UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2022

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____

Commission File Number 001-37687

EDITAS MEDICINE, INC.

(Exact name of registrant as specified in its charter)

Delaware	**46-4097528**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
11 Hurley Street **Cambridge, Massachusetts**	
(Address of principal executive offices)	**02141** **(Zip Code)**

(617) 401-9000
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	**EDIT**	**The Nasdaq Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

As of June 30, 2022, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's Common Stock held by non-affiliates of the registrant was approximately $633,806,647 based upon the closing price of the registrant's Common Stock on June 30, 2022.

The number of shares of the registrant's Common Stock outstanding as of February 17, 2023 was 68,970,188.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2023 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the end of the registrant's fiscal year ended December 31, 2022 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

Editas Medicine, Inc.
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References to Editas

Throughout this Annual Report on Form 10-K, the "Company," "Editas," "Editas Medicine," "we," "us," and "our," except where the context requires otherwise, refer to Editas Medicine, Inc. and its consolidated subsidiary, and "our board of directors" refers to the board of directors of Editas Medicine, Inc.

Special Note Regarding Forward-Looking Statements and Industry Data

This Annual Report on Form 10-K contains forward-looking statements regarding, among other things, the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, the timing for our receipt and presentation of data from our clinical trials and preclinical studies, potential of, and expectations for, our product candidates, the timing or likelihood of regulatory filings and approvals, our expectations regarding cash runway, and our business strategy, and other objectives for our operations. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section entitled "Risk Factors" in Part I that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data, which we obtained from our own internal estimates and research, as well as from industry and general publications and research, surveys, and studies conducted by third parties. Industry publications, studies, and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions are appropriate, neither such research nor these definitions have been verified by any independent source.

Risk Factor Summary:

- *We are dependent on the success of our lead product candidate, EDIT-301, which is in clinical development. Clinical trials of product candidates may not be successful. If we are unable to complete the clinical development of, obtain marketing approval for, or successfully commercialize this product candidate, either alone or with a collaborator, or if we experience significant delays in doing so, our business would be substantially harmed.*

- *We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.*

- *We will need substantial additional funding, which may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.*

- *We have never generated revenue from product sales and may never be profitable.*

- *We intend to identify and develop product candidates based on a novel genome editing technology, which makes it difficult to predict the time and cost of product candidate development.*

- *Regulatory requirements governing genetic medicines, and in particular any novel genetic medicines we may develop, have changed frequently and may continue to change in the future.*

- *Adverse public perception of genomic medicines, and genome editing in particular, may negatively impact regulatory approval of, or demand for, our potential products.*

- *The genome editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on CRISPR gene editing technology using Cas9 and Cas12a enzymes, but other genome editing technologies may be discovered that provide significant advantages over CRISPR/Cas9 or CRISPR/Cas12a.*

- *Except for EDIT-301, all of our ongoing product development programs are at the preclinical or research stage. Preclinical testing and clinical trials of product candidates may not be successful.*

- *If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any product candidates we develop, we may need to abandon or limit our further clinical development of those product candidates, and it may delay or prevent their regulatory approval, limit the commercial potential, or result in significant negative consequences following any potential marketing approval.*

- *We have not extensively tested any of our proposed delivery modes and product candidates in clinical trials.*

- *We face significant competition in an environment of rapid technological change, and our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours.*

- *Due to the novel nature of our technology and the potential for some of our product candidates to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for these product candidates.*

- *Genomic medicines are novel, and our product candidates may be complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products, or otherwise harm our business.*

- *We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we develop, for development of certain of our research programs, and to conduct our clinical trials and some aspects of our research and preclinical testing.*

- *If we are unable to obtain and maintain patent protection for any products we develop and for our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours.*

- *Our rights to develop and commercialize our technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.*

- *Some of our in-licensed patents are subject to priority and validity disputes. Our owned and in-licensed patents, patent applications and other intellectual property may be subject to further priority and validity disputes, and*

other similar intellectual property proceedings including inventorship disputes. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of the product candidates we develop.

- *Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of any of our product candidates.*

- *Our future success depends on our ability to attract and retain key executives and to attract, retain, and motivate qualified personnel.*

- *The market price of our common stock may be volatile, which could result in substantial losses for our stockholders.*

- *We do not expect to pay any dividends for the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investments.*

PART I

Item 1. Business

We are a clinical stage genome editing company dedicated to developing potentially transformative genomic medicines to treat a broad range of serious diseases. The promise of genomic medicines is supported by the advancing knowledge of the human genome and by harnessing the progress in technologies for cell therapy, gene therapy, and, most recently, gene editing. We believe this progress sets the stage for us to create medicines with the potential to have a durable benefit for patients. Our core capability in gene editing uses the technology known as CRISPR (clustered, regularly interspaced, short palindromic repeats) to allow us to create molecules that efficiently and specifically edit DNA. Our mission is to translate the promise of gene editing into a broad class of differentiated, transformational medicines for previously untreatable or under-treated diseases.

We have developed a proprietary gene editing platform based on CRISPR technology and we continue to expand its capabilities. CRISPR uses a protein-RNA complex composed of an enzyme, including either Cas9 (CRISPR associated protein 9) or Cas12a (CRISPR from *Prevotella* and *Francisella* 1, also known as Cpf1), bound to a guide RNA molecule designed to recognize a particular DNA sequence. Once the complex binds to the DNA sequence it is designed to recognize, the complex makes a specific cut in the DNA. We believe we are the only human genome editing company with a platform that includes CRISPR/Cas9, CRISPR/Cas12a, engineered forms of both of these CRISPR systems, and foundational intellectual property for both of these CRISPR systems. Because of the broad nature of this platform, we believe we can create gene editing molecules for over 95% of the human genome.

Our Strategy

We seek to be a leader in *in vivo* programmable gene editing, leveraging cutting edge gene editing technology to deliver therapies that simplify the usability for patients, minimize the burdens to patients and healthcare systems, and are meaningfully differentiated from the current standards of care. To achieve this, we are focused on advancing gene editing medicines to treat hemoglobinopathies, beginning with the continued development of our current *ex vivo* EDIT-301 program and leveraging the insights gained from this program to pursue next generation *in vivo* gene editing medicines targeting hematopoietic stem cells ("HSCs"). In parallel, we are pursuing the development of *in vivo* gene editing medicines for other organs and tissues that we believe will significantly differentiate our genome editing approach from the current standards of care for serious diseases. As part of these efforts, we are using existing strategic partnerships and collaborations and pursuing further opportunities to extend the reach of our intellectual property portfolio and access complementary technologies to expedite our drug discovery and clinical execution objectives.

Ex vivo *Hemoglobinopathies*

Using our proprietary AsCas12a enzyme, we can efficiently and specifically edit HSCs, which we believe can lead to best-in-class medicines for hemoglobinopathies. Our lead program, EDIT-301, is an experimental *ex vivo* gene-edited medicine to treat sickle cell disease ("SCD"), a severe inherited blood disease that causes premature death, and transfusion-dependent beta thalassemia ("TDT"), the most severe form of beta-thalassemia, an inherited blood disorder characterized by severe anemia. In the second quarter of 2022, we dosed the first patient in our Phase 1/2 clinical trial of EDIT-301, which we refer to as our RUBY trial, for the treatment of severe SCD, and in December 2022, announced initial clinical data from the first two patients treated in the RUBY trial. This clinical data supports human proof of concept by showing that EDIT-301 could safely increase expression of fetal hemoglobin to clinically meaningful levels and correct anemia in SCD patients. For additional information regarding these clinical data, please see "Business—Our Gene Editing Medicine Programs—Hemoglobinopathies." After completing sequential dosing of the first two patients, we have commenced parallel patient dosing in this trial, meaning that we can now dose multiple patients simultaneously, and are on track to dose 20 total patients by the end of 2023. We expect to provide clinical updates from the RUBY trial in mid-2023 and end of 2023.

In December 2021, the U.S. Food and Drug Administration ("FDA") cleared our Investigational New Drug ("IND") application for a Phase 1/2 clinical trial of EDIT-301 for the treatment of TDT. This trial, referred to as our EDITHAL trial, is designed to assess the safety, tolerability, and preliminary efficacy of EDIT-301 for the treatment of

TDT. We are on track to dose the first patient in this trial in the first quarter of 2023. We expect to provide data on this patient by the end of 2023.

We believe that our unique editing approach, and the initial data from the RUBY trial, support potential differentiation of our EDIT-301 experimental medicine. The CRISPR nuclease used in the program is a proprietary high fidelity, highly specific, engineered AsCas12a enzyme for which we have exclusively licensed the foundational intellectual property to develop and commercialize human therapeutics. This enzyme has demonstrated high efficiency editing of multipotent long-term HSCs for sustained efficacy and durability. Its use to target the HBG1 and HBG2 promoters to mimic naturally occurring human mutations, analogous to patients with naturally occurring hereditary persistence of fetal hemoglobin, is potentially a more effective approach with better long-term safety than other editing targets and mechanisms. We seek to further differentiate this program by developing milder conditioning protocols. The myeloablative busulfan conditioning regimen for HSC transplantation that is necessary for current gene editing therapies for SCD and TDT requires that patients undergo immunosuppression at the time of transplant and carries with it the long-term burdens of infertility and oncogenesis. We are in early stage research for the development of non-myeloablative patient preconditioning regimens for HSC transplantations. We believe that developing milder conditioning protocols will further position us to develop a potentially best-in-class medicine to treat SCD and TDT that improves the therapeutic proposition for patients.

In vivo *Medicines*

We are also pursuing the development of next generation *in vivo* administered gene editing medicines, in which the medicine is injected or infused into the patient to edit the cells inside their body. Leveraging our differentiated approach from our EDIT-301 program, we are initially focused on editing HSCs through targeted delivery of our AsCas12a enzyme to our clinically validated HBG1 and HBG2 promotor site. By editing HSCs directly in patients without transplantation, no myeloablative conditioning is required, thereby avoiding the adverse effects associated with current HSC transplantation protocols. We believe such a product could be used in multiple different healthcare settings with a much lower burden on patients and treatment sites.

Beyond hemoglobinopathies, our discovery and development efforts are focused on *in vivo* gene editing medicines in other organs and tissues, with the goal of selecting therapeutic targets we believe have a significant probability of technical, regulatory, and commercial success.

Business Development

We are pursuing the right combination of gene editing and targeted delivery tools through internal development and the in-licensing of complementary technologies, while also leveraging our intellectual property portfolio to drive potential out-licensing and partnership discussions that can accelerate the achievement of our goal of delivering lifesaving medicines to patients with previously untreatable or under-treated diseases.

In cellular therapy medicines, we are leveraging new and existing partnerships to progress engineered cell medicines to treat various cancers. We are advancing alpha-beta T-cell experimental medicines for the treatment of solid and liquid tumors in collaboration with Bristol Myers Squibb Company ("BMS") through its wholly owned subsidiary, Juno Therapeutics, Inc. ("Juno Therapeutics"). This collaboration, which leverages our Cas9 and AsCas12a platform technologies, has resulted in 11 programs. We have also entered into a non-exclusive collaboration and licensing agreement with Immatics N.V. to combine gamma-delta T cell adoptive cell therapies and gene editing to develop medicines for the treatment of cancer.

In January 2023, we announced the sale of our wholly owned oncology assets to Shoreline Biosciences, Inc. ("Shoreline"). Under the agreement, Shoreline acquired EDIT-202, our preclinical multiplexed edited induced human pluripotent stem cell ("iPSC")-derived natural killer ("iNK") cell medicine for the treatment of solid tumors, as well as an additional iNK program under development and certain related manufacturing technologies. We also exclusively licensed to Shoreline our rights to a proprietary knock-in gene editing technology referred to as SLEEK (SeLection by Essential-gene Exon Knock-in) for use in Shoreline's iNK platform and for oncology in Shoreline's iPSC-derived

macrophage platform, as well as non-exclusively licensed our AsCas12a gene editing technology. We believe that this transaction will enable this oncology program to more rapidly move towards clinical applications and benefit patients.

Our Core Capability — Gene Editing

Gene editing is the process of revising, removing, or repairing defective DNA *in situ*. In general, gene editing corrects the defective DNA in its native genomic location, and consequently the repaired genetic region retains the cell's normal control and feedback mechanisms. Gene editing typically takes advantage of naturally occurring DNA repair mechanisms, including non-homologous end joining ("NHEJ") and homology directed repair ("HDR"), to achieve its desired therapeutic outcome. Edits that are repaired by NHEJ typically disrupt a gene or eliminate a disease-causing mutation. Edits that are repaired by HDR, including targeted insertion, aim to correct or replace aberrant DNA sequences. The diversity of genetic drivers of disease demands a variety of solutions. Gene editing has the potential to deliver a variety of types of genome modification to address a broad range of diseases.

CRISPR technology uses a protein-RNA complex composed of a type of enzyme, referred to as a DNA endonuclease, bound to an RNA molecule, referred to as a guide RNA, that has been designed to recognize a particular DNA sequence. A DNA endonuclease is an enzyme that cleaves DNA. This combination of a DNA endonuclease and a guide RNA only bind and cut DNA when two criteria are met: first, the protein recognizes a short DNA specific to the enzyme called the protospacer adjacent motif ("PAM"), and second, the appropriate portion of the guide RNA matches the adjacent DNA sequence. The PAM sequence that is recognized by the DNA endonuclease creates a second layer of recognition in addition to the guide RNA. We believe that CRISPR technology has three principal advantages for genome editing:

- *Rapid, comprehensive, and systematic identification of product candidates.* The key targeting mechanism for the endonuclease, whether it is Cas9 or Cas12a, is a guide RNA, which can be rapidly replaced with a different guide RNA or optimized by changes as small as a single nucleotide. This allows for the flexible design, synthesis, and testing of hundreds of guide RNA/endonuclease combinations for each genetic target in order to find those that cut the DNA target with the optimal efficiency and specificity. In contrast, other commonly used DNA nucleases for gene editing have inherently limited flexibility. For example, zinc finger nucleases, engineered meganucleases, and transcription activator-like effector nucleases use proteins for DNA sequence recognition to bring the endonuclease to the site of the genome where cleavage is desired, requiring the creation of an entirely new protein for each target site.

- *Simultaneous and efficient targeting of multiple sites.* In CRISPR technology, multiple guide RNAs can be provided along with the same endonuclease, enabling the simultaneous and efficient targeting of multiple sites. This ability to target multiple DNA sequences expands the applicability of CRISPR technology and also creates the potential for self-regulating systems that control exposure to the editing machinery. To address more than one target, other gene editing technologies require the engineering, characterization, manufacture, and delivery of distinct nuclease proteins for each target.

- *Ability to achieve a range of different types of edits.* The inherent differences in Cas9 and Cas12a and the availability of different engineered variants of both enzymes allow for different types of cuts for gene editing. We are able to make a blunt cut, cut either strand of the DNA, or create overhangs of differing length. This may be a critical component of improved HDR-driven approaches because the type of DNA cut can influence the type of repair mechanism used by a cell in response to that cut. We believe the ability to modify CRISPR technology to allow for different types of cuts will expand the potential of our gene editing platform.

Our Gene Editing Platform

We have developed a proprietary gene editing platform that includes different natural and engineered variants of Cas9 and Cas12a. We have characterized different Cas9 and Cas12a enzymes for several reasons. Firstly, a lower molecular weight enzyme will have advantages for delivering the endonuclease using a viral vector due to the inherent size limitations of most such delivery systems. For example, the Cas9 enzyme from SaCas9 is significantly smaller than

that from *Streptococcus pyogenes* ("*S. pyogenes*" or "SpCas9") (3,159 vs. 4,104 base pairs), and this decreased size is important when working with adeno-associated viral vectors ("AAV") as a delivery vector, which has an effective packaging limit of approximately 4,700 base pairs. Secondly, we have gained access to modified versions of Cas12a and Cas12a guide RNAs that increase Cas12a activity. This increased activity may allow us to use Cas12a editing in more indications where editing at a Cas12a susceptible site is desirable from a biological perspective but technically difficult with the wild-type Cas12a editing system. EDIT-301 for SCD and TDT is one such example. Thirdly, identifying Cas9 and Cas12a enzymes with different editing properties will expand the number of potential editing sites in the human genome. The range of natural and engineered variants of Cas9 and Cas12a have significantly expanded the number of sites in the human genome that we can potentially target. As compared to the most commonly used, naturally occurring version of Cas9, from the bacterial species *S. pyogenes*, the range of endonucleases in our platform can target approximately ten times as many genomic sites. Thus, while the *S. pyogenes* Cas9 can target approximately 1 in 10 bases in the human genome, we have the potential to hit over 95% of all bases due to the wide range of endonucleases at our disposal.

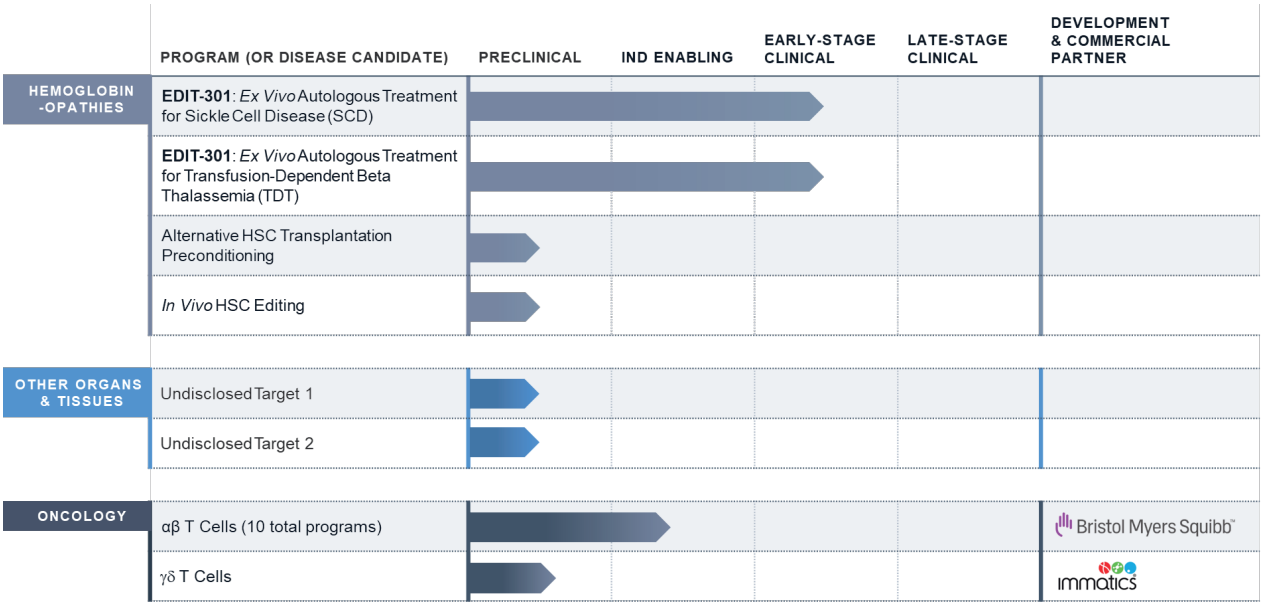
The guide RNA molecule is another component of our gene editing platform. We have made substantial advances in the design, synthesis, modification, analysis, and characterization of guide RNAs. For example, in order to accelerate and standardize the selection of guide RNAs, we have created proprietary analytical software that supports guide RNA design through single nucleotide polymorphism analysis, specificity prediction, and assessment of relative importance of potential off target sites. Of critical importance in determining the activity and specificity of an endonuclease-guide RNA complex is understanding the quality and composition of the guide RNA. The ability to understand the quality and composition of the guide RNA is an essential component to developing product candidates that have the potential to be safe and efficacious medicines. In order to understand the absolute composition of our guide RNAs, we utilize state-of-the-art mass spectrometry and sequencing methodologies.

