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients participating in clinical trials, consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our **products and** product candidates. There is a risk that our **products and** product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in: • impairment of our business reputation; • withdrawal of clinical study participants; • costs due to related litigation; • distraction of management' s attention from our primary business; • substantial monetary awards to patients or other claimants; • the inability to develop our product candidates or commercialize any approved product; and • decreased demand for any approved product. We carry product liability insurance and we believe our product liability insurance coverage is sufficient in light of our current clinical programs and approved ~~product~~ **products** ; however, we may not be able to maintain insurance coverage at commercially reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. Patients with the diseases targeted by our **products and** product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre- existing and potentially life- threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our **products and** product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain marketing approval for any approved product, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our **products and** product candidates the investigation into the circumstance may be time- consuming or inconclusive. These investigations may interrupt our sales efforts, delay our marketing approval process in other countries, or impact and limit the type of marketing approval our product candidates may receive or ~~any~~ **our** approved ~~product~~ **products** ~~maintains~~ **maintain** . As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations. **The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results. There has been increasing public focus by investors, patients, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, even if we are effective at addressing such concerns, we may experience increased costs as a result of executing upon our sustainability goals that may not be offset by any benefit to our reputation, which could have an adverse impact on our business and financial condition. In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.** Healthcare legislative reform measures may have a material adverse effect on our business and results of operations. The United States **has** ~~and many foreign jurisdictions have~~ enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our ~~potential products~~ **product candidates** , restrict or regulate post- approval activities and affect our ability to profitably sell ~~any product~~ **products** for which we **have** ~~obtain~~ **obtained** marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. ~~In~~ **A primary trend in** the ~~United States,~~ **U. S. healthcare industry and**

elsewhere is cost containment. Government authorities and ~~there~~ **other third party payers** have **attempted** ~~been and continue~~ to ~~be a number~~ **control costs by limiting coverage and the level** of ~~legislative initiatives to contain~~ **reimbursement for particular medical products and services, implementing reductions in Medicare and other** healthcare ~~costs~~ **funding and applying new payment methodologies** . For example, in March 2010, the ~~Patient Protection and~~ Affordable Care Act ~~, as amended by the Health Care and Education Reconciliation Act of 2010~~ (" **ACA** ~~Affordable Care Act~~ ") ~~,~~ was ~~passed~~ **enacted** , which ~~substantially changed the way health care is financed by both governmental and private insurers, and significantly impacts the U. S. pharmaceutical industry. The Affordable Care Act~~ , among other things, ~~addressed~~ **increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced** a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected **; extended manufacturer** ~~, increased the minimum~~ Medicaid ~~rebates~~ **rebate** ~~owed~~ **obligations to utilization** by ~~manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to~~ individuals enrolled in Medicaid managed care ~~organizations,~~ **plans;** established ~~annual fees and taxes on manufacturers of certain branded prescription drugs, expanded the types of entities eligible for the 340B drug discount program, and~~ a new Medicare Part D coverage gap discount program ~~, in which~~ **; subjected drug** manufacturers ~~must agree~~ to **new annual fees based on pharmaceutical companies' share** ~~offer 70 % (increased pursuant to the Bipartisan Budget Act~~ of ~~2018, effective as of 2019) point- of-~~ **sales to federal healthcare programs; imposed a new federal excise tax on the** sale ~~discounts off~~ **of** ~~negotiated prices of applicable~~ **certain medical devices; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in,** ~~brand~~ **and conduct comparative clinical effectiveness research** ~~drugs to eligible beneficiaries during their coverage gap period~~ , ~~as a condition~~ **along with funding** for **such research; and established a Center for** ~~the manufacturer' s outpatient drugs to be covered under~~ Medicare ~~Part D~~ **Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending** . Since its enactment, there have been ~~numerous~~ judicial, ~~administrative,~~ executive ~~,~~ and ~~legislative~~ **Congressional** challenges to certain aspects of the ~~Affordable Care Act~~ **ACA. On June 17** , **2021,** ~~and we expect there~~ **the U** ~~will be additional challenges and amendments to the Affordable Care Act in the future~~ . **S.** ~~Various portions of the Affordable Care Act are currently undergoing legal and constitutional challenges in the Fifth Circuit Court and the United States~~ Supreme Court **dismissed** . ~~It is unclear whether~~ the **most recent judicial** ~~Affordable Care Act will be overturned, repealed, replaced, or further amended. We cannot predict what effect further changes~~ **challenge** to the ~~Affordable Care Act would have~~ **ACA brought by several states without specifically ruling** on ~~our business~~ **the constitutionality of the ACA** . In addition, other legislative changes have been proposed and adopted **in the United States** since the **ACA** ~~Affordable Care Act~~ was enacted. ~~In August~~ **The Budget Control Act of** 2011, **among other things, led to reductions of Medicare payments to providers, which will remain in effect through 2031 unless additional Congressional action is taken. More recently, in March 2021,** President ~~Obama~~ **Biden** signed into law the ~~Budget Control~~ **American Rescue Plan** Act of ~~2011~~ **2021** , which **eliminates the statutory cap on the Medicaid drug rebate** , **currently set at 100 % of a drug' s AMP, beginning January 1, 2024. Most significantly, in August 2022, President Biden signed the Inflation Reduction Act of 2022 (" IRA") into law. This statute marks the most significant action by Congress with respect to the pharmaceutical industry since adoption of the ACA in 2010.