Our gene editing platform includes multiple modular delivery modes that can be efficiently adapted to deliver different CRISPR gene editing components to address the specific needs of each disease targeted. Our strategy is to leverage existing delivery technologies to target cell types of interest while developing next generation capabilities as warranted. We have developed a variety of delivery approaches, including electroporation for efficient delivery to blood cells *ex vivo*, lipid nanoparticles for non-viral *in vivo* delivery, and AAVs for *in vivo* viral delivery. We have made substantial advances in the *ex vivo* delivery of CRISPR systems to a number of cell types. We have been able to demonstrate greater than 90% *ex vivo* editing in HSCs using ribonucleoprotein complexes, which consist of the Cas9 or Cas12a endonuclease complexed with its guide RNA. These results are consistent across multiple cell donors and multiple target genes. In addition, we have taken advantage of the smaller *S. aureus* Cas9 and existing AAV technology to construct an "all-in-one" viral vector that is able to deliver the DNA coding for the nuclease protein and one or two guide RNAs directly to cells, which we believe has substantial advantages for manufacturing and delivery compared to approaches that rely on multiple vectors.

To optimize the specificity of our product candidates, there are a number of different aspects of the product configuration that we customize in addition to the sequence and quality of the guide RNA, including the length of the guide RNA, the type of Cas9 or Cas12a enzyme, including engineered forms, the delivery vector, the use of tissue-selective promoters, and the duration of exposure, all of which contribute to overall specificity.

Our Gene Editing Medicine Programs

Our research and development efforts are focused on hemoglobinopathies and developing next generation *in vivo* medicines, including *in vivo* editing of HSCs and other organs and tissues. Our product development strategy is to target diseases where gene editing can be used to enable or enhance therapeutic outcomes for patients, while maximizing probability of technical, regulatory and commercial success. We believe the therapeutic programs and delivery technologies we have chosen to pursue to date and those that are currently under development will demonstrate the depth and breadth of our ability to deploy our genome editing platform to develop differentiated, transformational medicines for previously untreatable or under-treated diseases. The following summarizes our product candidates, research programs and disease areas:



Ex vivo *Hemoglobinopothies*

We are developing an approach for gene editing in HSCs to support the advancement of research programs to treat non-malignant hematological diseases. Our most advanced program, EDIT-301, is an *ex vivo* gene edited medicine designed to treat SCD and TDT.

Sickle cell disease affects millions of people worldwide, including approximately 100,000 people in the United States, and over 300,000 babies are born annually with SCD globally. Transfusion-dependent beta thalassemia is relatively rare in the United States, affecting approximately 1,000 people, but is one of the most common autosomal recessive disorders in the world, found most often among individuals of Mediterranean, Middle Eastern, and South Asian descent. Patients suffering from SCD can experience vaso-occlusive events and other severe symptoms such as anemia, fatigue, hemolysis, stroke, and other end-organ damages, while those with TDT typically suffer from chronic anemia, often requiring lifelong blood transfusions that can result in iron overload that requires separate treatment. While allogeneic bone marrow transplantation can cure SCD, less than 20% of patients can find matched donors and there is a risk of serious complications. We are actively pursuing a distinct gene editing approach to treating these hemoglobinopathies. Our primary criteria for a successful product candidate include high and pancellular fetal hemoglobin ("HbF") with a best-in-class safety profile. To this end, we have developed EDIT-301, an experimental, autologous cell therapy that targets the HBG1/2 promoter and disrupts the binding site of the *BCL11A*, consistent with observed naturally occurring human mutations. These mutations mimic the asymptomatic condition of hereditary persistence of fetal hemoglobin ("HPFH"). By editing the HBG1/2 promoter in the beta-globin gene, we seek to generate protective changes that increase HbF production in a manner that is independent of erythropoietic stress, resulting in reduced sickling and vaso-occlusive events in sickle cell patients, and resolving anemia and transfusion dependence in beta thalassemia patients. We believe that mimicking a combination of HPFH mutations that elevate HbF could be more effective than recreating a single point mutation. EDIT-301 is the first experimental medicine in development generated using CRISPR/Cas12a (also known as Cpf1) gene editing.

We have focused our efforts on editing a site within the beta-globin locus that we believe has the potential to create superior expression of fetal hemoglobin since patients with elevated HbF levels have better clinical outcomes. We believe that EDIT-301 has the potential to impact beta-globin expression by increasing HbF and decreasing sickle globin. In particular, our preclinical data shows that EDIT-301 induces more HbF than the approach of targeting the *BCL11A* erythroid enhancer ("BC11Ae"). Likewise, we believe our approach will reduce the sickle globin and, therefore, not have to compete for alpha globin in the same cell unlike lentiviral gene therapy approaches. Our preclinical studies identified the potential that BC11Ae might result in deleterious lineage skewing when editing

the *BCL11Ae* locus. Finally, gene editing is more specific than lentiviral expression. To get the high levels of beta-globin required for an efficacious therapy, there will be cells in the CD34+ population, which are cells that contain the long-term stem cells that repopulate the hematopoietic lineages, that carry more than twenty copies of the viral genome. These random integration events have the potential to inadvertently activate or inactivate genes involved in cell function and tumorigenesis. As such, we believe our approach to editing the beta-globin locus provides the highest likelihood of providing clinical benefit in patients while minimizing potential safety risks.

Preclinical studies

Using our approach in preclinical studies, we tested the ability of CD34+ cells obtained from healthy donors and edited at the beta-globin locus to induce fetal hemoglobin. As predicted from our preclinical *in vitro* studies, editing at the beta-globin site with Cas12a caused a robust, pancellular induction of HbF of approximately 45% above the background levels.

We also tested CD34+ cells obtained from sickle cell patients, which we edited at the beta-globin locus. These studies showed that editing was highly efficient and reproducible, with approximately 90% editing in multiple sickle patient donors. We found that EDIT-301 derived red blood cells had more than 50% HbF expression. Further, EDIT-301 derived red blood cells had a significant improvement in deformability, which could aid red blood cell transit without sickling, and a four-fold decrease in sickling, when subjected to reduced oxygen levels compared to unedited control cells. These data suggest EDIT-301 can provide potential clinical benefit for sickle patients. *In vivo* studies revealed editing was highly efficient with greater than 90% editing in bone marrow cells from mice infused with edited CD34+ cells 16 weeks post-infusion. In these mice, HbF expression was increased by approximately 50% in the red blood cells derived from these edited cells. We also observed that approximately 90% of these cells were HbF positive, demonstrating that HbF expression was pan-cellular, which we believe is likely a critical property for potential clinical benefit. For these reasons, we believe our approach of editing the hemoglobin locus to increase HbF has the potential to generate differentiated medicines to benefit patients with sickle cell disease and TDT.

Clinical trial

In January 2021, the FDA cleared the start of enrollment and dosing of patients in the first phase of our Phase 1/2 RUBY clinical trial of EDIT-301 for the treatment of SCD, and in July 2022, the FDA removed its partial clinical hold, enabling us to include efficacy data from patients in a future marketing application for EDIT-301. This trial is a single-arm, open-label, multi-center Phase 1/2 study designed to assess the safety and efficacy of EDIT-301 in patients with SCD. Enrolled patients receive a single administration of EDIT-301.

In December 2022, we announced initial clinical data from the first two patients treated in the RUBY trial, which supports human proof of concept by showing that EDIT-301 could safely increase expression of fetal hemoglobin to clinically meaningful levels and correct anemia in SCD patients. The clinical data included safety data from the first two patients and efficacy data from the first patient treated. Both treated patients demonstrated successful neutrophil and platelet engraftment. Patient 1 achieved neutrophil engraftment at 23 days after EDIT-301 infusion and platelet engraftment at 19 days after EDIT-301 infusion. Patient 2 achieved neutrophil engraftment 29 days after EDIT-301 infusion and platelet engraftment 37 days after EDIT-301 infusion. Additionally, neither patient had experienced any vaso-occlusive events since treatment with EDIT-301, at five and 1.5 months follow up, respectively. At five months post-treatment, the first patient treated with EDIT-301 had a total hemoglobin of 16.4 g/dL, an HbF of 45.4%, and a mean corpuscular HbF of 13.8 pg/red blood cell, exceeding the 10.0 pg/red blood cell threshold to suppress red blood cell sickling. Additionally, HbF increase in the first patient was highly pancellular, with F cells steadily increasing to reach greater than 95% of red blood cells. EDIT-301 was well-tolerated in the two patients and demonstrated a safety profile consistent with myeloablative conditioning with busulfan and autologous HSC transplant. No serious adverse events occurred, and no adverse events reported were related to treatment with EDIT-301.

In December 2021, the FDA cleared our IND application for our Phase 1/2 EDITHAL clinical trial of EDIT-301 for the treatment of TDT. This trial is designed to assess the safety, tolerability, and preliminary efficacy of EDIT-301 for the treatment of TDT.

We have increased our investment in our EDIT-301 program to expand our editing capacity and accelerate clinical trial enrollment and dosing. We are also activating additional trial sites and continue to screen patients. After completing sequential dosing of the first two patients, we have commenced parallel patient dosing in the RUBY trial and are on track to dose 20 total patients by the end of 2023. We expect to provide clinical updates from the RUBY trial in mid-2023 and end of 2023. We also are on track to dose the first patient in the EDITHAL trial in the first quarter of 2023, and expect to provide data on this patient by the end of 2023.

In Vivo *Gene Editing Medicines*

We seek to additionally develop targeted *in vivo* gene editing medicines, initially focused on HSCs but expanding to other organs and tissues in the future. Initial clinical data from our *ex vivo* EDIT-301 program demonstrated successful hemoglobin induction, creating a foundation for development of *in vivo* HSC gene editing medicines. We believe that the ability to edit HSCs directly in patients without transplantation will allow the treatment of larger patient populations due to the elimination of the current myeloablative conditioning requirement, enabling access to such a product across health systems with a lower burden on patients and treatment centers. We are also in the discovery stage in developing *in vivo* gene editing medicines for other organs and tissues.

We previously achieved human proof of concept for our most advanced *in vivo* gene editing medicine for inherited retinal diseases ("IRDs"), EDIT-101. EDIT-101 is designed to treat a specific genetic form of retinal degeneration called Leber congenital amaurosis 10 ("LCA10"), a CEP290-related retinal degenerative disorder. EDIT-101 uses an AAV5 vector to deliver the DNA encoding SaCas9 and two guide RNAs to photoreceptor cells in the eye. In mid-2019, we initiated a Phase 1/2 clinical trial of EDIT-101, referred to as the BRILLIANCE trial, which was designed to assess the safety, tolerability, and efficacy of EDIT-101 in up to five cohorts of patients. In November 2022, we announced clinical data from the trial, including safety and efficacy data from all 14 patients treated in the study to that date. EDIT-101 was tolerated with no ocular serious adverse events or dose-limiting toxicities observed. Most adverse events were mild and expected for subretinal delivery. Three out of 14 treated subjects met a responder threshold having experienced clinically meaningful improvements in best corrected visual acuity and demonstrated consistent improvements in two of the following three additional endpoints: full field sensitivity test, visual function navigation course, or the visual function quality of life. Two of the three responders were homozygous for IVS26 mutation. Despite this proof of concept, we were not able to identify any baseline characteristics of the treatment responder patients that could pre-select a responder patient population other than zygosity, or the degree to which both copies of a chromosome or gene have the same genetic sequence. Since LCA10 patients homozygous for CEP290 IVS26 mutation represent an estimated population of approximately 300 in the United States, we paused further patient enrollment in the trial and determined not to progress the program independently. We have also terminated our AAV IRD platform, including EDIT-103 for the treatment of rhodopsin-assoiated autosomal dominant retinitis pigmentosa, and are seeking to divest those assets.

Partnerships

Through new and existing partnerships, we are also progressing multiple cellular therapy medicines for the treatment of different cancers. In our collaboration with BMS, we are researching and developing engineered alpha-beta T cell therapies to treat solid and liquid tumors leveraging our platform technologies, including Cas9 and AsCas12a. Engineered T cells, including alpha-beta T cells, have shown encouraging clinical activity against multiple cancers, culminating in recent approvals of such therapies in the United States. Because of these promising results, there is significant interest in the medical community in expanding the application of this technology across a broader range of cancers and patients. We believe that our genome editing technology has the potential to improve multiple properties of these alpha-beta T cell therapies. Alpha-beta cells are part of the adaptive immune system and recognize tumors with endogenous alpha-beta T cell receptors or CARs or engineered T cell receptors ("eTCRs"). If we are successful, genome-edited engineered alpha-beta T cells have the potential to significantly expand the types of cancers treatable by CAR/ eTCR alpha-beta T cells and to improve the outcomes of these therapies. Through our collaboration with BMS, we have applied our Cas9 and AsCas12a platform technologies to multiple gene targets in order to improve the efficacy and safety of CAR/eTCR alpha-beta T cells directed against a range of tumor types. In addition, we have optimized

genome editing components and delivery methods compatible with engineered alpha-beta T cell manufacturing methods developed by BMS. To date, this collaboration has resulted in 11 programs. We are also leveraging our AsCas12a technology in a non-exclusive collaboration with Immatics N.V. to advance gamma-delta T cell therapies for the treatment of cancer.

Our Collaborations and Licensing Strategy

BMS Collaboration and License Agreement

In May 2015, we entered into a collaboration and license agreement with Juno Therapeutics, a subsidiary of BMS, for the research and development of engineered T cells with CARs and eTCRs that have been genetically modified to recognize and kill other cells. We and BMS amended and restated this agreement in May 2018 and November 2019 (the "BMS Collaboration Agreement") and, in connection with the amendment and restatement in November 2019, we entered into a license agreement with BMS (such agreement, the "BMS License Agreement," and together with the BMS Collaboration Agreement, the "BMS Agreements"). Under the terms of the BMS Collaboration Agreement, we received an upfront payment of $25.0 million, amendment fees totaling $75.0 million and have received milestone payments totaling $20.0 million, in addition to certain opt-in fees.

The BMS Agreements relate to technology used to edit or modify the genome of a cell in connection with the research, development, manufacture, commercialization or other exploitation of T cells that express or have ever expressed T cell receptor dimers consisting of an alpha (α) chain and a beta (β) chain (such cells, "Alpha-beta T Cells"), and T cells derived from pluripotent stem cells or any other precursor cell (such cells, "Other Derived T Cells"), subject to certain exclusions for certain of our existing obligations. The exploitation of Alpha-beta T Cells and Other Derived T Cells specifically excludes the exploitation of T Cells that express a T cell receptor dimer consisting of a gamma (γ) chain and a delta (δ) chain, which we refer to as gamma-delta T Cells.

During the research term under the BMS Collaboration Agreement, we may research ribonucleoprotein complexes comprising an RNA-guided engineered nuclease paired with an oligonucleotide ("RNP Complexes") that recognize or modulate the expression of up to twenty gene targets selected by BMS (each, a "Research Program") for the purpose of identifying the RNP Complexes that may be used in the creation of potential drug development candidates. The initial research term is five years from the November 2019 effective date of the BMS Collaboration Agreement. BMS may extend the research term for up to two one-year periods upon written notice to us and payment to us of a mid to high single digit million-dollar payment upon each extension. BMS' right to extend the research term for the second one-year period is subject to our consent.

Under the BMS Collaboration Agreement, if BMS elects to opt-in with respect to a Research Program, it shall make a mid-six digit dollar payment to us and we shall amend the BMS License Agreement to include such Research Program by executing a licensed program addendum for such Research Program. Following BMS' opt-in for each program we shall grant to BMS an exclusive (even as to us), royalty-bearing worldwide right and license under specified intellectual property rights to research, develop, manufacture commercialize or otherwise exploit the RNP Complexes in such Research Program to create products containing, incorporating, comprising or containing Alpha-beta T Cells and/or Other Derived T Cells, in each case modified using the RNP Complexes in such Research Program (each, a "BMS Licensed Product").

We are entitled to receive high single-digit to low double-digit percentage royalties on net sales made by BMS, its affiliates and sublicensees of any BMS Licensed Products, subject to reductions in certain circumstances. We are also entitled to receive development milestones totaling up to $135.0 million in the aggregate upon achievement of certain clinical milestones and specified regulatory approvals and commercial milestone payments totaling up to $60.0 million in the aggregate for each of the first two BMS Licensed Products to achieve specified net sales milestones.

We have agreed during the term of the BMS Collaboration Agreement not to use (directly or indirectly), or license others to use, genome editing technology in connection with any research, development, manufacture, commercialization or other exploitation of any Alpha-beta T Cells or Other Derived T Cells. Our exclusivity obligation will not apply to activities related to (i) any identified RNP Complexes in a program for which BMS elects not to

exercise its opt-in right, (ii) certain of our existing obligations to third parties, and (iii) certain existing programs of an acquiror of our company in a change of control.