** ~~among~~ **Among** other things, ~~created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation' s automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, 2 % per fiscal year through 2025 unless Congress takes additional action. These reductions were extended through 2029 through subsequent legislative amendments. In January 2013, the American Taxpayer Relief Act of 2012, among other~~ **the IRA requires** ~~things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U. S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer~~ **manufacturers** ~~patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration' s budget proposal for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price~~ 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** ~~allow some states to negotiate drug prices~~ **price** ~~under Medicaid,~~ **increases that outpace inflation (first due in 2023);** 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 ~~eliminate cost sharing~~ **implement many of these provisions through guidance, as opposed to regulation,** for ~~generic drugs for low- income patients~~ **the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated, and while the impact of the IRA on our business and the pharmaceutical industry cannot yet be fully determined, it is likely to be significant** . At the **U. S.** state level, legislatures have increasingly passed legislation and implemented 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. We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in

a similar reduction in payments from private third- party payers. ~~The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to commercialize any products for which we obtain marketing approval.~~ There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our ~~potential~~ products **and product candidates**. Such reforms could have an adverse effect on anticipated revenue from **products and** product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates. Our ~~computer~~ **information technology** systems, or those of our third- party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product candidates' development programs and **activities related to our approved products and** have a material adverse effect on our reputation, business, financial condition or results of operations. Our ~~computer~~ **information technology** systems and those of our current or future third- party collaborators, service providers, contractors and consultants may fail and are vulnerable to **attack,** damage **and interruption** from computer viruses **and malware (e. g. ransomware)** , **malicious code, natural disasters, terrorism, war, telecommunication and electrical failures, hacking, cyberattacks, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, sophisticated nation- state and nation- state- supported actors or** unauthorized access ~~, natural disasters, terrorism, war and telecommunication and electrical failures. The size and complexity of our~~ **or** ~~information technology~~ **use by persons inside our organizations, or persons with access to** systems **inside** ~~, and those of our collaborators, service providers, contractors and consultants, and the large amounts of information stored on those systems make those systems vulnerable to service interruptions, security breaches, or~~ **our organization** ~~other failures, resulting from inadvertent or intentional actions by our employees or those of third- party business partners, or from cyber- attacks by malicious third parties~~. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized groups and individuals with a wide range of motives and expertise. ~~In addition to extracting sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial- of- service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information.~~ The prevalent use of mobile devices **and unauthorized applications** also increases the risk of data security incidents. ~~If~~ **As a result of the COVID- 19 pandemic, and continued hybrid working environment,** we **may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also** experience **security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if we were to experience** a ~~material~~ system failure, accident or security breach that causes interruptions in our operations or the operations of third- party collaborators, service providers, contractors and consultants, it could result in significant reputational, financial, legal, regulatory, business or operational harm. For example, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or **our products and** product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. In addition, we rely on third- party service providers for management of the manufacture and delivery of drug product to patients in the commercial context, including for chain of identity and chain of custody. We also rely on third- party service providers for aspects of our internal control over financial reporting and such service providers may experience a material system failure or fail to carry out their obligations in other respects, which may impact our ability to produce accurate and timely financial statements, thus harming our operating results, our ability to operate our business, and our investors' view of us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to material failures, security breaches, cyberattacks and other related breaches. Any failure or perceived failure by us or any third- party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations to third parties, or any data security incidents or other security breaches that result in the unauthorized access, release or transfer of sensitive information, including personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us. These events could cause third parties to lose trust in us or could result in claims by third parties asserting that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of

operations ~~. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm~~ . While we have implemented data security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents. **Further, our insurance coverage may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.** Risks related to the separation of our oncology programs and portfolio We may incur operational difficulties or be exposed to claims and liabilities as a result of the separation of 2seventy bio. On November 4, 2021, we distributed all of the outstanding shares of 2seventy bio, Inc. (" 2seventy") common stock to our stockholders in connection with the separation of our oncology programs and portfolio. In connection with the distribution, we entered into a separation agreement and various other agreements (including a tax matters agreement, an employee matters agreement, transition services agreements and an intellectual property license agreement). These agreements govern the separation and distribution and the relationship between us and 2seventy going forward, including with respect to potential tax- related losses associated with the separation and distribution. They also provide for the performance of services by each company for the benefit of the other for a period of time. The separation agreement provides for indemnification obligations designed to make 2seventy financially responsible for many liabilities that may exist relating to its business activities, whether incurred prior to or after the distribution, including any pending or future litigation, but we cannot guarantee that 2seventy will be able to satisfy its indemnification obligations. It is also possible that a court would disregard the allocation agreed to between us and 2seventy and require us to assume responsibility for obligations allocated to 2seventy. Third parties could also seek to hold us responsible for any of these liabilities or obligations, and the indemnity rights we have under the separation agreement may not be sufficient to fully cover all of these liabilities and obligations. Even if we are successful in obtaining indemnification, we may have to bear costs temporarily. In addition, our indemnity obligations to 2seventy, including those related to assets or liabilities allocated to us, may be significant. These risks could negatively affect our business, financial condition or results of operations. ~~The separation~~ **If the distribution of shares** of 2seventy ~~continues to involve a number of additional risks, including, among other things, the potential that management's and our employees' attention will be significantly diverted by the provision of transitional services or that we may incur other operational challenges or difficulties as a result of the separation. Certain of the agreements described above provide for the performance of services by each company for the benefit of the other for a period of time. If 2seventy is unable to satisfy its obligations under these agreements, we could incur losses and may not have sufficient resources available for such services. These arrangements could also lead to disputes over rights to certain shared property and over the allocation of costs and revenues for products and operations. Our inability to effectively manage the transition activities and related events could adversely affect our business, financial condition or results of operations. We may fail to realize some or all of the anticipated benefits of the separation of 2seventy. The anticipated operational, financial, strategic and other benefits of the separation of 2seventy may not be achieved. The combined value of the common stock of the two publicly- traded companies may not be equal to or greater than what the value of our common stock would have been had the separation not occurred. The combined value of the common stock of the two companies could be lower than anticipated for a variety of reasons, including the failure of either company to operate and compete effectively as an independent company. The common stock price of each company may experience periods of extreme volatility. In addition, following the separation we are smaller and less diversified, with a narrower business focus, and may be more vulnerable to changing market conditions. The separation also presents a number of significant risks to our internal processes, including the failure to maintain an adequate control environment due to changes to our infrastructure technology systems and financial reporting processes. Completion of the separation of 2seventy resulted in substantial changes in our board of directors and management. Completion of the separation of 2seventy resulted in substantial changes in our board of directors and management. In particular, our former chief executive officer, Nick Leschly, resigned from that position (although Mr. Leschly continues to serve on our board of directors). In addition, Philip Gregory, our former chief scientific officer, and Chip Baird, our former chief financial officer, resigned from their positions with us to join management positions with 2seventy. Furthermore, Dan Lynch, Ramy Ibrahim, Denice Torres, William Sellers, Sarah Glickman and Marcela Maus resigned as members of our board of directors upon the completion of the separation. These senior officer and board level changes could be disruptive to our operations, present significant management challenges and could harm our business. The separation may result in disruptions to, and harm our relationships with, our strategic business partners. Uncertainty related to the separation may lead the suppliers, research organizations, and other parties with which we currently do business or may do business in the future to terminate or attempt to negotiate changes in our existing business relationships, or cause them to delay entering into business relationships with us or consider entering into business relationships with parties other than us. These disruptions could have a material and adverse effect on our business, prospects, financial condition and results of operations. If the distribution of shares of 2seventy bio~~ , together with certain related transactions, does not qualify as a transaction that is generally tax- free for U. S. federal income tax purposes, we and our stockholders could be subject to significant tax liabilities. The completion of the distribution **of shares of 2seventy** was conditioned upon, among other things, our receipt of a private letter ruling from the **U. S. Internal Revenue Service (the"** IRS **")** , and an opinion from Goodwin Procter LLP, both satisfactory to our board of directors and both continuing to be valid, together confirming that the distribution, together with certain related transactions, generally is tax- free for U. S. federal income tax purposes under Sections 355 and 368 (a) (1) (D) of the **U. S. Internal Revenue** Code **of 1986, as amended (the" Code")** . We have received a favorable private letter ruling from the IRS addressing one significant issue of the qualification of the distribution under Section 355 of the Code. However, the private letter ruling does not address the remaining issues that are relevant to determining whether the distribution, together with certain related transactions, qualifies as a transaction that is generally tax- free for U. S. federal income tax purposes. **This can include events that occur following the distribution such as subsequent public offerings by us or 2seventy or share sales to persons that engaged in negotiations over share purchases prior to the distribution. Subsequent tax opinions have been obtained by us and**