We have agreed during the term of any licensed program addendum under the BMS License Agreement not to use (directly or indirectly), or license others to use, any genome editing technology that modulates or recognizes a gene target covered by such licensed program addendum for the conduct of any research, development, manufacture, commercialization or other exploitation with respect to any product that constitutes, incorporates, comprises or contains any Alpha-beta T Cell or Other Derived T Cells.

The BMS Collaboration Agreement continues in effect until the later of expiration of the research term or expiration of the last to expire of BMS' right to opt-in with respect to any Research Program. BMS may terminate the BMS Collaboration Agreement in its discretion upon six months' prior written notice to us. Either party may terminate the BMS Collaboration Agreement for uncured material breach of the other party, provided that the breaching party has had sixty days to cure such breach, or in the event of insolvency or bankruptcy of the other party.

The BMS License Agreement continues in effect on a BMS Licensed Product-by-BMS Licensed Product and country-by-country basis until the expiration of the royalty term with respect to such licensed product in such country and in its entirety upon the expiration of all royalty terms with respect to all BMS Licensed Products in all countries. BMS may terminate the BMS License Agreement in its entirety or on a BMS Licensed Product-by-BMS Licensed Product basis in its discretion upon ninety days' prior written notice to us. Either party may terminate the BMS License Agreement on a BMS Licensed Product-by-BMS Licensed Product basis in the event of an uncured material breach of the other party, provided that the breaching party has had sixty days to cure such breach, or in the event of insolvency or bankruptcy of the other party. We have the right to terminate the BMS License Agreement on a program-by-program basis in the event that BMS fails to make any undisputed payment to us and has not cured such payment breach within the cure period. Other than BMS' right to wind-down its operations with respect to BMS Licensed Products during the twelve months following the date of effectiveness of termination, all licenses and other exclusive rights granted under the BMS License Agreement shall terminate.

Allergan Agreement

In March 2017, we entered into a strategic alliance and option agreement with Allergan Pharmaceuticals International Limited (together with its affiliates, "Allergan") to discover, develop, and commercialize new gene editing medicines for a range of ocular disorders. Pursuant to this agreement, we granted Allergan an exclusive option to exclusively license from us up to five collaboration development programs for the treatment of ocular disorders.

Allergan was acquired by AbbVie Inc. in May 2020. On August 5, 2020, we entered into a termination agreement with Allergan pursuant to which, among other things, we and Allergan terminated the strategic alliance and option agreement and the co-development and commercialization agreement. As a result of the termination of our collaboration with Allergan, we regained full global rights to research, develop, manufacture, and commercialize our ocular product candidates, including EDIT-101 for the treatment of LCA10. Under the termination agreement, Allergan granted us a non-exclusive, royalty-bearing right and license, including the right to grant sublicenses (through multiple tiers), to certain Allergan know-how that is necessary to develop, manufacture and commercialize EDIT-101. In addition, we are obligated to use commercially reasonable efforts to develop and commercialize a product directed to each of four collaboration targets, one of which is LCA10. Under this agreement, we will make certain payments on achievements of clinical and regulatory milestones up to $20.0 million for each target program and aggregated sales milestones for all products covered by the termination agreement up to $90.0 million. We are also obligated to pay royalties in a low-single digit percentage, subject to reduction under specified circumstances, on net sales of specified products. Our obligation to pay royalties will expire on a country-by-country and product-by-product basis upon the later of the expiration of regulatory-based exclusivity with respect to such product in such country and the tenth anniversary of the first commercial sale of such product.

Intellectual Property Licenses

We are a party to a number of license agreements under which we license patents, patent applications, and other intellectual property from third parties. The licensed intellectual property covers, in part, CRISPR-related compositions of matter and their use for genome editing. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. We consider the following license agreements to be material to our business.

The Broad Institute and President and Fellows of Harvard College License Agreement

In October 2014, we entered into a license agreement with The Broad Institute, Inc. ("Broad") and the President and Fellows of Harvard College ("Harvard"), for specified patent rights. In December 2016, we amended and restated this license agreement and further amended the agreement in March 2017 (as amended, the "Cas9-I License Agreement"). Among other things, the Cas9-I License Agreement amended the original license agreement by excluding additional fields from the scope of the exclusive license granted to us; converting the exclusive license to three specified targets to a non-exclusive license, subject to specified limitations; revising certain provisions relating to the rights of Harvard and Broad to grant further licenses under specified circumstances to third parties that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of our exclusive license; and providing Harvard and Broad with certain rights to designate, and reserve all rights to, gene targets for which the designating institution has an interest in researching and developing products that would otherwise be covered by rights licensed to us. The licenses granted to us under the Cas9-I License Agreement include rights to certain patents solely owned by Harvard (the "Harvard Cas9-I Patent Rights"), certain patents co-owned by the Massachusetts Institute of Technology ("MIT") and Broad, certain patents co-owned by MIT, The Rockefeller University ("Rockefeller"), and Broad, and certain patents co-owned by MIT, Broad and Harvard. We refer to all the patents and patent applications licensed to us under the Cas9-I License Agreement as the Harvard/Broad Cas9-I Patent Rights.

Certain patent applications in the Harvard/Broad Cas9-I Patent Rights are jointly owned by Rockefeller. In February 2017, Broad and Rockefeller entered into an inter-institutional agreement pursuant to which Rockefeller authorized Broad to act as its sole and exclusive agent for the purposes of licensing Rockefeller's rights in such Harvard/Broad Cas9-I Patent Rights and any additional related patents or patent applications that Rockefeller may jointly own with Broad. The March 2017 amendment to the Cas9-I License Agreement included a license to Rockefeller's rights in such patents and patent applications.

The Harvard/Broad Cas9-I Patent Rights are directed, in part, to certain CRISPR/Cas9 compositions of matter and their use for genome editing and to certain CRISPR/Cas9 related delivery technologies. Pursuant to the Cas9-I License Agreement, and as of December 31, 2022, we have certain rights under 71 U.S. patents, 50 pending U.S. patent applications, 33 European patents and related validations, 23 pending European patent applications, and other related patent applications in jurisdictions outside of the United States and Europe.

Pursuant to the Cas9-I License Agreement, Harvard and Broad granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the Harvard/Broad Cas9-I Patent Rights to make, have made, use, sell, offer for sale, have sold, import, and export products and services in the field of the prevention and treatment of human disease, subject to certain limitations and retained rights. The exclusive license granted by Broad and Harvard excludes certain fields, including the modification of animals or animal cells for the creation and sale of organs suitable for xenotransplantation into humans; the research, development and commercialization of products or services in the field of livestock applications; plant-based agricultural products; and, subject to certain limitations, products providing nutritional benefits. Moreover, the license granted by Broad is non-exclusive with respect to the treatment of medullary cystic kidney disease 1 and three other specified targets, subject to the limitation that for such three targets, each of Broad and Harvard is only permitted to grant a non-exclusive license to one third party at a time with respect to each such target within the field of exclusive license granted to us. Harvard and Broad also granted us a non-exclusive, worldwide, royalty-bearing, sublicensable license to the Harvard/Broad Cas9-I Patent Rights for all purposes, with the exception that the non-exclusive license to certain Harvard Cas9-I Patent Rights excludes the modification of animals or animal cells for the creation and sale of organs suitable for xenotransplantation into humans and the development and commercialization of products or services in the field of livestock applications. In addition to the exclusions described

above, the following are excluded from the scope of both the exclusive and non-exclusive licenses granted to us under the Cas9-I License Agreement: human germline modification; the stimulation of biased inheritance of particular genes or traits within a population of plants or animals; the research, development, manufacturing, or commercialization of sterile seeds; and the modification of the tobacco plant with specified exceptions.

We are obligated to use commercially reasonable efforts to research, develop, and commercialize products for the prevention or treatment of human disease under the Cas9-I License Agreement. Also, we are required to achieve certain development milestones within specified time periods for products incorporating the technologies covered by the Harvard/Broad Cas9-I Patent Rights. Harvard and Broad have the right to terminate our license with respect to the Harvard/Broad Cas9-I Patent Rights covering the technology or technologies with respect to which we fail to achieve these development milestones.

The licenses granted by Broad and Harvard to us under the Cas9-I License Agreement are subject to retained rights of the U.S. government in the Harvard/Broad Cas9-I Patent Rights and the rights retained by Broad, Harvard, MIT, and Rockefeller on behalf of themselves and other academic, government and non-profit entities, to practice the Harvard/Broad Cas9-I Patent Rights for research, educational, or teaching purposes. In addition, certain rights granted to us under the Cas9-I License Agreement are further subject to a non-exclusive license to the Howard Hughes Medical Institute for research purposes. Our exclusive license rights also are subject to rights retained by Broad, Harvard, MIT, and Rockefeller any third party to research, develop, make, have made, use, offer for sale, sell, have sold, import or otherwise exploit the Harvard/Broad Cas9-I Patent Rights and licensed products as research products or research tools, or for research purposes.

We have the right to sublicense our licensed rights provided that the sublicense agreement must be in compliance and consistent with the terms of the Cas9-I License Agreement. Any sublicense agreement cannot include the right to grant further sublicenses without the written consent of Broad and Harvard. In addition, any sublicense agreements must contain certain terms, including a provision requiring the sublicensee to indemnify Harvard, Broad, MIT, and Howard Hughes Medical Institute according to the same terms as are provided in the Cas9-I License Agreement and a statement that Broad, Harvard, MIT, and Howard Hughes Medical Institute are intended third party beneficiaries of the sublicense agreement for certain purposes.

Under the agreement, Harvard and Broad also retained rights to grant further licenses under specified circumstances to third parties, other than specified entities, that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of our exclusive license from Harvard and Broad. If a third party requests a license under the Harvard/Broad Cas9-I Patent Rights for the development and commercialization of a product that would be subject to our exclusive license grant from Harvard and Broad under the Cas9-I License Agreement, Harvard and Broad may notify us of the request (the "Cas9-I Third Party Proposed Product Requests"). Our process to address Cas9-I Third Party Proposed Product Requests has been conformed to the same process established in our Cpf1 license agreement described below.

The Cas9-I License Agreement also provides Broad with the right, after a specified period of time and subject to certain limitations, to designate gene targets for which Broad, whether alone or together with an affiliate or third party, has an interest in researching and developing products that would otherwise be covered by rights licensed to us under the Cas9-I License Agreement. Broad may not so designate any gene target for which we, directly or through any of our affiliates, sublicensees, or collaborators, are researching, developing, or commercializing a product, or for which we can demonstrate to Broad's reasonable satisfaction that we are interested in researching, developing, and commercializing a product, that we have a commercially reasonable research, development, and commercialization plan to do so, and we commence and continue reasonable commercial efforts under such plan. If we directly or through any of our affiliates, sublicensees, or collaborators, are not researching, developing, or commercializing a product directed toward the gene target designated by Broad and are not able to develop and implement a plan reasonably satisfactory to Broad, Broad is entitled to reserve all rights under the Cas9-I License Agreement, including the right to grant exclusive or non-exclusive licenses to third parties, to develop and commercialize products directed to such gene target and our license granted with respect to such gene target will terminate, and we will not be entitled under the Cas9-I License Agreement to develop and commercialize products directed to that gene target.

Under the Cas9-I License Agreement, we paid Broad and Harvard an upfront license fee in the low six figures and issued a single-digit percentage of shares of our common stock to Broad (with Broad holding a right to request re-issuance to its designees, including MIT or MIT's designee) and Harvard. We also must pay an annual license maintenance fee ranging from the low- to mid-five figures to the low-six figures, depending on the calendar year. This annual license maintenance fee is creditable against royalties owed on licensed products and services in the same year as the maintenance fee is paid. We are obligated to reimburse Broad and Harvard for expenses associated with the prosecution and maintenance of the Harvard/Broad Cas9-I Patent Rights, including expenses associated with any interference proceedings in the USPTO, any opposition proceedings in the EPO, or any other *inter partes* or other post grant proceedings in these or other jurisdictions where we are seeking patent protection. Therefore, we are obligated to reimburse Broad and/or Harvard for expenses associated with the interference and opposition proceedings involving patents licensed to us under this agreement (described in more detail under "Risk Factors—Risks Related to Our Intellectual Property—Some of Our In-Licensed Patents are Subject to Priority and Validity Disputes" in Part I, Item 1A of this Annual Report on Form 10-K).

Broad and Harvard are collectively entitled to receive clinical and regulatory milestone payments totaling up to $14.8 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. If we undergo a change of control during the term of the Cas9-I License Agreement, these clinical and regulatory milestone payments will be increased by a certain percentage in the mid double-digits. We are also obligated to make additional payments to Broad and Harvard, collectively, of up to an aggregate of $54.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. Broad and Harvard are collectively entitled to receive clinical and regulatory milestone payments totaling up to $4.1 million in the aggregate per licensed product approved in the United States and at least one jurisdiction outside the United States for the prevention or treatment of a human disease that afflicts fewer than a specified number of patients in the aggregate in the United States or a specified number of patients per year in the United States, which we refer to as an ultra-orphan disease. We are also obligated to make additional payments to Broad and Harvard, collectively, of up to an aggregate of $36.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of an ultra-orphan disease.

Broad and Harvard, collectively, are entitled to receive mid single-digit percentage royalties on net sales of licensed products for the prevention or treatment of human disease, and ranging from low single-digit to high single-digit percentage royalties on net sales of other licensed products and services, made by us, our affiliates, or our sublicensees. The royalty percentage depends on the licensed product and licensed service, and whether such licensed product or licensed service is covered by a valid claim within the Harvard/Broad Cas9-I Patent Rights. If we are legally required to pay royalties to a third party on net sales of our licensed products because such third party holds patent rights that cover such licensed product, then we can credit up to a mid double-digit percentage of the amount paid to such third party against the royalties due to Harvard and Broad in the same period. Our obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the Harvard/Broad Cas9-I Patent Rights that cover the composition, manufacture, or use of each covered product or service in each country or the tenth anniversary of the date of the first commercial sale of the licensed product or licensed service. If we sublicense any of the Harvard/Broad Cas9-I Patent Rights to a third party pursuant to our exclusive license under the Cas9-I License Agreement, Broad and Harvard, collectively, had the right to receive a low to mid double-digit percentage of the sublicense income, which percentage decreased to a low double-digit percentage in 2018 and may still decrease to a low of a high single-digit percentage for licensed products for the prevention or treatment of human disease under sublicenses executed after we meet a certain clinical milestone.

Broad and Harvard retain control of the prosecution of their respective patent rights. If an interference is declared or a derivation proceeding is initiated, with respect to any Harvard/Broad Cas9-I Patent Rights, then our prosecution related rights, including our right to receive correspondence from a patent office, will be suspended with respect to the patent rights involved in the interference or derivation proceeding until, under some circumstances, we enter into a common interest agreement with that institution. Nevertheless, we remain responsible for the cost of such interference or derivation proceeding. We are responsible for the cost of the interference proceeding and appeal with respect to these patents and this patent application. Broad and Harvard are required to maintain any application or patent within the Harvard/Broad Patents Rights so long as we meet our obligation to reimburse Broad and Harvard for expenses

related to prosecution and there is a good faith basis for doing so. If we cease payment for the prosecution of any Harvard/Broad Patent Right, then any license granted to us with respect to such Harvard/Broad Patent Right will terminate.

We have the first right, but not the obligation, to enforce the Harvard/Broad Cas9-I Patent Rights with respect to our licensed products so long as certain conditions are met, such as providing Broad and Harvard with evidence demonstrating a good faith basis for bringing suit against a third party. We are solely responsible for the costs of any lawsuits we elect to initiate and cannot enter into a settlement without the prior written consent of Broad and Harvard (and MIT and Rockefeller, if applicable). Any sums recovered in such lawsuits will be shared between us, Broad, and Harvard.

Unless terminated earlier, the term of the Cas9-I License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Harvard/Broad Cas9-I Patent Rights in such country. However, our royalty obligations, discussed above, may survive expiration or termination. We have the right to terminate the agreement at will upon four months' written notice to Broad and Harvard. Broad and Harvard may terminate the agreement upon a specified period of notice in the event of our uncured material breach, such notice period varying depending on the nature of the breach. Both Broad and Harvard may terminate the Cas9-I License Agreement immediately if we challenge the enforceability, validity, or scope of any Harvard/Broad Patent Right or assist a third party to do so, or in the event of our bankruptcy or insolvency. Neither Broad nor Harvard acting alone has the right to terminate the Cas9-I License Agreement. However, Broad and Harvard may separately terminate the licenses granted to us with respect to their respective patent rights upon the occurrence of the same events that would give rise to the right of both institutions acting collectively to terminate the Cas9-I License Agreement.

The Broad Institute—Cpf1 License Agreement

In December 2016, we entered into a license agreement with Broad, for specified patent rights ("Cpf1 Patent Rights") related primarily to Cas12a compositions of matter and their use for gene editing (as amended, the "Cpf1 License Agreement"). Pursuant to the Cpf1 License Agreement, Broad, on behalf of itself, Harvard, MIT, Wageningen University ("Wageningen"), and the University of Tokyo ("Tokyo" and collectively with the other institutions, the "Cpf1 Institutions") granted us an exclusive, worldwide, royalty-bearing, sublicensable license to the Cpf1 Patent Rights, to make, have made, use, have used, sell, offer for sale, have sold, export and import products solely in the field of the prevention or treatment of human disease using gene therapy, editing of genetic material, or targeting of genetic material, subject to certain limitations and retained rights (collectively, the "Exclusive Cpf1 Field"), as well as a non-exclusive, worldwide, royalty-bearing, sublicensable license to the Cpf1 Patent Rights for all other purposes, subject to certain limitations and retained rights. The licenses granted to us under the Cpf1 License Agreement exclude certain fields, including human germline modification; the stimulation of biased inheritance of particular genes or traits within a population of plants or animals; the research, development, manufacturing, or commercialization of sterile seeds; and the modification of the tobacco plant with specified exceptions.

Tokyo and the National Institute of Health ("NIH") are joint owners on certain Cpf1 Patent Rights. Broad has only granted a license to us with respect to its interests and to Tokyo's interests in these U.S. patent applications but not to any foreign equivalents thereof. Broad does not, and does not purport to, grant any rights in NIH's interest in these U.S. patent applications under our agreement. As a result, we may not have exclusive rights under any U.S. patents that issue from these U.S. patent applications and we may not have any rights under any foreign patents that issue from any foreign equivalents thereof.

Pursuant to the Cpf1 License Agreement, and as of December 31, 2022, we have certain rights under 7 U.S. patents, 12 pending U.S. patent applications, 5 European patents and related validations, 6 pending European patent applications, and other related patent applications in jurisdictions outside of the United States and Europe.

We are obligated to use commercially reasonable efforts to research, develop, and commercialize licensed products in the Exclusive Cpf1 Field. We are also required to achieve certain development milestones within specified time periods for products covered by the Cpf1 Patent Rights, with Broad having the right to terminate the Cpf1 License Agreement if we fail to achieve these milestones within the required time periods. We have the right to sublicense our

licensed rights provided that the sublicense agreement must be in compliance and consistent with the terms of the Cpf1 License Agreement. Any sublicense agreement cannot include the right to grant further sublicenses without the written consent of Broad. In addition, any sublicense agreements must contain certain terms, including a provision requiring the sublicensee to indemnify the Cpf1 Institutions according to the same terms as are provided in the Cpf1 License Agreement and a statement that the Cpf1 Institutions are intended third party beneficiaries of the sublicense agreement for certain purposes.

The licenses granted to us under the Cpf1 License Agreement are subject to retained rights of the U.S. government in the Cpf1 Patent Rights and rights retained by the Cpf1 Institutions on behalf of themselves and other academic, government and non-profit entities, to practice the Cpf1 Patent Rights for research, teaching, or educational purposes. Our exclusive license rights also are subject to rights retained by the Cpf1 Institutions for themselves and any third party to research, develop, make, have made, use, offer for sale, sell, have sold, import or otherwise exploit the Cpf1 Patent Rights and licensed products as research products or research tools, or for research purposes.

Under the Cpf1 License Agreement, Broad also retained rights to grant further licenses under specified circumstances to third parties that wish to develop and commercialize products that target a particular gene and that otherwise would fall within the scope of our exclusive license from Broad. If a third party requests a license under the Cpf1 Patent Rights for the development and commercialization of a product that would be subject to our exclusive license grant from Broad (a "Cpf1 Third Party Proposed Product Request"), Broad may notify us of such request. A Cpf1 Third Party Proposed Product Request must be accompanied by a research, development and commercialization plan reasonably satisfactory to Broad, including evidence that the third party has, or reasonably expects to have, access to any necessary intellectual property and funding. Broad may not grant a Cpf1 Third Party Proposed Product Request (i) if we, directly or through any of our affiliates, sublicensees, or collaborators are researching, developing, or commercializing a product directed to the same gene target that is the subject of the Cpf1Third Party Proposed Product Request ("Cpf1 Licensee Product") and we can demonstrate such ongoing efforts to Broad's reasonable satisfaction, or (ii) if we, directly or through any of our affiliates or sublicensees, wish to do so either alone or with a collaboration partner, and we can demonstrate to Broad's reasonable satisfaction that we are interested in researching, developing, and commercializing a Cpf1 Licensee Product, that we have a commercially reasonable research, development, and commercialization plan to do so, and we commence and continue reasonable commercial efforts under such plan. If we, directly or through any of our affiliates, sublicensees, or collaborators, are not researching, developing, or commercializing a Cpf1 Licensee Product nor able to develop and implement a plan reasonably satisfactory to Broad, Broad may grant an exclusive or non-exclusive license to the third party on a gene target-by-gene target basis.

The Cpf1 License Agreement also provides Broad with the right, subject to certain limitations, to designate gene targets for which Broad, whether alone or together with a Cpf1 Institution, affiliate or third party, has an interest in researching and developing products that would otherwise be covered by rights licensed to us under the Cpf1 License Agreement. Broad may not so designate any gene target for which we, directly or through any of our affiliates, sublicensees, or collaborators, are researching, developing, or commercializing a product, or for which we can demonstrate to Broad's reasonable satisfaction that we are interested in researching, developing, and commercializing a product, that we have a commercially reasonable research, development, and commercialization plan to do so, and we commence and continue reasonable commercial efforts under such plan. If we, directly or through any of our affiliates, sublicensees, or collaborators, are not researching, developing, or commercializing a product directed toward the gene target designated by Broad and are not able to develop and implement a plan reasonably satisfactory to Broad, Broad is entitled to reserve all rights under the Cpf1 License Agreement, including the right to grant exclusive or non-exclusive licenses to third parties, to develop and commercialize products directed to such gene target, our license with respect to such gene target will terminate, and we will not be entitled under the Cpf1 License Agreement to develop and commercialize products directed to such gene target.

Under the Cpf1 License Agreement, we paid Broad and Wageningen an aggregate upfront license fee in the mid seven digits and issued to Broad and Wageningen promissory notes (the "Initial Promissory Notes") in an aggregate principal amount of $10.0 million, which we settled in full in 2017. Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to $20.0 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. If we undergo a change of control

during the term of the Cpf1 License Agreement, certain of these clinical and regulatory milestone payments will be increased by a certain percentage in the mid double-digits. We are also obligated to make additional payments to Broad and Wageningen, collectively, of up to an aggregate of $54.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of a human disease that afflicts at least a specified number of patients in the aggregate in the United States. Broad and Wageningen are collectively entitled to receive clinical and regulatory milestone payments totaling up to $6.0 million in the aggregate per licensed product approved in the United States, the European Union and Japan for the prevention or treatment of an ultra-orphan disease. We are also obligated to make additional payments to Broad and Wageningen, collectively, of up to an aggregate of $36.0 million upon the occurrence of certain sales milestones per licensed product for the prevention or treatment of an ultra-orphan disease.

Broad and Wageningen, collectively, are entitled to receive mid single-digit percentage royalties on net sales of products for the prevention or treatment of human disease, and ranging from sub single-digit to high single-digit percentage royalties on net sales of other products and services, made by us, our affiliates, or our sublicensees. The royalty percentage depends on the product and service, and whether such licensed product or licensed service is covered by a valid claim within the Cpf1 Patent Rights. If we are legally required to pay royalties to a third party on net sales of our products because such third party holds patent rights that cover such licensed product, then we can credit up to a mid double-digit percentage of the amount paid to such third party against the royalties due to Broad and Wageningen in the same period. Our obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the Cpf1 Patent Rights that covers each licensed product or licensed service in each country or the tenth anniversary of the date of the first commercial sale of the product or service. If we sublicense any of the Cpf1 Patent Rights to a third party, Broad and Wageningen, collectively, have the right to receive high single-digit to low double-digit percentages of the sublicense income, depending on the stage of development of the products or services in question at the time of the sublicense.

Under the Cpf1 License Agreement, Broad and Wageningen are also entitled, collectively, to receive success payments in the event our market capitalization reaches specified thresholds ascending from a high nine digit dollar amount to $10.0 billion ("Market Cap Success Payments") or sale of our company for consideration in excess of those thresholds, ("Company Sale Success Payments," which with the Market Cap Success Payments, the "Success Payments"). Market Cap Success Payments are payable by us in cash, in shares of our common stock, with such shares being valued for such purpose at the closing price of our common stock as reported the Nasdaq Stock Market for the trading day immediately preceding the date of such payment if our common stock was then listed on the Nasdaq Stock Market, or in the form of promissory notes (the "Promissory Notes"). The Promissory Notes bear interest at 4.8% per annum. Principal and interest on the Promissory Notes are payable on, subject to certain exceptions, 150 days following issuance (or if earlier, a specified period of time following a sale of our company). We could elect to make any payment of amounts outstanding under the Promissory Notes either in the form of cash or, subject to certain conditions, in shares of our common stock of equal value, with such shares being valued for such purpose at the closing price of our common stock as reported the Nasdaq Stock Market for the trading day immediately preceding the date of such payment if our common stock was then listed on the Nasdaq Stock Market. In the event of a change of control of our company or a sale of our company, we are required to pay all remaining principal and accrued interest on the Promissory Notes in cash within a specified period following such event. Following a change in control of our company, Market Cap Success Payments are required to be made in cash. Company Sale Success Payments are payable solely in cash. In 2017, two Market Cap Success Payments of $5.0 million each became due and payable and we issued Promissory Notes in such amounts, which we fully settled by issuing shares of our common stock in 2017 and 2018. In December 2020, an additional Market Cap Success Payment of $15.0 million became due and payable, which we settled through the issuance of shares of our common stock in January 2021. The remaining Success Payments that may be paid to Broad and Wageningen range from a low-eight digit dollar amount to a mid-eight digit dollar amount, and collectively will not exceed, in aggregate, $100.0 million, which maximum would be payable only if we achieve a market capitalization threshold of $10.0 billion and have at least one product candidate covered by a claim of a patent right licensed to us under either the Cpf1 License Agreement or the Cas9-I License Agreement that is or was the subject of a clinical trial pursuant to development efforts by us or any of our affiliates or sublicensees.

In addition, in the event that a sale of our company or change of control has occurred and the maximum amount of potential Success Payments under the Cpf1 License Agreement has not been paid to Broad and Wageningen, Broad and Wageningen are entitled to receive, upon the subsequent achievement of specified regulatory milestones,

percentages ranging from high single digits to mid-to-low double digits of the remaining unpaid maximum amount of Success Payments. Broad and Wageningen are further entitled to receive up to the full remaining unpaid maximum amount of Success Payments upon the subsequent achievement of specified sales milestones. All such post-sale or post-change of control milestone payments are required to be made in cash.

Broad retains control of the prosecution and maintenance of the Cpf1 Patent Rights. We have the right to provide input in the prosecution of the Cpf1 Patent Rights, including to direct Broad to file and prosecute patents in certain countries. We are also obligated to reimburse Broad and Wageningen for all unreimbursed expenses incurred by them in connection with the prosecution and maintenance of the Cpf1 Patent Rights prior to the date of the Cpf1 License Agreement, and to reimburse Broad for expenses associated with the prosecution and maintenance of the Cpf1 Patent Rights following the date of the Cpf1 License Agreement.

We have the first right, but not the obligation, to enforce the Cpf1 Patent Rights with respect to our licensed products in the Exclusive Cpf1 Field so long as certain conditions are met, such as providing Broad and the applicable Cpf1 Institutions with evidence demonstrating a good faith basis for bringing suit against a third party. We are solely responsible for the costs of any lawsuits we elect to initiate and cannot enter into a settlement without the prior written consent of Broad. Any sums recovered in such lawsuits will be shared between Broad, Wageningen, and us.

Unless terminated earlier, the term of the Cpf1 License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the Cpf1 Patent Rights in such country. However, our royalty obligations, discussed above, may survive expiration or termination. We have the right to terminate the Cpf1 License Agreement at will upon four months' written notice to Broad. Either party may terminate the Cpf1 License Agreement upon a specified period of notice in the event of the other party's uncured material breach of a material obligation, such notice period varying depending on the nature of the breach. Broad may terminate the Cpf1 License Agreement immediately if we challenge the enforceability, validity, or scope of any Cpf1 Patent Right or assist a third party to do so, or in the event of our bankruptcy or insolvency.

Other Broad Agreements

In addition to the Cas9-I License Agreement and the Cpf1 License Agreement, in December 2016, we entered into a license agreement with Broad for certain Cas9 compositions of matter and their use for gene editing (the "Cas9-II Agreement"), and, in December 2018, we entered into a Sponsored Research Agreement with Broad providing for Broad to conduct research useful or relevant to genome editing in the field of genomic medicines for the prevention of treatment of human diseases with funding from us (the "Sponsored Research Agreement"). Under the Cas9-II Agreement and the Sponsored Research Agreement, we have potential obligations with respect to success payments, which are described in Note 8 to the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K.

Intellectual Property

Our success depends in part on our ability to obtain and maintain proprietary protection for our platform technology, programs, and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets, and operate without infringing valid and enforceable intellectual property rights of others. We seek to protect our proprietary position by, among other things, exclusively licensing and filing U.S. and certain foreign patent applications related to our platform technology, existing and planned programs, and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know-how, continuing technological innovation, and confidential information to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We seek to protect our proprietary technology and processes, in part, by 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.

Our in-licensed patents and patent applications cover various aspects of our genome editing platform technology, including CRISPR systems that employ Cas9 including *S. aureus* Cas9, high-fidelity Cas9 nucleases and Cas9 PAM variants, self-inactivating forms of Cas9, Cas9 nickases, CRISPR systems that employ Cas12a including Cas12a nickases and other variants and self-inactivating forms of Cas12a, and also CRISPR systems that employ viral vectors for delivery, single guide RNAs, or modified guide RNAs, including guide nucleic acids containing both DNA and RNA components. We also have filed patent applications and have in-licensed rights to filed patent applications directed to each of the four components of our genome editing platform technology. We intend to pursue, when possible, additional patent protection, including composition of matter, method of use, and process claims, directed to each component of our platform technology. We also intend to obtain rights to existing delivery technologies through one or more licenses from third parties.

Notwithstanding these efforts, we cannot be sure that patents will be granted with respect to any patent applications we have licensed or filed or may license or file in the future, and we cannot be sure that any patents we have licensed or patents that may be licensed or granted to us in the future will not be challenged, invalidated, or circumvented or that such patents will be commercially useful in protecting our technology. Moreover, trade secrets can be difficult to protect. While we have confidence in the measures we take to protect and preserve our trade secrets, such measures can be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. For more information regarding the risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property."

The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984 extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug or a method for using it may be extended.

CRISPR

As of December 31, 2022, we owned 24 U.S. patents, 69 pending U.S. non-provisional patent applications, 14 European patents and related validations, 63 pending European patent applications, 10 pending U.S. provisional patent applications, seven pending PCT patent applications, and other related patent applications in jurisdictions outside the United States and Europe that are related to our CRISPR technology and which include claims directed to our genome editing platform, including our directed editing component, as well as composition of matter and method of use claims for our therapeutic programs. Four of these U.S. patents, one of these European patents and their U.S., European and foreign counterpart applications are co-owned with Broad and Iowa and we have obtained an exclusive license to such co-ownership rights from these third parties in the field of prevention or treatment of human disease using gene therapy or genome editing. In addition, 13 of these pending U.S. non-provisional patent applications are co-owned with certain of our collaborators because they encompass inventions developed under our collaborations. Our current issued U.S. patents, if the appropriate maintenance fees are paid, are expected to expire between 2034 and 2038, excluding any additional term for patent term adjustments or patent term extensions. If issued as U.S. patents, and if the appropriate maintenance fees are paid, the U.S. patent applications would be expected to expire between 2035 and 2042, excluding any additional term for patent term adjustments or patent term extensions.

As of December 31, 2022, we in-licensed 114 U.S. patents, 54 European patents and related validations, and approximately 430 pending patent applications, including 86 pending U.S. non-provisional patent applications, 52 pending European patent applications, and other related patents and patent applications in jurisdictions outside the United States and Europe that are related to our CRISPR technology collectively from various universities and institutions. The patents and patent applications outside of the United States and Europe are held primarily in Canada, Japan, and Australia, although some of our in-licensed patent families were filed in a larger number of countries. The claims from our in-licensed portfolio include claims to compositions of matter, methods of use, and certain processes.

These include claims directed to CRISPR systems that employ Cas9 including Cas9 nickases, *S. aureus* Cas9, high-fidelity Cas9 nucleases, Cas9 PAM variants and self-inactivating forms of Cas9, CRISPR systems that employ Cas12a including Cas12a nickases and other variants and self-inactivating forms of Cas12a, and also CRISPR systems that employ viral vectors for delivery, single guide RNAs, or modified guide RNAs. Our current in-licensed U.S. patents, if the appropriate maintenance fees are paid, are expected to expire between 2033 and 2037, excluding any additional term for patent term adjustments or patent term extensions. If issued as U.S. patents, and if the appropriate maintenance fees are paid, the U.S. patent applications would be expected to expire between 2034 and 2037, excluding any additional term for patent term adjustments or patent term extensions.

Our in-licensed patents and patent applications claim the inventions of investigators at various universities and institutions and the majority of these licensed patents and patent applications are licensed on an exclusive basis. The exclusive licenses are, in some cases, limited to certain technical fields. Certain U.S. patent applications licensed to us by Broad include Tokyo and NIH as joint applicants. Broad has only granted a license to us with respect to its interests and to Tokyo's interests in these U.S. patent applications but not to any foreign equivalents thereof. Broad does not and does not purport to grant any rights in NIH's interest in these U.S. patent applications under our agreement. As a result, we may not have exclusive rights under any U.S. patents that issue from these U.S. patent applications and we may not have any rights under any foreign patents that issue from any foreign equivalents thereof. For more information regarding these license agreements, please see the section of this Annual Report on Form 10-K titled "Business —Intellectual Property Licenses."

Trademarks

As of December 31, 2022, our registered trademark portfolio consisted of registrations in the United States for EDITAS, EDITAS in Stylized Letters and the Infinity Logo, registrations in Australia, China, the European Union, Japan, Switzerland and the United Kingdom for EDITAS, registrations in Australia, China, the European Union, Japan, Switzerland and the United Kingdom for the Infinity Logo, registrations in the European Union and United Kingdom for UDITAS, registrations in the European Union, Switzerland and the United Kingdom for SLEEK, and registrations in Australia, the European Union and United Kingdom for the Double Helix Design.

Competition

The biotechnology and pharmaceutical industries, including in the gene therapy, genome editing and cell therapy fields, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, development experience, and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical, biotechnology companies, governmental agencies, and public and private research institutions. Any product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology, and other related markets that utilize technologies encompassing genomic medicines to create therapies, including genome editing and gene therapy. There are additional companies that are working to develop therapies in areas related to our research programs. Our platform and product focus is the development of therapies using CRISPR technology specifically for genome editing. Other companies developing CRISPR Cas9 or Cas12a technology or therapies using CRISPR Cas9 or Cas12a technology include Artisan Bio, Caribou Biosciences, CRISPR Therapeutics, EdiGene, ERS Genomics, Excision Biotherapeutics, Graphite Bio, Inscripta, Intellia Therapeutics, Sigma-Aldrich, ToolGen, and Vertex Pharmaceuticals. In addition, there have been and may continue to be discoveries of new CRISPR-based gene editing technologies. There are additional companies developing therapies using related CRISPR genome editing technologies, including other CRISPR nucleases, base editing, prime editing and gene writing. These companies include Arbor Biotechnologies, Beam Therapeutics, Chroma Medicine, Emendo Biotherapeutics, Integra Therapeutics, KSQ Therapeutics, Locus Biosciences, Mammoth Biosciences, Metagenomi, Poseida Therapeutics, Prime Medicine, Scribe Therapeutics, Tessera Therapeutics, Tome Biosciences, Tune Therapeutics, and Verve Therapeutics. There are also companies developing therapies using transcription activator-like effector nucleases, meganucleases, Mega-TALs and zinc finger nucleases. These companies include 2Seventy Bio, Allogene Therapeutics, bluebird bio, Cellectis, Precision Biosciences, and Sangamo Therapeutics.