2seventy in connection with certain post- distribution sales of 2seventy' s shares. The IRS private letter ruling ~~and~~ **, the** opinion of Goodwin Procter LLP **and tax opinions related to certain subsequent post- distribution sales of 2seventy shares** were based, among other things, on various facts and assumptions, as well as certain representations, statements and undertakings from us and 2seventy ~~bio~~ (including those relating to the past and future conduct of us and 2seventy ~~bio~~) and were subject to certain caveats. If any of these facts, assumptions, representations, statements or undertakings is, or becomes, inaccurate or incomplete, or if we or 2seventy ~~bio~~ breach any of our respective covenants relating to the separation, the IRS private letter ruling and tax opinion may be invalid. Moreover, the opinion is not binding on the IRS or any courts. Accordingly, notwithstanding receipt of the IRS private letter ruling and an opinion of Goodwin Procter LLP **at the time of the distribution** , the IRS could determine that the distribution and certain related transactions should be treated as taxable transactions for U. S. federal income tax purposes. If the distribution, together with certain related transactions, were to fail to qualify as a transaction that is generally tax- free under Sections 355 and 368 (a) (1) (D) of the Code, in general, for U. S. federal income tax purposes, we would recognize taxable gain as if we have sold 2seventy ~~bio~~ ' s distributed common stock in a taxable sale for its fair market value and our stockholders who receive shares of 2seventy ~~bio~~ common stock in the distribution would be subject to tax as if they had received a taxable distribution equal to the fair market value of such shares. In connection with the distribution, we and 2seventy ~~bio~~ entered into a tax matters agreement pursuant to which each party is responsible for certain liabilities and obligations following the distribution. In general, under the terms of the tax matters agreement, if the distribution, together with certain related transactions, were to fail to qualify as a transaction that is generally tax- free for U. S. federal income tax purposes under Sections 355 and 368 (a) (1) (D) of the Code, and if and to the extent that such failure results from a prohibited change of control in us under Section 355 (e) of the Code, or an acquisition of our stock or assets or certain actions, omissions or failures to act, by us, then we will bear any resulting taxes, interest, penalties and other costs. If and to the extent that such failure results from a prohibited change of control in 2seventy ~~bio~~ under Section 355 (e) of the Code or an acquisition of 2seventy ~~bio~~ stock or assets or certain actions by 2seventy ~~bio~~ , then 2seventy ~~bio~~ will be obligated to indemnify us for any resulting taxes, interest, penalties and other costs, including any reductions in our net operating loss carryforwards or other tax assets. If such failure does not result from a prohibited change of control in **us** ~~bluebird bio~~ or 2seventy ~~bio~~ under Section 355 (e) of the Code and both we and 2seventy ~~bio~~ are responsible for such failure, liability will be shared according to relative fault. If neither we nor 2seventy ~~bio~~ is responsible for such failure, we will bear any resulting taxes, interest, penalties and other costs. Risks related to our intellectual property If we are unable to obtain or protect intellectual property rights related to our **products and** product candidates, we may not be able to compete effectively in our markets. We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our **products and** product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in- license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our **products and** product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our **products and** product candidates or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. If the patent applications we hold or have in- licensed with respect to our programs or **our products and** product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, **our current and** future products. Several patent applications covering our **products and** product candidates have been filed recently. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a **product or** product candidate under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by a third- party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications. In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know- how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know- how, and information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not

have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know- how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA' s disclosure policies may change in the future, if at all. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non- patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition. Third- party claims of intellectual property infringement may prevent or delay our development and commercialization efforts. Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, ex parte reexaminations, post- grant review, and inter partes review proceedings before the U. S. Patent and Trademark Office (" U. S. PTO") and corresponding foreign patent offices. Numerous U. S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our **products and** product candidates may be subject to claims of infringement of the patent rights of third parties. Third parties have asserted and in the future may assert that we are employing their proprietary technology without authorization **. For example, as discussed in Part I, Item 3," Legal Proceedings", San Rocco Therapeutics, LLC, formerly known as Errant Gene Therapeutics, LLC has alleged that our use of the BB305 lentiviral vector in connection with the beti- cel program infringes U. S. Patent Nos. 7, 541, 179 and 8, 058, 061, and seeks equitable, injunctive and monetary relief, including royalties, treble damages, attorney fees and costs** . There may be third- party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third- party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our **products and** product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such **product or** product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third- party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product **or product** candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our **products or** product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and ~~attorneys'~~ **attorney** **'s** fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. We may not be successful in obtaining or maintaining necessary rights to gene therapy product components and processes for our ~~development~~ pipeline through acquisitions and in- licenses. Presently we have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates and commercialize our ~~potential~~ products. Because our programs may involve additional **technologies** ~~product candidates~~ that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in- license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others **. For instance, our growth strategy depends in part upon our ability to leverage advancements in complementary technologies such as in reduced toxicity conditioning or in stem cell mobilization** . We may be unable to acquire or in- license any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third- party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. For example, we sometimes collaborate with U. S. and foreign academic institutions to accelerate our preclinical research or clinical development under written agreements with these

institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution' s rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third- party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third- party intellectual property rights, our business, financial condition and prospects for growth could suffer. 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 are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. Pursuant to an intellectual property license agreement with 2seventy, we granted sublicenses to 2seventy to certain existing license agreements. If we fail to comply with our obligations under these agreements, we or 2seventy materially breach these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. We may need to obtain licenses from third parties to advance the development of our product candidates or allow commercialization of our ~~potential~~ products, and we have done so from time to time. We may fail to obtain any of these 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 develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected **products or** product candidates, which could harm our business significantly. We cannot provide any assurances that third- party patents do not exist which might be enforced against our current product candidates, approved ~~product~~ **products**, or future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and / or other forms of compensation to third parties. In many cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. 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 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. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected approved ~~product~~ **products** or product candidates. We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time- consuming and unsuccessful. Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and / or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including patent eligible subject matter, lack of novelty, obviousness or non- enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U. S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, post grant review, and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our ~~potential~~ products **and product candidates**. Such a loss of patent protection would have a material adverse impact on our business. Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial

amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. We employ individuals who 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 independent contractors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee' s former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We have had in the past, and we may also have in the future, ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our **products and** product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and / or applications will be due to be paid to the U. S. PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and / or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non- U. S. patent agencies. The U. S. PTO and various non- U. S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non- compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business. Changes in U. S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our potential products. As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time- consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide- ranging patent reform legislation. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U. S. Congress, the federal courts, and the U. S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. 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, but enforcement is not as strong as that in the United States. These products may compete with our ~~potential~~ 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 or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent 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 and 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 rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Risks related to ownership of our common stock The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the price at which you purchase them. Companies trading in the stock market in general, and The Nasdaq Global Select Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and biotechnology and pharmaceutical industry factors **, such as the recent volatility and disruption experienced in the global economy and rising interest and inflation rates,** may negatively affect the market price of our common stock, regardless of our actual operating performance. The market price of our common stock has been volatile in the past, and may continue to be volatile for the foreseeable future. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following: • adverse results or delays in preclinical or clinical studies; • reports of adverse events **, either from patients participating** in **our clinical trials** ~~our~~ **or in connection with sales of our commercial** ~~product~~ **products** ~~candidates~~ or other gene therapy products ~~, or~~ in **the market** ~~clinical studies of such products~~ ; • inability to obtain additional funding; • any delay in filing ~~an IND or~~ **our** BLA for **lovo- cel** ~~any of our product candidates~~ , and any adverse development or perceived adverse development with respect to the regulatory authority' s review of **such** ~~that IND or~~ BLA; • failure to successfully manage the commercial launch of **ZYNTEGLO** ~~beti- cel, eli- cel,~~ or **SKYSONA or of** lovo- cel following marketing approval ~~,~~ **(** if and when obtained **)** , including failure to manage our supply chain operations in the coordination and delivery of drug product to patients at qualified treatment centers; • failure to obtain sufficient pricing and reimbursement for **ZYNTEGLO or SKYSONA or** ~~beti- cel, eli- cel, or~~ **for** lovo- cel from private and governmental payers ~~following marketing approval, if and when obtained~~ ; • failure to obtain market acceptance and adoption of **ZYNTEGLO** ~~beti- cel, eli- cel,~~ or **SKYSONA or of** lovo- cel ~~following marketing approval, if and when obtained; • developments concerning the separation of our programs into two independent, publicly- traded companies~~ ; • failure to maintain our existing strategic collaborations or enter into new collaborations; • failure by us or our licensors and strategic collaboration partners to prosecute, maintain or enforce our intellectual property rights; • changes in laws or regulations applicable to future products; • inability to obtain adequate product supply for **ZYNTEGLO** ~~beti- cel~~ , **SKYSONA** ~~eli- cel,~~ or lovo- cel, or the inability to do so at acceptable prices; • adverse regulatory decisions; • announcements of clinical trial results or progress in the development of programs by our competitors, and the introduction of new products, services or technologies by our competitors; • failure to meet or exceed financial projections we may provide to the public; • failure to meet or exceed the financial projections of the investment community; • the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community; • ~~the effects of the separation of 2seventy bio; •~~ announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic collaboration partner or our competitors; • disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; • additions or departures of key scientific or management personnel; • significant lawsuits, including patent or stockholder litigation; • changes in the market valuations of similar companies; • sales of our common stock by us or our stockholders in the future; and • trading volume of our common stock. Actual or potential sales of our common stock by our employees, including our executive officers, pursuant to pre- arranged stock trading plans could cause our stock price to fall or prevent it from increasing for numerous reasons, and actual or potential sales by such persons could be viewed negatively by other investors. In accordance with the guidelines specified under Rule 10b5- 1 of the Securities Exchange Act of 1934, as amended, and our policies regarding stock transactions, a number of our employees, including executive officers and members of our board of directors, have adopted and may continue to adopt stock trading plans pursuant to which they have arranged to sell shares of our common stock from time to time in the future. Generally, sales under such plans by our executive officers and directors require public filings. Actual or potential sales of our common stock by such persons could cause the price of our common stock to fall or prevent it from increasing for numerous reasons. Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall. Additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, **including under our Equity Distribution Agreement with Goldman Sachs & Co. LLC,** 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, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. Pursuant to our 2013 Stock Option and Incentive Plan (the" 2013 Plan") **we are** ~~our management is~~ authorized to grant stock options and other equity- based awards to our employees, directors and consultants. The number of shares available for future grant under the 2013 Plan automatically increases each year by up to 4 % of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors or compensation committee to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2013 Plan each year. ~~If our board~~ **In January 2023, the number** of ~~directors~~ **shares of common stock available** ~~or~~ **for** ~~compensation committee elects to~~ **issuance under the 2013 Plan was increased by approximately 3. 3 million shares as a result of this automatic** increase **provision. The 2013 Plan will expire in 2023 and we will need** ~~the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price~~ to ~~fall~~ **adopt a new plan subject to shareholder approval** . We **also** make equity grants to certain new employees joining the ~~company~~ **Company** pursuant to an inducement plan, and our compensation committee may elect to increase the number of shares available for future grant without stockholder approval. We also have an Employee Stock Purchase Plan and any shares of common stock purchased pursuant to that plan will also cause dilution. We ~~are~~ **may be** subject to securities class action litigation, which may result in

substantial costs and a diversion of management' s attention and resources, which could harm our business. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities, and we ~~are litigating~~ **have in the past litigated** class action complaints in the United States District Court for the District of Massachusetts and for the District of Delaware, filed by purported stockholders against us and certain of our directors and officers. We may face additional securities class action litigation in the future. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years, and we expect to experience continued stock price volatility. Defending against ~~the current litigation and~~ any future litigation could result in substantial costs and a diversion of management' s attention and resources, which could harm our business. Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited. Under ~~Section~~ **Sections** 382 **and 383** of the ~~Internal Revenue~~ Code ~~of 1986, as amended~~, if a corporation undergoes an " ownership change, " generally defined as a **cumulative change of** greater than 50 % ~~change~~ (by value) in its equity ownership over a three- year period, the corporation' s ability to use its pre- change net operating loss carryforwards (" NOLs") and other pre- change tax attributes (such as research **and development** tax credits) to offset its post- change income **and taxes** may be limited. We have completed several financings since our inception ~~and prior to our initial public offering in 2013~~, which we believe have resulted in **shifts** ~~a change~~ in **our equity ownership** ~~control as defined by IRC Section 382~~. We completed a study through December 2020 confirming no ownership changes have occurred since our initial public offering in 2013. We may **have experienced ownership changes since December 2020, and we may** also experience ownership changes in the future as a result of subsequent shifts in our ~~stock~~ **equity** ownership **, some of which are outside our control** . ~~As~~ **If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre- change NOLs or other pre- change tax attributes if we undergo** a ~~result~~ **future ownership change. Accordingly** , if we earn net taxable income, our ability to use our pre- change ~~net operating loss carryforwards~~ **NOLs and other pre- change tax attributes** to offset U. S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. We do not intend to pay cash dividends on our common stock so any returns will be limited to the value of our stock. We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. Provisions in our amended and restated certificate of incorporation and by- laws, as well as provisions of Delaware law, could make it more difficult for a third- party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management. Our amended and restated certificate of incorporation, amended and restated by- laws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and by- laws, include provisions that: • authorize " blank check " preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock; • create a classified board of directors whose members serve staggered three- year terms; • specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president; • prohibit stockholder action by written consent; • establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors; • provide that our directors may be removed only for cause; • provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum; • specify that no stockholder is permitted to cumulate votes at any election of directors; • expressly authorize our board of directors to modify, alter or repeal our amended and restated by- laws; and • require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated by- laws. These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15 % of our outstanding voting stock to merge or combine with us. Any provision of our amended and restated certificate of incorporation or amended and restated by- laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock. Our amended and restated certificate of incorporation and amended and restated by- laws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us. Our amended and restated certificate of incorporation and amended and restated by- laws specify that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders, other than suits brought to enforce any liability or duty created by the Securities Exchange Act of 1934, as amended (the " Exchange Act ") or any other claim for which the federal courts have exclusive jurisdiction and any action that the Court of Chancery of the State of Delaware has dismissed for lack of subject matter jurisdiction, which may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated by- laws also specify that, unless we consent in writing to the selection of an alternate forum, the United States District Court for the District of Massachusetts shall be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended (the " Securities Act "). Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation and amended and restated by- laws described above. We believe these provisions benefit us by providing increased consistency in the application

of Delaware law by chancellors particularly experienced in resolving corporate disputes or federal judges experienced in resolving Securities Act disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi- forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees, and agents as it may limit any stockholder' s ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees, or agents and result in increased costs for stockholders to bring a claim. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation and by- laws has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation and amended and restated by- laws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation or amended and restated by- laws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition, or results of operations. Changes in tax law **and regulations** could adversely affect our business ~~and~~ **,** financial condition ~~. The rules dealing with U. S. federal, state,~~ and ~~local~~ **results of operations. New** income **, sales, use or** ~~taxation are constantly under review by persons involved in the~~ **other** ~~legislative process and by the IRS and the U. S. Treasury Department. Changes to~~ tax laws ~~(~~ **, statutes, rules, regulations or ordinances could be enacted at any time,** which ~~changes may have retroactive application)~~ could ~~adversely~~ affect ~~us or holders~~ **the tax treatment** of ~~our common stock. In recent years, many~~ **any of** ~~such changes have been made and changes are likely to continue to occur~~ -- **our** ~~in the~~ future **earnings** . ~~Future changes in~~ **Further, existing** tax laws **, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. Generally, future changes in applicable tax laws and regulations, or their interpretation and application, potentially with retroactive effect,** could have **an** ~~a material~~ adverse effect on our business, ~~cash flow,~~ financial ~~condition~~ **conditions** ~~or~~ **and** results of operations **. We are unable to predict whether such changes will occur and, if so, the ultimate impact on our business** . We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock. **Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price. The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets continue to deteriorate or the United States enters a recession, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. In addition, there is a risk that one or more of our CROs, suppliers or other third- party providers may not survive an economic downturn or recession. As a result, our business, results of operations and price of our common stock may be adversely affected.**