In addition to competition from other genome editing therapies, gene therapies or cell medicine therapies, any products that we may develop may also face competition from other types of therapies, such as small molecule, antibody, protein, oligonucleotide, or ribonucleic acid therapies. There are also companies developing therapies related to our development programs. For hemoglobinopathies, these companies include Acceleron Pharma, Aruvant Therapeutics, Beam Therapeutics, bluebird bio, Cellectis, CRISPR Therapeutics, EdiGene, Global Blood Therapeutics, Graphite Bio, Intellia Therapeutics, Novartis Pharmaceuticals, Sangamo Therapeutics, and Vertex Pharmaceuticals.

In addition, many of our current or potential competitors, either alone or with their collaboration partners, may have greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety, convenience, and availability of reimbursement.

If our current programs are approved for the indications for which we are currently planning clinical trials, they may compete with other products currently under development, including genome editing and gene therapy products. Competition with other related products currently under development may include competition for clinical trial sites, patient recruitment, and product sales.

Manufacturing

We currently perform some manufacturing activities such as the production of RNP Complexes for our various internal programs, as well as cell processing for EDIT-301. We may also agree to produce RNP Complexes for our partners. These activities are performed on site at our existing facilities or at current good manufacturing practice-compliant space leased by us. We contract with third parties for the manufacturing of all other materials for preclinical studies and our clinical trials. We have limited manufacturing operations and do not own or operate any substantial manufacturing facilities for large-scale production of our program materials. While we have limited early-phase clinical manufacturing capabilities, we currently have no plans to build our own late-stage clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing and reliance on collaboration partners is relatively cost-efficient and has eliminated the need for substantial direct investment in manufacturing facilities and additional staff early in development. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee our contract manufacturers. We expect third-party manufacturers to be capable of providing sufficient quantities of our program materials to meet anticipated needs for preclinical studies and clinical trials. To meet our projected needs for commercial manufacturing, third parties with whom we currently work might need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our preclinical, clinical, and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

Commercialization

We currently intend to build the commercial infrastructure in the United States and Europe necessary to effectively support the commercialization of all of our programs, if and when we first believe a regulatory approval of a product candidate under one of our programs in a particular geographic market appears probable. The commercial infrastructure for orphan products typically consists of a targeted, specialty sales force that calls on a limited and focused

group of physicians supported by sales management, medical liaisons, internal sales support, an internal marketing group, and distribution support.

Additional capabilities important to the orphan marketplace include the management of key accounts such as managed care organizations, group purchasing organizations, specialty pharmacies, and government accounts. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any product candidate we may develop will be approved.

Outside of the United States and Europe, where appropriate, we may elect in the future to utilize strategic partners, distributors, or contract sales forces to assist in the commercialization of our products. In certain instances, we may consider building our own commercial infrastructure.

As product candidates advance through our pipeline, our commercial plans may change. In particular, some of our research programs target potentially larger indications. Data, the size of the development programs, the size of the target market, the size of a commercial infrastructure, and manufacturing needs may all influence our strategies in the United States, Europe, and the rest of the world.

Government Regulation and Licensure of Products

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, pricing, reimbursement, sales, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Licensure and Regulation of Biologics in the United States

In the United States, our candidate products would be regulated as biological products, or biologics, under the Public Health Service Act (the "PHSA") and the Federal Food, Drug and Cosmetic Act (the "FDCA") and its implementing regulations and guidances. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and their approval by regulatory authorities, is generally referred to as a sponsor. The failure to comply with the applicable U.S. requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may subject a sponsor to delays in the conduct of the study, regulatory review and approval, and/or administrative or judicial sanctions.

A sponsor seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the FDA's Good Laboratory Practice ("GLP") regulations and standards;

- completion of the manufacture, under current Good Manufacturing Practices ("cGMP") conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;

- design of a clinical protocol and submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;

- approval by an independent institutional review board ("IRB") representing each clinical site before each clinical trial may be initiated;

- performance of adequate and well-controlled human clinical trials to establish the safety, potency, and purity of the product candidate for each proposed indication, in accordance with current Good Clinical Practices ("GCP");

- preparation and submission to the FDA of a Biologic License Application ("BLA") for a biologic product requesting marketing for one or more proposed indications, including submission of detailed information on the manufacture and composition of the product in clinical development and proposed labelling;

- review of the product by an FDA advisory committee, where appropriate or if applicable;

- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, strength, quality, and purity, and, if applicable, the FDA's current good tissue practice ("GTP") for the use of human cellular and tissue products;

- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCPs and the integrity of clinical data in support of the BLA;

- payment of user Prescription Drug User Free Act ("PDUFA") securing FDA approval of the BLA and licensure of the new biologic product; and

- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy ("REMS") and any post-approval studies required by the FDA.

Preclinical Studies and Investigational New Drug Application

Before testing any biologic product candidate in humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential for efficacy and toxicity in animal studies. These studies are generally referred to as IND-enabling studies. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin or recommence.

As a result, submission of the IND may result in the FDA not allowing the trials to commence or allowing the trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the IND process, it may choose to impose a partial or complete clinical hold. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls. This order issued by the FDA would delay either a proposed clinical study or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. This could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational products for patients who may benefit from investigational therapies. FDA regulations allow access to investigational products under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the investigational product under a treatment protocol or treatment IND application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act (the "Cures Act"), passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests, it must make that policy publicly available. Although these requirements were rolled out over time, they have now come into full effect. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the investigational drug or biologic receives designation as a Breakthrough Therapy, Fast Track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its investigational products available to eligible patients as a result of the Right to Try Act.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain regulatory requirements of the FDA in order to use the trial as support for an IND or application for marketing approval. Specifically, the FDA requires that such trials be conducted in accordance with GCP, including review and approval by an independent ethics committee and informed consent from subjects. The GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign trials are conducted in a manner comparable to that required for clinical trials in the United States.

Further, each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects, and the possible liability of the institution. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. These reports must include a development safety update report, or DSUR. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board ("DSMB"). This group may recommend continuation of the study as planned, changes in study conduct, or cessation of the study at designated check points based on certain available data from the study to which only the DSMB has access. Finally, research activities involving infectious agents, hazardous chemicals, recombinant DNA, and genetically altered organisms and agents may be subject to review and approval of an Institutional Biosafety Committee in accordance with NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- *Phase 1* clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion, and pharmacodynamics in healthy humans or, on occasion, in patients, such as patients suffering from LCA10, sickle cell disease or cancer.

- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.

- *Phase 3* clinical trials may proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy, and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a biologic; such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement or to request a change in the product labeling. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

Sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017, and both NIH and the FDA have recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Although the FDA has historically not enforced these reporting requirements due to HHS's long delay in issuing final implementing regulations, those regulations have now been issued and the FDA has issued several Notices of Noncompliance to manufacturers since April 2021.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, a BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

For products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease.

Special Regulations and Guidance Governing Gene Therapy Products

It is possible that the procedures and standards applied to gene therapy products and cell therapy products may be applied to any CRISPR product candidates we may develop, but that remains uncertain at this point. The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material and/or by integrating into the host genome and which are administered as nucleic acids, viruses, or genetically engineered microorganisms. The products may be used to modify cells *in vivo* or transferred to cells *ex vivo* prior to administration to the recipient.

Within the FDA, the Center for Biologics Evaluation and Research ("CBER") regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Cellular, Tissue and Gene Therapies, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The NIH, including its Novel and Exceptional Technology Research Advisory Committee ("NExTRAC"), also advises the FDA on gene therapy issues and other issues related to emerging biotechnologies. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

The FDA has issued various guidance documents regarding gene therapies, including recent final guidance documents released in January 2020 relating to chemistry, manufacturing and controls information for gene therapy INDs, long-term follow-up after the administration of gene therapy products, gene therapies for rare diseases and gene therapies for retinal disorders, as well as draft guidance in January 2021 for Human Gene Therapy for Neurodegenerative Diseases. Although the FDA has indicated that these and other guidance documents it previously issued are not legally binding, compliance with them is likely necessary to gain approval for any gene therapy product candidate. The guidance documents provide additional factors that the FDA will consider at each of the above stages of development and relate to, among other things, the proper preclinical assessment of gene therapies; the chemistry, manufacturing, and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire.

Until 2019, most gene therapy clinical trials required pre-review by the predecessor of NExTRAC before being submitted for approval by the IRBs and any local biosafety boards. In 2019, the NIH eliminated the pre-review process and going forward, the review of future gene therapy clinical trial protocols would be largely handled by IRBs. Furthermore, in 2019, the NIH removed from public access the Genetic Modification Clinical Research Information System database, which previously contained substantial amounts of safety and other patient information regarding human gene therapy studies performed to date.

Compliance with cGMP and GTP Requirements

Before approving a BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

For a gene therapy product, the FDA also will not approve the product if the manufacturer is not in compliance with GTP. These standards are found in FDA regulations and guidances that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products ("HCT/Ps"), which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission, and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether foreign or domestic, is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request,

electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Submission and Filing of a BLA

The results of product candidate development, preclinical testing, and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting license to market the product. The BLA must contain extensive manufacturing information and detailed information on the composition of the product and proposed labeling as well as payment of a user fee. Under federal law, the submission of most BLAs is subject to an application user fee, which for federal fiscal year 2023 is approximately $3.25 million for an application requiring clinical data. The sponsor of a licensed BLA is also subject to an annual program fee, which for fiscal year 2023 is more than $394,000. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In pertinent part, FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor.

On the other hand, once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the sponsor, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests or if the sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with a BLA submission, including component manufacturing (e.g., active pharmaceutical ingredients), finished product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. With passage of FDORA, Congress clarified FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to FDA as well as other persons holding study records or involved in the study process.

In connection with its review of a BLA, the FDA may refer the application to an advisory committee for review, evaluation, and recommendation as to whether the application should be approved. In particular, the FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates, and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on a BLA

Under the PHSA, the FDA may approve a BLA if it determines that the product is safe, pure, and potent and the facility where the product will be manufactured meets standards designed to ensure that it continues to be safe, pure, and potent.

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of non-clinical and clinical trial sites to assure compliance with GCPs, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA will issue a complete response letter ("CRL"), which will contain the conditions that must be met in order to secure final approval of the application, and when possible will outline recommended actions the sponsor might take to obtain approval of the application. Sponsors that receive a CRL may submit to the FDA information that represents a complete response to the issues identified by the FDA. Such resubmissions are classified under PDUFA as either Class 1 or Class 2. The classification of a resubmission is based on the information submitted by a sponsor in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has two months to review a Class 1 resubmission and six months to review a Class 2 resubmission. The FDA will not approve an application until issues identified in the complete response letter have been addressed.

If the FDA approves a new product, it may limit the approved indications for use of the product. It may also require that contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's safety after approval. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use ("ETASU"). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Expedited Review Programs

The FDA is authorized to expedite the review of applications in several ways. None of these expedited programs, however, changes the standards for approval but they may help expedite the development or approval process of product candidates.

- *Fast Track designation*: Candidate products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.

- *Breakthrough Therapy designation.* To qualify for the Breakthrough Therapy program, product candidates must be intended to treat a serious or life-threatening condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a Breakthrough Therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.

- *Priority review.* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

- *Accelerated approval.* Drug or biologic products studied for their safety and effectiveness in treating serious or life-threatening conditions and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials.

  With passage of the Food and Drug Omnibus Reform Act, or FDORA, in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to FDA every six months (until the study is completed; and use expedited procedures to withdraw accelerated approval of an NDA or BLA after the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the agency to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

- *Regenerative advanced therapy.* With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to Breakthrough Therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA have imposed as part of the approval process. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money, and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release,

the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Orphan Drug Designation and Exclusivity

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the biologic for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for tax credits and market exclusivity for seven years following the date of the product's marketing approval if granted by the FDA. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. A product becomes an orphan when it receives orphan drug designation from the Office of Orphan Products Development at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process like any other product.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first drug. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same product for the same indication for seven years, except in certain limited circumstances. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies, and the FDA has recently issued guidance indicating it would consider two gene therapy products for the same indication to be different, thus each eligible for orphan drug exclusivity, if they express different transgenes or have or use different vectors, so long as those differences are not "minor." The FDA will determine whether two vectors from the same viral class are the same on a case-by-case basis and may consider additional key features in assessing sameness. If a product designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor or the sponsor is unable to provide sufficient quantities.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, FDA announced that, in matters beyond the scope of that court order, FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory

exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Biosimilars and Exclusivity

The 2010 Patient Protection and Affordable Care Act, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"). The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. A biosimilar is a biological product that is highly similar to an existing FDA-licensed "reference product." To date, the FDA has approved a number of biosimilars and the first interchangeable biosimilar product was approved on July 30, 2021, and a second product previously approved as a biosimilar was designated as interchangeable in October 2021. The FDA has also issued numerous guidance documents outlining its approach to reviewing and licensing biosimilars and interchangeable biosimilars under the PHSA, including a draft guidance issued in November 2020 that seeks to provide additional clarity to manufacturers of interchangeable biosimilars.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. In December 2022, Congress clarified through FDORA that FDA may approve multiple first interchangeable biosimilar biological products so long as the products are all approved on the first day on which such a product is approved as interchangeable with the reference product.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such 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. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. There have been recent government proposals to reduce the 12-year reference product exclusivity period, but none has been enacted to date. At the same time, since passage of the BPCIA, many states have passed laws or amendments to laws, which address pharmacy practices involving biosimilar products.

Patent Term Restoration and Extension

A patent claiming a new biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of the IND and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for

which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

FDA Approval of Companion Diagnostics

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

The 2014 guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a biologic product candidate generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption ("IDE") regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a product are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE.

In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple drug or biological oncology products, when appropriate. This guidance builds upon existing policy regarding the labeling of companion diagnostics. In its 2014 guidance, the FDA stated that if evidence is sufficient to conclude that the companion diagnostic is appropriate for use with a specific group of therapeutic products, the companion diagnostic's intended use/indications for use should name the specific group of therapeutic products, rather than specific products. The 2020 guidance expands on the policy statement in the 2014 guidance by recommending that companion diagnostic developers consider a number of factors when determining whether their test could be developed, or the labeling for approved companion diagnostics could be revised through a supplement, to support a broader labeling claim such as use with a specific group of oncology therapeutic products (rather than listing an individual therapeutic product(s)).

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval ("PMA") simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the sponsor must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. For federal fiscal year 2023, the standard fee is $441,547 and the small business fee is $110,387.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing

processes and those of its suppliers are required to comply with the applicable portions of the Quality System Regulation, which covers the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, a sponsor will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application ("MAA") and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval

Before the new Clinical Trials Regulation, (EU) No 536/2014, or the Clinical Trials Regulation, came into application in January 2022, requirements for the conduct of clinical trials in the European Union, or EU, were set forth in Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP. This system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, a sponsor must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the sponsor may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the Clinical Trials Regulation, (EU) No 536/2014, or the Clinical Trials Regulation, was adopted. The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The Clinical Trials Regulation came into application in all the EU Member States on January 31, 2022, repealing Clinical Trials Directive 2001/20/EC. According to the transitional provisions, if a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation became applicable, the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

Parties conducting certain clinical studies must, as in the U.S., post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the EU

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority Medicines ("PRIME") scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated EMA contact and rapporteur from the Committee for Human Medicinal Products ("CHMP") or Committee for Advanced Therapies are appointed early in the PRIME scheme facilitating increased understanding of the product at the EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Pediatric Studies

Sponsors developing a new medicinal product must agree upon a Pediatric Investigation Plan ("PIP") with the EMA's pediatric committee ("PDCO"), and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies (e.g., because the relevant disease or condition occurs only in adults). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date.

Marketing Authorization

To obtain a marketing authorization for a product under the European Union regulatory system, a sponsor must submit an MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in European Union Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to a sponsor established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, a sponsor must demonstrate compliance with all measures included in an EMA-approved PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. Pursuant to Regulation (EC) No. 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. Manufacturers must demonstrate the quality, safety, and efficacy of their products to the EMA, which provides an opinion regarding the MAA. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Specifically, the grant of marketing authorization in the European Union for products containing viable human tissues or cells such as gene therapy medicinal products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC lays down specific rules concerning the authorization, supervision, and pharmacovigilance of gene therapy medicinal products, somatic cell therapy medicinal products, and tissue engineered products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety, and efficacy of their products to EMA which provides an opinion regarding the

application for marketing authorization. The European Commission grants or refuses marketing authorization in light of the opinion delivered by EMA.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting an initial assessment of a product. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts such a request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Specialized Procedures for Gene Therapies

The grant of marketing authorization in the European Union for gene therapy products is governed by Regulation 1394/2007/EC on advanced therapy medicinal products, read in combination with Directive 2001/83/EC of the European Parliament and of the Council, commonly known as the Community code on medicinal products. Regulation 1394/2007/EC includes specific rules concerning the authorization, supervision, and pharmacovigilance of gene therapy medicinal products. Manufacturers of advanced therapy medicinal products must demonstrate the quality, safety, and efficacy of their products to the EMA, which provides an opinion regarding the MAA. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

Regulatory Data Protection in the European Union

In the European Union, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the drug on the EU market (in the case of the centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities, and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union under Directive 2001/83EC, as amended.

Reimbursement and Pricing of Prescription Pharmaceuticals

In the E.U., similar political, economic and regulatory developments to those in the United States may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the U.S. and the E.U., reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the E.U., the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, pharmaceutical firms may be required to conduct a clinical trial that compares the cost-effectiveness of the product to other available therapies.

Orphan Drug Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the sponsor must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized European Union marketing authorization. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the European Commission or the member states can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the product is sufficiently profitable not to justify market exclusivity.

Pediatric Exclusivity

Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six-month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) even where the trial results are negative. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Patent Term Extensions in the European Union and Other Jurisdictions

The European Union also provides for patent term extension through Supplementary Protection Certificates, or SPCs. The rules and requirements for obtaining an SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. These periods can be extended for six additional months if pediatric exclusivity is obtained, which is described in detail below. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's withdrawal from the EU took place on January 31, 2020. The EU and the UK reached an agreement on their new partnership in the Trade and Cooperation Agreement, ("the Agreement"), which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the EU and the UK will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the UK is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA"), became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the UK's withdrawal from the EU.

Since a significant proportion of the regulatory framework for pharmaceutical products in the UK covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the UK. For example, the UK is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA, and a separate marketing authorization will be required to market our product candidates in the UK Until 31 December 2023, it is possible for the MHRA to rely on a decision taken by the European Commission on the approval of a new marketing authorization via the centralized procedure.

As with other issues related to Brexit, there are open questions about how personal data will be protected in the UK and whether personal information can transfer from the EU to the UK. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the UK will remain lawful under GDPR. The United Kingdom government has already determined that it considers all European Union and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the European Union/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the UK as being "essentially adequate" for purposes of data transfer from the EU to the UK, although this decision may be re-evaluated in the future.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, 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. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

In July 2020, the Court of Justice of the European Union, ("CJEU"), invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EU to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EU to the United States. Additionally, in October 2022, President Joe Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The EC initiated the process to adopt an adequacy decision for the EU-US Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU. Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR, including in relation to data transfers.

Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may seek regulatory approval by the FDA or other government authorities. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. Even if any product candidates we may develop are approved, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors

will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for any product candidates we may develop will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies (so called health technology assessments) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Arrangements with providers, consultants, third-party payors, and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase,

order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent or knowingly making, using, or causing to made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- the federal civil monetary penalty and false statement laws and regulations relating to pricing and submission of pricing information for government programs, including penalties for knowingly and intentionally overcharging 340b eligible entities and the submission of false or fraudulent pricing information to government entities;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for health care benefits, items or services;

- the Foreign Corrupt Practices Act, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act ("PPACA"), as amended by the Health Care Education Reconciliation Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services ("CMS") within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the PPACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act. Under subsequent legislation, these Medicare sequester reductions were suspended and reduced through June 2022 with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the PPACA are invalid as well. In June 2021, the U.S. Supreme Court dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and

Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program ("SIP"), to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Infrastructure Investment and Jobs Act to January 1, 2026 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at 2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any

of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), the U.S. Department of Health and Human Services, or HHS, has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

In 2018, California passed into law the California Consumer Privacy Act (the "CCPA"), which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation (the "GDPR"), including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act (the "CPRA"), which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition, other states, including Virginia, Colorado, Utah, and Connecticut already have passed state privacy laws. Virginia's privacy law also went into effect on January 1, 2023, and the laws in the other three states will go into effect later in the year. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be

subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, 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. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Additional Regulations

In addition to the foregoing, state, and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservation and Recovery Act, and the Toxic Substances Control Act, affect our business. These and other laws govern the use, handling, and disposal of various biologic, chemical, and radioactive substances used in, and wastes generated by, operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. Equivalent laws have been adopted in third countries that impose similar obligations.

Human Capital

As of February 1, 2023, we had 226 full-time employees, including 113 employees with M.D. or Ph.D. degrees. Of these full-time employees, 140 employees are engaged in research and development activities. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We anticipate that we will increase headcount in our manufacturing and clinical organizations as we accelerate the clinical development of EDIT-301 to treat SCD and TDT, and in our research organization to strengthen our discovery engine and technological capabilities.

At Editas, we seek to unlock the full potential of gene editing technology, and we recognize that our success is driven by our dynamic, passionate and diverse team. We work together with integrity, guided by our distinct culture, to develop transformative medicines for people living with serious diseases around the world. At the center of our culture are our core values, which guide and define the behaviors that make our culture unique and enable us to bring our best selves forward to achieve our mission of translating the promise of gene editing into a broad class of differentiated, transformational medicines for previously untreatable or under-treated diseases:

- Engagement – We are active within our teams, Editas, and the broader community.
- Teamwork – We succeed together through collaboration, communication, and mutual respect.
- Drive – We are focused to urgently deliver transformative medicines to patients.
- Resilience – We adapt and learn from setbacks and proactively prepare for future challenges.
- Accountability – We hold ourselves, our teams, and Editas responsible for both our successes and failures.

Our Commitment to Diversity, Equity and Inclusion

We strongly believe that our greatest strength comes from the people who make up our team. Each employee brings diverse perspectives, backgrounds, and thinking styles, and, by embracing and celebrating these differences, we strengthen our culture and further our mission to pioneer a new field of genome editing. We are committed to preserving and further cultivating our diverse and inclusive workforce, including in our senior management team, to ensure an environment where employees feel empowered to achieve their fullest potential.

As of December 31, 2022, approximately 52% of our full-time employees were women and 48% of our senior management (director level and above) were women. As of December 31, 2022, approximately 45% of our full-time employees identify as racially/ethnically diverse and 33% of our senior management identify as racially/ethnically diverse.

Recruitment, Retention and Development

Successful execution of our strategy is dependent on attracting, retaining and motivating a diverse team of highly skilled employees at all levels. We believe a key component of recruiting, retaining and motivating our employees is our total compensation package. For this reason, we provide employees with competitive compensation, including market-competitive salary and equity awards, along with competitive benefits packages, including medical, dental, vision and life insurance, an employee stock purchase plan, flexible spending accounts, short- and long-term disability and matching contributions to a 401(k) tax-deferred savings plan. We also provide annual cash incentive bonus opportunities that are tied to both company performance and individual performance to foster a pay-for-performance culture. We regularly benchmark these total rewards against our industry peers to ensure we remain competitive and attractive to potential new hires.

We believe that continued learning and development, training and other resources are also an essential part of retaining our employees and creating a culture of learning and leadership. We encourage our employees to participate and take advantage of a variety of learning and development resources, including online skills courses, professional development events, and external training programs based on individual needs. We have also implemented formal coaching and mentoring programs, which enable employees to connect with, and learn and develop from, individuals across our company.

Communication and Engagement

We recognize that our employees perform best when they know how their work contributes to our overall strategy. To achieve this, we emphasize open and direct communication through the use of a variety of channels, including quarterly all-company business updates from the senior management team, fireside chats with new members of the board of directors and our executive management team, open forums and company-wide written communications, and postings on our company intranet.

In addition, we periodically conduct employee surveys to gauge employee engagement and solicit feedback, and enhance our understanding of the views of our employees, work environment and culture. The results from engagement surveys are used to implement programs and processes designed to enhance employee engagement and improve the employee experience.

Health, Wellness and Safety

Employee safety and well-being is of paramount importance to us. In addition to traditional benefits such as healthcare, flexible time off, paid parental leave, and retirement benefits, we offer a variety of benefits and resources to support employees' physical and mental health, including a lifestyle spending allowance that employees may allocate to certain wellness programs and a third-party employee assistance program, which help us both attract talent and help to realize a healthier workforce.

Our Corporate Information

We were incorporated under the name Gengine, Inc. as a Delaware corporation in September 2013, and we changed our name to Editas Medicine, Inc. in November 2013. Our principal executive offices are located at 11 Hurley St., Cambridge, Massachusetts, 02141, and our telephone number is (617) 401-9000.

Available Information

We maintain an internet website at www.editasmedicine.com and make available free of charge through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act of 1934, or the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or the SEC.

You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors & Media," as a source of information about us.

The information on our website is not incorporated by reference into this Annual Report on Form 10-K and should not be considered to be a part of this Annual Report on Form 10-K. Our website address is included in this Annual Report on Form 10-K as an inactive technical reference only.

Item 1A. Risk Factors

Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Annual Report on Form 10-K and other filings with the Securities and Exchange Commission (the "SEC"), press releases, communications with investors, and oral statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events, or otherwise.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net losses were $220.4 million, $192.5 million, and $116.0 million for the years ended December 31, 2022, 2021 and 2020, respectively. As of December 31, 2022, we had an accumulated deficit of $1.1 billion. We have financed our operations primarily through public offerings of our common stock, our collaboration with Bristol Myers Squibb Company ("BMS") through its wholly owned subsidiary, Juno Therapeutics, Inc. ("Juno Therapeutics"), and payments under our former strategic alliance with Allergan Pharmaceuticals International Limited (which was acquired by AbbVie Inc. in May 2020 and is referred to together with its affiliates as "Allergan"). We have devoted substantially all of our efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- progress the clinical development of EDIT-301 to treat severe sickle cell disease ("SCD") and transfusion-dependent beta-thalassemia ("TDT");
- continue our current research programs, including *ex vivo* treatments for hemoglobinopothies and *in vivo* gene editing medicines, and our preclinical and clinical development of product candidates from our current research programs;
- seek to identify additional research programs and additional product candidates;
- initiate preclinical testing and clinical trials for any product candidates we identify and develop;
- maintain, expand, and protect our intellectual property portfolio and provide reimbursement of third-party expenses related to our patent portfolio;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;

- ultimately establish a sales, marketing, and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;
- further develop our genome editing platform;
- hire additional clinical, quality control, and scientific personnel;
- add operational, financial, and management information systems and personnel, including personnel to support our product development;
- acquire or in-license other medicines and technologies;
- validate a commercial-scale current Good Manufacturing Practices ("cGMP") manufacturing facility; and
- continue to operate as a public company.

We are in the early stages of the clinical development of EDIT-301 and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. To become and remain profitable, we must develop and eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including identifying product candidates, completing preclinical testing and clinical trials of product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing, and selling those medicines for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. Other than EDIT-301, we are currently only in the preclinical testing stages for our most advanced research programs. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business, or continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investments in us.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce, or eliminate our research and product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we identify, continue the research and development of, initiate clinical trials of, and seek marketing approval for, product candidates. In addition, if we obtain marketing approval for any product candidates we develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, manufacturing, and distribution are not the responsibility of a collaborator. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and product development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents, and marketable securities at December 31, 2022 and anticipated interest income will enable us to fund our operating expenses and capital expenditure requirements into 2025. Our future capital requirements will depend on many factors, including:

- the scope, progress, results, and costs of drug discovery, preclinical development, laboratory testing, and clinical or natural history study trials for the product candidates we develop;
- the costs of progressing the clinical development of EDIT-301 to treat SCD and TDT;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;

- the costs, timing, and outcome of regulatory review of the product candidates we develop;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for any product candidates for which we receive regulatory approval;
- the success of our collaboration with BMS;
- whether BMS exercises any of its options to extend the research program term and/or to additional research programs under our collaboration;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other medicines and technologies;
- the costs of reimbursing our licensors for the prosecution and maintenance of the patent rights in-licensed by us; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, even if we successfully identify and develop product candidates and those are approved, we may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. We do not have any significant committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders may be materially diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

If we raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates, or we may have to grant licenses on terms that may not be favorable to us.

Our short operating history may make it difficult for our stockholders to evaluate the success of our business to date and to assess our future viability.

We were founded and commenced operations in the second half of 2013. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates, undertaking preclinical studies and initiating clinical trials. Except for EDIT-301, all of our research programs are still in the preclinical or research stage of development, and the risk of failure of all of our research programs is high. We have not yet demonstrated an ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for

successful commercialization. In addition, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown factors.

We expect that our financial condition and operating results will continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We have never generated revenue from product sales and may never be profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, product candidates we may identify for development. We do not anticipate generating revenues from product sales for the next several years, if ever.

Even if one or more of the product candidates we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the U.S. Food and Drug Administration (the "FDA"), the European Medicines Agency (the "EMA"), or other regulatory authorities to perform clinical and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

Risks Related to Discovery, Development, and Commercialization

We are dependent on the success of our lead product candidate, EDIT-301, which is in clinical development. Clinical trials of product candidates may not be successful. If we are unable to complete the clinical development of, obtain marketing approval for, or successfully commercialize this product candidate, either alone or with a collaborator, or if we experience significant delays in doing so, our business would be substantially harmed.

In January 2023, we implemented a strategic reprioritization of our portfolio to focus on hemoglobinopathies and *in vivo* gene editing, and in connection with that paused patient enrollment in our clinical EDIT-101 program, terminated our AAV IRD platform, and divested our preclinical wholly owned iNK programs. As a result, we have one ongoing clinical-stage program, EDIT-301. We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of EDIT-301 for the treatment of SCD and TDT.

Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize EDIT-301. Because our business is significantly dependent upon this one product candidate, any setback in the clinical development or the obtaining of regulatory approval for EDIT-301 would have a material adverse effect on our business and prospects.

The success of our EDIT-301 program will depend on several factors, including the following:

- successful enrollment and completion of our RUBY Phase 1/2 clinical trial of EDIT-301 for the treatment of SCD and our EDITHAL Phase 1/2 clinical trial of EDIT-301 for the treatment of TDT, as well as any additional clinical trials of EDIT-301 that we undertake;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the performance of our future collaborators, if any;

- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- establishment of arrangements with third-party manufacturers to obtain finished drug products that are appropriately packaged for sale;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors following any marketing approval; and
- our ability to compete with other therapies, including therapies that are further advanced in clinical development.

Many of these factors are beyond our control, including the outcome of clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize EDIT-301, on our own or with any future collaborator, or experience delays as a result of any of these or other factors, our business would be substantially harmed.

We intend to identify and develop product candidates based on a novel genome editing technology, which makes it difficult to predict the time and cost of product candidate development. No therapeutic products that utilize genome editing technology have been approved in the United States or in Europe.

We have concentrated our research and development efforts on our genome editing platform, which uses CRISPR technology. Our future success depends on the successful development of this novel genome editing therapeutic approach. To date, no therapeutic product that utilizes genome editing, including CRISPR technology, has been approved in the United States or Europe. It is difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our genome editing platform, or any similar or competitive genome editing platforms, will result in the identification, development, and regulatory approval of any medicines. There can be no assurance that any development problems we experience in the future related to our genome editing platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process or transferring that process to commercial partners. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we develop on a timely or profitable basis, if at all.

Regulatory requirements governing genetic medicines, and in particular any novel genetic medicines we may develop, have changed frequently and may continue to change in the future.

Regulatory requirements governing genetic and cellular medicines, and in particular any novel genetic medicine products we may develop, have changed frequently and may continue to change in the future, including, for example, the draft guidance document titled “Human Gene Therapy Products Incorporating Human Genome Editing” issued by the FDA in March 2022. We are aware of a limited number of genetic medicines that have received marketing authorization from the FDA and EMA. Even with respect to more established products in the genetic medicine field, the regulatory

landscape is still developing. For example, the FDA has established the Office of Tissues and Advanced Therapies (formerly the Office of Cellular, Tissue and Gene Therapies) within CBER to consolidate the review of genetic medicines and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Genetic medicine clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH also are potentially subject to review by the Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC; however, the NIH announced that the RAC will only publicly review clinical trials if the trials cannot be evaluated by standard oversight bodies and pose unusual risks.

The same applies in the European Union. The EMA's Committee for Advanced Therapies ("CAT") is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a genetic medicinal candidate that is submitted to the CHMP before CHMP adopts its final opinion. In the European Union, the development and evaluation of a genetic medicinal product must be considered in the context of the relevant European Union guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for genetic medicinal products and require that we comply with these new guidelines. As a result, the procedures and standards applied to genetic medicines and cell therapy products may be applied to any product candidates we may develop, but that remains uncertain at this point.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of any product candidates we may develop or lead to significant post-approval limitations or restrictions. As we advance any product candidates we may develop, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of these product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

Although the FDA decides whether individual genetic medicine protocols may proceed, the RAC public review process, if undertaken, can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put an IND on a clinical hold even if the RAC has provided a favorable review or an exemption from in-depth, public review. If we were to engage an NIH-funded institution to conduct a clinical trial, that institution's IBC as well as its IRB would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of genetic medicine products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of any product candidates we may develop. Similarly, the EMA may issue new guidelines concerning the development and marketing authorization for genetic medicine products and require that we comply with these new guidelines.

As we are initially seeking to identify and develop product candidates to treat diseases using novel technologies, there is heightened risk that the FDA, the EMA or other regulatory authority may not consider the clinical trial endpoints that we propose to provide clinically meaningful results. Even if the endpoints are deemed clinically meaningful, we may not achieve these endpoints to a degree of statistical significance, particularly because many of the diseases we are targeting with our platform have small patient populations, making development of large and rigorous clinical trials more difficult.

Adverse developments in post-marketing experience or in clinical trials conducted by others of genetic medicines or cell therapy products may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for development or approval of any product candidates we may develop or limit the use of products utilizing non-viral genetic medicinal technologies, either of which could materially harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as the product candidates we may develop can be more expensive and take longer than for other, better known or more extensively studied pharmaceutical or other product candidates. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing non-viral genetic medicine technology in a

timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our research programs or the commercialization of resulting products.

In addition, ethical, social and legal concerns about genetic medicine, genetic testing and genetic research could result in additional regulations or prohibiting the processes we may use. Federal and state agencies, congressional committees and foreign governments have expressed their intentions to further regulate biotechnology. More restrictive regulations or claims that any product candidates we may develop are unsafe or pose a hazard could prevent us from commercializing any products. New government requirements may be established that could delay or prevent regulatory approval of any product candidates we may develop under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be.

As we advance any product candidates we may develop through clinical development, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. These regulatory review committees and advisory groups and any new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of any product candidates we may develop or lead to significant post-approval limitations or restrictions. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue.

We may not be successful in our efforts to identify, develop, or commercialize potential product candidates.

The success of our business depends primarily upon our ability to identify, develop, and commercialize products based on our genome editing platform. Other than EDIT-301, all of our ongoing product development programs are still in the preclinical or research stage of development. Our research programs, including those subject to our collaboration with BMS, may fail to identify potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products impractical to manufacture or commercialize, or unlikely to receive marketing approval.

The occurrence of these events may force us to abandon our development efforts for a program or programs, which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Research programs to identify new product candidates require substantial technical, financial, and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

For example, in November 2022 we announced updated clinical data from our Phase 1/2 BRILLIANCE trial of EDIT-101 to treat Leber congenital amaurosis. This data demonstrated a favorable safety profile and provided proof of concept. However, we were not able to identify any baseline characteristics of the treatment responder patients that could pre-select a responder patient population other than zygosity. The identified responder patient population was determined to be too small to progress the program independently. We have since paused patient enrollment in this program.

The genome editing field is relatively new and is evolving rapidly. We are focusing our research and development efforts on CRISPR gene editing technology using Cas9 and Cas12a enzymes, but other genome editing technologies may be discovered that provide significant advantages over CRISPR/Cas9 or CRISPR/Cas12a, which could materially harm our business.

To date, we have focused our efforts on genome editing technologies using CRISPR and the Cas9 and Cas12a (also known as Cpf1) enzymes. Other companies have previously undertaken research and development of genome editing technologies using zinc finger nucleases, engineered meganucleases, and transcription activator-like effector nucleases, but to date none has obtained marketing approval for a product candidate. There can be no certainty that the

CRISPR/Cas9 or CRISPR/Cas12a technology will lead to the development of genomic medicines, that other genome editing technologies will not be considered better or more attractive for the development of medicines or that either Cas9 or Cas12a, the two CRISPR associated proteins that we use, may be useful or successful in developing therapeutics. For example, Cas9 or Cas12a may be determined to be less attractive than other CRISPR enzymes, including CRISPR enzymes that have yet to be discovered. Similarly, a new genome editing technology that has not been discovered yet may be determined to be more attractive than CRISPR. Moreover, if we decide to develop genome technologies other than CRISPR technology using a Cas9 or Cas12a enzyme, we cannot be certain we will be able to obtain rights to such technologies. Any of these factors could reduce or eliminate our commercial opportunity, and could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Except for EDIT-301, all of our product development programs are at the preclinical or research stage. Preclinical testing and clinical trials of product candidates may not be successful. If we are unable to commercialize any product candidates we develop or experience significant delays in doing so, our business will be materially harmed.

Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on our successful development and eventual commercialization of product candidates that we have identified or may identify in the future. Our research programs, including any with collaborators, may fail to identify potential product candidates for clinical development for a number of reasons, or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the product candidates impractical to manufacture, unmarketable, or unlikely to receive marketing approval. Any potential product candidates we identify will require preclinical and clinical activities and studies, regulatory review and approval in each jurisdiction in which we intend to market the products, substantial investment, establishing manufacturing capabilities, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. We currently generate no revenue from sales of any product and we may never be able to develop or commercialize a marketable product.

If serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any product candidates we develop, we may need to abandon or limit our further clinical development of those product candidates.

We have limited experience in evaluating product candidates in human clinical trials, having dosed our first patient in a clinical trial in 2020, and our proposed delivery modes, combined with CRISPR technology, have a limited history, if any, of being tested clinically. It is impossible to predict when or if any product candidates we develop will ultimately prove safe in humans, including EDIT-301. In the genomic medicine field, there have been several significant adverse events from gene therapy treatments in the past, including reported cases of leukemia and death. There can be no assurance that genome editing technologies will not cause severe or undesirable side effects.

A significant risk in any genome editing product is that the edit will be “off-target” and cause serious adverse events, undesirable side effects, or unexpected characteristics. For example, off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA. We cannot be certain that off-target editing will not occur in any of our clinical studies. There is also the potential risk of delayed adverse events following exposure to genome editing therapy due to the potential for persistent biological activity of the genetic material or other components of products used to carry the genetic material.

If any product candidates we develop are associated with serious adverse events, or undesirable side effects, or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

If any of the product candidates we develop or the delivery modes we rely on cause undesirable side effects, it could delay or prevent their regulatory approval, limit the commercial potential, or result in significant negative consequences following any potential marketing approval.

Our product candidates that we are testing or may test in clinical trials, including EDIT-301, or that are developed may be associated with off-target editing or other serious adverse events, undesirable side effects, or unexpected characteristics. In addition to serious adverse events or side effects caused by any product candidate we develop and test, the administration process or related procedures also can cause undesirable side effects. If any such events occur, our clinical trials could be suspended or terminated. If we are unable to demonstrate that such adverse events were caused by factors other than our product candidate, the FDA, the EMA or other regulatory authorities could order us to cease further development of, or deny approval of, any product candidates we are able to develop for any or all targeted indications. Even if we are able to demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of any product candidate we develop, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, result of operations, and prospects significantly.

If we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy ("REMS") to ensure that the benefits of treatment with such product candidate outweighs the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. Furthermore, if we or others later identify undesirable side effects caused by any of our product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of any product candidates we may identify and develop and could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We have not extensively tested any of our proposed delivery modes and product candidates in clinical trials.

Our proposed delivery modes, combined with our product candidates, have a limited history of being evaluated in human clinical trials. Any of our product candidates, including EDIT-301 to treat SCD and TDT, may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical trials.

There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit, or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development.

Any such adverse events may cause us to delay, limit, or terminate planned clinical trials, any of which would

have a material adverse effect on our business, financial condition, results of operations, and prospects.

Because we are developing product candidates for the treatment of diseases in which there is little clinical experience using new technologies, there is increased risk that the FDA, the EMA, or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

During the regulatory review process, we will need to identify success criteria and endpoints such that the FDA, the EMA, or other regulatory authorities will be able to determine the clinical efficacy and safety profile of our product candidates. As we are seeking to identify and develop product candidates to treat diseases in which there is little clinical experience using new technologies, there is heightened risk that the FDA, the EMA, or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results. Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoints to a degree of statistical significance. This may be a particularly significant risk for many of the genetically defined diseases for which we plan to develop product candidates because many of these diseases have small patient populations, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. The FDA weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. Any product candidates we develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval. No genome editing therapeutic product has been approved in the United States or in Europe.

If clinical trials of any product candidates we identify and develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of any of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy in humans of any such product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

We or our collaborators may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates we may identify and develop, including:

- delays in reaching a consensus with regulators on trial design;
- regulators, institutional review boards (“IRBs”) or independent ethics committees (“IECs”) not authorizing us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching or failing to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective contract research organizations (“CROs”) and clinical trial sites;
- clinical trials of any product candidates we develop producing negative or inconclusive results, and us deciding, or regulators requiring us, to conduct additional clinical trials or abandon product development or research programs;
- the number of patients required for clinical trials of any product candidates we develop may be larger than we anticipate; enrollment of suitable participants in these clinical trials may be delayed or slower than we anticipate; or patients may drop out of these clinical trials at a higher rate than we anticipate;

- our third-party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- regulators, IRBs, or IECs requiring that we or our investigators suspend or terminate clinical research or clinical trials of any product candidates we develop for various reasons, including noncompliance with regulatory requirements, a finding of undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks or after an inspection of our clinical trial operations or trial sites;

- the supply or quality of any product candidates we develop or other materials necessary to conduct clinical trials of any product candidates we develop being insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing, and delivery of any product candidates we develop to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;

- occurrence of serious adverse events associated with any product candidates we develop that are viewed to outweigh their potential benefits; and

- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

If we or our collaborators are required to conduct additional clinical trials or other testing of any product candidates we develop beyond those that we currently contemplate, if we or our collaborators are unable to successfully complete clinical trials or other tests of any product candidates we develop, or if the results of these trials or tests are not positive or only modestly positive, or if there are safety concerns, we or our collaborators may:

- be delayed in obtaining marketing approval for any such product candidates we develop, or not obtain marketing approval at all;

- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

- be subject to changes in the way the product is administered;

- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;

- have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;

- be sued; or

- experience damage to our reputation.

Product development costs will also increase if we or our collaborators experience delays in testing or marketing approvals. We do not know whether clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates we develop, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize any product candidates we develop, any of which may harm our business, financial condition, results of operations, and prospects.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary

regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate or continue clinical trials for any of our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States, or as needed to provide appropriate statistical power for a given trial. In addition, if patients are unwilling to participate in our genome editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy, or genome editing fields, competitive clinical trials for similar patient populations, clinical trials in competing products, or for other reasons, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of any product candidates we develop may be delayed. Moreover, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as any product candidates we develop, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors, including:

- severity of the disease under investigation;
- size of the patient population and process for identifying patients;
- design of the trial protocol;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- ability to obtain and maintain patient informed consent;
- risk that enrolled patients will drop out before completion of the trial;
- eligibility and exclusion criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;
- perceived risks and benefits of genome editing as a therapeutic approach;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment;
- the ongoing COVID-19 pandemic; and
- proximity and availability of clinical trial sites for prospective patients.

The eligibility criteria of our clinical trials further limits the pool of available trial participants. Additionally, the process of finding and diagnosing patients may prove costly. The COVID-19 pandemic, including related restrictions imposed by regulatory authorities and constraints on healthcare provider capacity, has previously impacted and may in the future impact our ability to timely enroll trial participants and conduct our studies.

Our ability to successfully initiate, enroll, and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- different standard-of-care for patients with a particular disease;
- inability to locate qualified local consultants, physicians, and partners; and
- potential burden of complying with a variety of foreign laws, medical standards, and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

Enrollment delays in our clinical trials may result in increased development costs for any of our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. If we or our collaborators have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit, or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations, and prospects.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and our product candidates for specific indications among many potential options. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such event could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If we are unable to successfully identify patients who are likely to benefit from therapy with any medicines we develop, or experience significant delays in doing so, we may not realize the full commercial potential of any medicines we may develop.

Our success may depend, in part, on our ability to identify patients who are likely to benefit from therapy with any of our medicines, which may require those potential patients to have their DNA analyzed for the presence or absence of a particular sequence. If we, or any third parties that we engage to assist us, are unable to successfully identify such patients, or experience delays in doing so, then:

- our ability to develop any product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- any product candidates we develop may not receive marketing approval if safe and effective use of such product candidates depends on an in vitro diagnostic; and
- we may not realize the full commercial potential of any product candidates we develop that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our medicines.

As a result, we may be unable to successfully develop and realize the commercial potential of any product candidates we may identify and develop, and our business, financial condition, results of operations, and prospects would be materially adversely affected.

Even if we complete the necessary clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate we develop, and any such approval may be for a more narrow indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if any product candidates we develop meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or a REMS. These regulatory authorities may require precautions or contra-indications with respect to conditions of use, or they may grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of any product candidates we develop. Any of the foregoing scenarios could materially harm the commercial prospects for any product candidates we develop and materially adversely affect our business, financial condition, results of operations, and prospects.

Even if any product candidates we develop receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors, and others in the medical community necessary for commercial success.

The commercial success of any of our product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors, and others in the medical community. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages compared to alternative treatments;
- the limitation to our targeted patient population and limitations or warnings contained in approved labeling by the FDA or other regulatory authorities;
- the ability to offer our medicines for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the clinical indications for which the product candidate is approved by the FDA, the European Commission, or other regulatory agencies;
- public attitudes regarding genomic medicine generally and genome editing technologies specifically;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, as well as their willingness to accept a therapeutic intervention that involves the editing of the patient's genome;
- product labeling or product insert requirements of the FDA, the EMA, or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- relative convenience and ease of administration;

- the timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

If any of our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues, and we may not become profitable.

Adverse public perception of genomic medicines, and genome editing in particular, may negatively impact regulatory approval of, or demand for, our potential products.

Our potential therapeutic products involve editing the human genome. The clinical and commercial success of our potential products will depend in part on public understanding and acceptance of the use of genome editing therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that genome editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Adverse public attitudes may adversely impact our ability to enroll clinical trials. Moreover, our success will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

In addition, genome editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of genome editing technology to human embryos or the human germline. For example, academic scientists in several countries, including the United States, have reported on their attempts to edit the genome of human embryos as part of basic research and, in November 2018, Dr. Jiankui He, a Chinese biophysics researcher who was an associate professor in the Department of Biology of the Southern University of Science and Technology in Shenzhen, China, announced he had created the first human genetically edited babies, twin girls and helped create a second gene-edited pregnancy. The announcement was negatively received by the public, in particular by those in the scientific community. In the United States, germline editing for clinical application has been expressly prohibited since enactment of a December 2015 U.S. FDA ban on such activity. Prohibitions are also in place in the United Kingdom, across most of Europe, in China, and many other countries around the world. In the United States, the NIH has announced that it would not fund any use of genome editing technologies in human embryos, noting that there are multiple existing legislative and regulatory prohibitions against such work, including the Dickey-Wicker Amendment, which prohibits the use of appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. Laws in the United Kingdom prohibit genetically modified embryos from being implanted into women, but embryos can be altered in research labs under license from the Human Fertilisation and Embryology Authority. Basic research on embryos is more tightly controlled in many other European countries.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of genome editing technologies in human embryos and heightened regulatory scrutiny could prevent or delay our development of product candidates. More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair our development and commercialization of product candidates or demand for any products we may develop.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any of our product candidates, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing, or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing, and commercial support infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize our medicines on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;
- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support, and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to market and sell any medicines we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face significant competition in an environment of rapid technological change, and our competitors may achieve regulatory approval before us or develop therapies that are safer or more advanced or effective than ours.

The development and commercialization of new drug products is highly competitive. Moreover, the biotechnology and pharmaceutical industries, including in the gene therapy, genome editing and cell therapy fields, are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. We will face competition with respect to any of our product candidates now and in the future from major pharmaceutical companies, specialty pharmaceutical companies, and biotechnology companies worldwide. Potential competitors also include academic institutions, government agencies, and other public and private research organizations that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we have research programs. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches.

Our platform and product focus is the development of therapies using CRISPR technology specifically for genome editing. Other companies developing CRISPR Cas9 or Cas12a technology or therapies using CRISPR Cas9 or Cas12a technology include Artisan Bio, Caribou Biosciences, CRISPR Therapeutics, EdiGene, ERS Genomics, Excision Biotherapeutics, Graphite Bio, Inscripta, Intellia Therapeutics, Sigma-Aldrich, ToolGen, and Vertex Pharmaceuticals. In addition, there have been and may continue to be discoveries of new CRISPR-based gene editing technologies. There are additional companies developing therapies using related CRISPR genome editing technologies, including other CRISPR nucleases, base editing, prime editing and gene writing. These companies include Arbor Biotechnologies, Beam Therapeutics, Chroma Medicine, Emendo Biotherapeutics, Integra Therapeutics, KSQ Therapeutics, Locus Biosciences, Mammoth Biosciences, Metagenomi, Poseida Therapeutics, Prime Medicine, Scribe Therapeutics, Tessera Therapeutics, Tome Biosciences, Tune Therapeutics, and Verve Therapeutics. There are also companies developing therapies using transcription activator-like effector nucleases, meganucleases, Mega-TALs and zinc finger nucleases. These companies include 2Seventy Bio, Allogene Therapeutics, bluebird bio, Cellectis, Precision Biosciences, and Sangamo Therapeutics. In addition to competition from other genome editing therapies, gene therapies or cell medicine therapies, any products that we may develop may also face competition from other types of therapies, such as small molecule, antibody, protein, oligonucleotide, or ribonucleic acid therapies. There are also companies developing therapies related to our development programs. For hemoglobinopathies, these companies include Acceleron Pharma, Aruvant Therapeutics, Beam Therapeutics, bluebird bio, Cellectis, CRISPR Therapeutics, EdiGene, Global Blood Therapeutics, Graphite Bio, Intellia Therapeutics, Novartis Pharmaceuticals, Sangamo Therapeutics, and Vertex Pharmaceuticals.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology, and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or non-competitive. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we develop against competitors.

In addition, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

If we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices, or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing, and reimbursement for new medicines vary widely from country to country. Some countries require approval of the sale price of a medicine before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a medicine in a particular country, but then be subject to price regulations that delay our commercial launch of the medicine, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the medicine in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any of our product candidates obtain marketing approval.

Our ability to commercialize any medicines successfully also will depend in part on the extent to which

reimbursement for these medicines and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. For example, the Inflation Reduction Act of 2022 (the "IRA") includes several measures intended to lower the cost of prescription drugs and related healthcare reforms, including limits on price increases and subjecting an escalating number of drugs to annual price negotiations with The Centers for Medicare & Medicaid Services. We cannot be sure whether additional legislation or rulemaking related to the IRA will be issued or enacted, or what impact, if any, such changes will have on the profitability of any of our drug candidates, if approved for commercial use, in the future. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any medicine that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved medicines, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any medicine will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the medicine and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost medicines and may be incorporated into existing payments for other services. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved medicines we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines, and our overall financial condition.

Due to the novel nature of our technology and the potential for some of our product candidates to offer therapeutic benefit in a single administration or limited number of administrations, we face uncertainty related to pricing and reimbursement for these product candidates.

The pricing and reimbursement of any of our product candidates, if approved, must be adequate to support the necessary commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to any of our product candidates, e.g., for administration of our product to patients, is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products. In addition, it may be necessary for us to develop new reimbursement models in order to realize adequate value. Payors may not be able or willing to adopt such new models, and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary but we are unsuccessful in developing them, or if such models are not adopted by payors, our business, financial condition, results of operations, and prospects could be adversely affected.

We expect the cost of a single administration of genomic medicine products to be substantial, when and if they achieve regulatory approval. We expect that coverage and reimbursement by government and private payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of any such product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of any product candidates we develop will be paid by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or will be reimbursed by government authorities, private health coverage insurers, and other third-party payors. Coverage and reimbursement by a third-party payor may depend upon several factors, including the third-party

payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective, and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement for a product from third-party payors is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical, and cost-effectiveness data. There is significant uncertainty related to third-party coverage and reimbursement of newly approved products. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. If coverage and reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any of our product candidates. Even if coverage is provided, the approved reimbursement amount may not be adequate to realize a sufficient return on our investment. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any product candidates we develop will be harmed.

If the market opportunities for any of our product candidates are smaller than we believe they are, our revenues may be adversely affected, and our business may suffer. If the target patient population for a product candidate we develop is small, we will need to successfully identify patients and achieve a significant market share to maintain profitability and growth.

Some of our programs may focus on treatments for rare genetically defined diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of these diseases. The number of patients in the United States, Europe, and elsewhere may turn out to be lower than expected, and patients may not be amenable to treatment with our products, or may become increasingly difficult to identify or gain access to, all of which would adversely affect our business, financial condition, results of operations, and prospects.

Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any medicines that we may develop.

We face an inherent risk of product liability exposure related to the testing in human clinical trials of any of our product candidates and will face an even greater risk if we commercially sell any medicines that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or medicines that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and

- the inability to commercialize any medicines that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage if we successfully commercialize any medicine. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we or any contract manufacturers and suppliers we engage fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We and any contract manufacturers and suppliers we engage are subject to numerous federal, state, and local environmental, health, and safety laws, regulations, and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air, and water; and employee health and safety. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. We also could incur significant costs associated with civil or criminal fines and penalties.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research and product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological or hazardous waste insurance coverage, and our commercial general liability and umbrella liability policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Any third-party contract manufacturers and suppliers we engage will also be subject to these and other environmental, health, and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Genomic medicines are novel, and our product candidates can be complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs, limit the supply of our products, or otherwise harm our business.

Our product candidates can require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims, or insufficient inventory. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, EMA or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA, and other regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA, or other regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials, including the ongoing Phase 1/2 clinical trial for EDIT-301, or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations, and prospects.

We also may encounter problems hiring and retaining the experienced scientific, quality control, and manufacturing personnel needed to manage our manufacturing process, which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. Some of the raw materials that we anticipate will be required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall, or restriction on the use of biologically derived substances in the manufacture of any product candidates we develop could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially harm our development timelines and our business, financial condition, results of operations, and prospects.

Any problems in our manufacturing process or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs. Problems in third-party manufacturing process or facilities also could restrict our ability to ensure sufficient clinical material for any clinical trials we may be conducting or are planning to conduct and meet market demand for any products we commercialize.

Risks Related to Our Dependence on Third Parties

We expect to depend on collaborations with third parties for the research, development, and commercialization of certain of the product candidates we develop or for development of certain of our research programs. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates or research programs.

We anticipate seeking third-party collaborators for the research, development, and commercialization of certain of the product candidates we develop or for development of certain of our research programs. Our likely collaborators include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them and, if applicable, whether they exercise any additional options to commercialize a product. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs or any of our product candidates and alliance arrangements we may enter into under which our research programs or product candidates may be involved pose the following risks to us:

- Collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations.

- Collaborators may not pursue development and commercialization of any product candidates we develop or may elect not to continue or renew development or commercialization programs based on clinical trial

results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities.

- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing.

- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our medicines or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.

- Collaborators with marketing and distribution rights to one or more medicines may not commit sufficient resources to the marketing and distribution of such medicine or medicines.

- Collaborators may not properly obtain, maintain, enforce, or defend our intellectual property or proprietary rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation.

- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development, or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.

- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control.

- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished, or terminated.

If our collaborations do not result in the successful development and commercialization of products, or if one of our collaborators terminates its agreement with us, we may not receive any milestone or royalty payments under such collaborations. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval, and commercialization described in this Annual Report on Form 10-K apply to the activities of our collaborators.

If we are not able to establish collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our product development and research programs and the potential commercialization of any of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates and research programs, we may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates or programs.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement

for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators or allies. For example, under our amended and restated collaboration with BMS, we may not use directly or indirectly, or license others to use, genome editing technology in connection with any research, development, manufacture, commercialization or other exploration of certain T cells, subject to certain exceptions, as more fully described in "Part I—Business—Our Collaborations and Licensing Strategy" of this Annual Report on Form 10-K. Collaborations are also complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop product candidates or bring them to market and generate product revenue.

We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research, or testing.

We currently rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, our product development activities would be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording, and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates we develop and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any

performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we develop or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of materials for our research programs, preclinical studies and clinical trials and expect to continue to do so and for commercialization of any product candidates that we develop. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, product candidates, or any medicines that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

We have a limited ability to manufacture materials for our research programs and preclinical studies and we do not operate any significant manufacturing facilities. We primarily rely on third-party contract manufacturing organizations ("CMOs") for the manufacture of our materials for preclinical and clinical studies and expect to continue to do so and for commercial supply of any product candidates that we develop and for which we or our collaborators obtain marketing approval.

Even though we have established supply agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, safety, and pharmacovigilance and related reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or medicines, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business, financial condition, results of operations, and prospects. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Our current and anticipated future dependence upon others for the manufacture of any of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any products we develop and for our technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize any of our product candidates, and our technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our CRISPR platform technology and any proprietary product candidates and technology we develop. We seek to protect our proprietary position by in-licensing intellectual property relating to our platform technology and filing patent applications in the United States and abroad related to our technologies and product candidates that are important to our business. If we or our licensors and/or collaborators are unable to obtain or maintain patent protection with respect to our CRISPR platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations, and prospects could be materially harmed.

No consistent policy regarding the scope of claims allowable in the field of genome editing, including CRISPR technology, has emerged in the United States. The scope of patent protection outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. With respect to both in-licensed and owned intellectual property, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output in time to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we license or own issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any patents that we hold or in-license may be challenged, narrowed, circumvented, or invalidated by third parties. Consequently, we do not know whether any of our platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. For example, we are aware that third parties have suggested the use of the CRISPR technology in conjunction with a protein other than Cas9 or Cas12a. Our owned and in-licensed patents may not cover CRISPR technology in conjunction with a protein other than Cas9 or Cas12a. If our competitors commercialize the CRISPR technology in conjunction with a protein other than Cas9 or Cas12a, our business, financial condition, results of operations, and prospects could be materially adversely affected.

The issuance of a patent is not conclusive as to its inventorship, scope, validity, or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Our licensors are currently, and we or our licensors may in the future become, subject to a third-party pre-issuance submission of prior art to the United States Patent and Trademark Office (the "USPTO") or opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceedings and other similar proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, we, or one of our licensors, may have to participate in interference proceedings declared by the USPTO to determine priority of invention or in post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge priority of invention or other features of patentability. Such challenges may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. As discussed below, some of our in-licensed patents are subject to interference, opposition and *ex parte* re-examination proceedings and therefore subject to these risks.

In addition, given the amount of time required for the development, testing, and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our owned and in-licensed patents and patent applications are, and may in the future be, co-owned with third parties. If we are unable to obtain an exclusive license to

any such third party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co-owners of our owned and in-licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Furthermore, our owned and in-licensed patents and patent applications may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in-licensed patent rights and technology was funded in part by the U.S. government. As a result, the U.S. government has certain rights to such patent rights and technology. These rights may permit the U.S. government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. Any exercise by the government of any of the foregoing rights could harm our competitive position, business, financial condition, results of operations, and prospects.

Our rights to develop and commercialize our technology and product candidates are subject, in part, to the terms and conditions of licenses granted to us by others.

We are heavily reliant upon licenses to certain patent rights and proprietary technology from third parties that are important or necessary to the development of our genome editing technology, including our CRISPR technology, and product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses. For example, pursuant to our license agreements with The Broad Institute, Inc. ("Broad"), and Broad and the President and Fellows of Harvard College ("Harvard"), the licensors may, under certain circumstances, grant a license to the patents that are the subject of such license agreements to a third party. Such third party would have full rights to the patent rights that are the subject of such licenses, which could impact our competitive position and enable a third party to commercialize products similar to our future product candidates and technology. The terms of these license agreements are described more fully under "Part I—Business—Our Collaborations and Licensing Strategy" in this Annual Report.

In addition, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. For example, pursuant to each of our intellectual property licenses with Broad and Harvard, our licensors retain control of preparation, filing, prosecution, and maintenance, and, in certain circumstances, enforcement and defense of their patents and patent applications. Therefore, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. Additionally, we are required to reimburse our licensors for all of their expenses related to the prosecution, maintenance, enforcement and defense of patents and patent applications that we in-license from them, and we anticipate that our obligation to reimburse our licensors for expenses related to these matters will continue to be substantial.

Our licensors may have relied on third party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents and patent applications we in-license. For example, certain patent applications licensed to us by Broad are co-owned with NIH. Broad does not and does not purport to grant any rights in NIH's interest in these patent applications under our agreement. If other third parties have ownership rights to our in-licensed patents and patent applications, they may be able to license such patents and patent applications to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Some of our in-licensed patents are subject to priority and validity disputes. In addition, our owned and in-licensed patents, patent applications and other intellectual property may be subject to further priority and validity disputes,

and other similar intellectual property proceedings including inventorship disputes. If we or our licensors are unsuccessful in any of these proceedings, we may be required to obtain licenses from third parties, which may not be available on commercially reasonable terms or at all, or to cease the development, manufacture, and commercialization of one or more of the product candidates we develop, which could have a material adverse impact on our business.

Certain U.S. patents and a U.S. patent application directed to CRISPR/Cas9 that are co-owned by the Broad Institute and the Massachusetts Institute of Technology ("MIT"), and in some cases Harvard (collectively referred to as "Broad"), and in-licensed by us were involved in a first interference with a U.S. patent application that is co-owned by the University of California, the University of Vienna, and Emmanuelle Charpentier (collectively referred to "CVC"). An interference is a proceeding in United States Patent and Trademark Office (the "USPTO") before the Patent Trial and Appeal Board of the USPTO ("PTAB") to determine priority of invention of the subject matter of patent claims filed by different parties. In this first interference, the PTAB made a judgment of no interference-in-fact in favor of the Broad, which was upheld on appeal. This decision was final and bars any further interference between the same parties for claims to the same invention that was considered in the interference. As a result of this decision, the U.S. patents and application that we in-license from the Broad and others were not modified or revoked.

On June 24, 2019, the PTAB declared a second interference between certain pending U.S. patent applications that are co-owned by CVC and certain U.S. patents and a U.S. patent application that are co-owned by Broad and in-licensed by us. Most of the Broad U.S. patents and the patent application that are involved in the second interference were also part of the first interference. The invention that was considered in the first interference related to a method involving contacting a target DNA in a eukaryotic cell with certain defined CRISPR/Cas9 components for the purpose of cleaving or editing that target DNA molecule or modulating transcription of at least one gene encoded thereon. The second interference is directed to a different invention, namely a eukaryotic cell comprising a target DNA and certain defined CRISPR/Cas9 components including a single molecule guide RNA that are capable of cleaving or editing the target DNA molecule.

On September 10, 2020, the PTAB granted Broad's motion for priority benefit while denying CVC priority benefit to their two earliest provisional patent applications. As a result, Broad entered the priority phase of the interference as "Senior Party" while CVC remained the "Junior Party" for purposes of determining which entity was the first to invent the inventions at issue. On February 28, 2022, the PTAB issued a decision regarding the priority phase of the interference determining that Broad was the first entity to invent the claims at issue. This decision has been appealed by CVC and the Broad has cross-appealed. It is uncertain when or in what manner the U.S. Court of Appeals for the Federal Circuit will act on these appeals.

On December 14, 2020, the PTAB, declared two new interferences involving a pending U.S. patent application that is owned by ToolGen, Inc. (the "ToolGen application"). One of the two interferences is between the ToolGen application and certain U.S. patents and U.S. patent applications that are co-owned by Broad and in-licensed by us. Most of the Broad U.S. patents and patent applications that are involved in the interference with ToolGen are also part of the second interference with CVC. The other ToolGen interference is between the same ToolGen application and the U.S. patent applications that are co-owned by CVC and involved in the second interference with Broad. The claims in ToolGen's patent application relate to a mammalian cell with a CRISPR/Cas system comprising a codon optimized nucleic acid encoding a Cas9 polypeptide with a nuclear localization signal and a single-molecule guide RNA that, together, are capable of forming a Cas9/RNA complex that mediates double stranded cleavage of a target nucleic acid sequence. On September 28, 2022, the PTAB suspended both of these interferences until the U.S. Court of Appeals for the Federal Circuit issues a mandate in the pending appeals related to the second interference between Broad and CVC.

On June 21, 2021, the PTAB declared two new interferences involving a pending U.S. patent application owned by Sigma-Aldrich (the "Sigma-Aldrich application"). One of the two new interferences is between the Sigma-Aldrich application and certain U.S. patents and U.S. patent applications that are co-owned by Broad and in-licensed by us. The other Sigma interference is between the same Sigma-Aldrich application and the U.S. patent applications that are co-owned by CVC. Most of the Broad U.S. patents and patent applications that are involved in the interference with Sigma-Aldrich are also part of the concurrent interferences with CVC and ToolGen. The claims in Sigma-Aldrich's application relate to a method for modifying a chromosomal sequence in a eukaryotic cell by integrating a donor sequence into that

chromosomal sequence. These methods use a CRISPR/Cas9 system comprising a Cas9 polypeptide with a nuclear localization signal, a guide RNA, and a donor sequence that, together, are capable of mediating double stranded cleavage and repair of a target nucleic acid sequence leading to integration of the donor sequence into the chromosomal sequence. On December 14, 2022, the PTAB suspended both of these interferences until the U.S. Court of Appeals for the Federal Circuit issues a mandate in the pending appeals related to the second interference between Broad and CVC.

As a result of these declarations of interference, five parallel adversarial proceedings in the USPTO before the PTAB have been initiated – the patent interferences between Broad and CVC, Broad and ToolGen, CVC and ToolGen, Broad and Sigma-Aldrich, and CVC and Sigma-Aldrich. We cannot predict with any certainty how long each interference proceeding will take. It is also possible that other third parties may seek to become a party to these interferences.

Our owned and in-licensed patents and patent applications are, or may in the future become, subject to validity disputes in the USPTO and other foreign patent offices. For example, a request for ex parte re-examination was filed with the USPTO on February 16, 2016 against a U.S. patent that we have in-licensed from Broad, which is involved in certain of the interferences. The request for ex parte re-examination was granted on May 9, 2016 thereby initiating a re-examination procedure between the USPTO and The Broad Institute, acting on behalf of itself and MIT. The PTAB has suspended the re-examination noting that it has jurisdiction over any file that involves a patent involved in an interference. It is uncertain when the PTAB will lift the suspension. If The Broad Institute is unsuccessful during the re-examination, the patent in question may be revoked or narrowed, which could have a material adverse effect on the scope of our rights under such patent.

We or our licensors may also be subject to claims that former employees, collaborators, or other third parties have an interest in our owned or in-licensed patents or patent applications, or other intellectual property rights as an inventor or co-inventor. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents, patent applications or other intellectual property rights, such co-owners may be able to license their rights to other third parties, including our competitors. In addition, we may need the cooperation of any such co-owners to enforce any patents, including any patents that issue from patent applications, against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on the conduct of our business, financial condition, results of operations, and prospects.

We or our licensors are subject to and may in the future become a party to similar proceedings or priority disputes in Europe or other foreign jurisdictions. For example, certain European patents that we have in-licensed from Broad have been revoked in their entirety by the European Patent Office Opposition Division (the "Opposition Division"). Certain other European patents that we have in-licensed from Broad were maintained with amended patent claims. Certain of these decisions have been appealed by both Broad and the opposing party(s), and it is uncertain when or in what manner the Boards of Appeal will act on these appeals. The Opposition Division has also initiated opposition proceedings against certain other European patents that we have in-licensed from Broad. The European Patent Office opposition proceedings may involve issues including, but not limited to, procedural formalities related to filing the European patent application, priority, and the patentability of the involved claims. In view of certain arguments made by the third parties against the revoked patents and similar arguments made by the third parties against other in-licensed European patents under opposition, the opposition proceedings may lead to the revocation of certain additional in-licensed European patents. The loss of priority for, or the loss of, these European patents could have a material adverse effect on the conduct of our business. One or more of the third parties that have filed oppositions against these European patents or other third parties may file future oppositions against other European patents that we in-license or own. There may be other oppositions against these European patents that have not yet been filed or that have not yet been made available to the public.

If we or our licensors are unsuccessful in any patent related disputes, including interference proceedings, patent oppositions, re-examinations, or other priority, inventorship, or validity disputes to which we or they are subject (including any of the proceedings discussed above), we may lose valuable intellectual property rights through the loss of one or more patents owned or licensed or our owned or licensed patent claims may be narrowed, invalidated, or held unenforceable. In addition, if we or our licensors are unsuccessful in any inventorship disputes to which we or they are subject, we may lose valuable intellectual property rights, such as exclusive ownership of, or the exclusive right to use,

our owned or in-licensed patents and patent applications. If we or our licensors are unsuccessful in any interference proceeding or other priority or inventorship dispute, we may be required to obtain and maintain licenses from third parties, including parties involved in any such interference proceedings or other priority or inventorship disputes. Such licenses may not be available on commercially reasonable terms or may be non-exclusive or may not be available at all. If we are unable to obtain and maintain such licenses, we may need to cease the development, manufacture, and commercialization of one or more of the product candidates we develop. The loss of exclusivity or the narrowing of our owned and in-licensed patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects. Even if we are successful in any interference proceeding or other priority, inventorship, or validity disputes, it could result in substantial costs and be a distraction to our management and other employees.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. In addition, our intellectual property license agreements may not always include worldwide rights. For example, certain U.S. patent applications licensed to us by Broad include The University of Tokyo ("Tokyo") and NIH as joint applicants. Broad has only granted a license to us with respect to its interests and to Tokyo's interests in these U.S. patent applications but not to any foreign equivalents thereof. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents and our intellectual property rights or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment, and other requirements imposed by government patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees, and various other government fees on patents and applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned or licensed patents and applications. In certain circumstances, we rely on our licensing

partners to pay these fees due to U.S. and non-U.S. patent agencies. The USPTO and various non-U.S. government agencies require compliance with several procedural, documentary, fee payment, and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In some cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in a partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We have entered into license agreements with third parties and may need to obtain additional licenses from our existing licensors and others to advance our research or allow commercialization of product candidates we develop. It is possible that we may be unable to obtain any additional licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third party patents do not exist which might be enforced against our current technology, including CRISPR genome editing technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

In each of our license agreements, and we expect in our future agreements, we are responsible for bringing any actions against any third party for infringing on the patents we have licensed. Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, including the amount, if any, that may become due and payable to our

licensors in connection with sublicense income. If these events were to occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

We may not be successful in obtaining necessary rights to any product candidates we develop through acquisitions and in-licenses.

We currently have rights to intellectual property, through licenses from third parties, to identify and develop product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of genome editing technology and filing patent applications potentially relevant to our business. For example, we are aware of third party patents and patent applications that may be construed to cover our CRISPR technology and product candidates. In order to avoid infringing these third party patents, or patents that issue from these third party patent applications, we may find it necessary or prudent to obtain licenses from such third party intellectual property holders. We may also require licenses from third parties for certain non-CRISPR technologies including certain delivery methods that we are evaluating for use with product candidates we develop. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest in such patents. However, we may be unable to secure such licenses or otherwise acquire or in-license any compositions, methods of use, processes, or other intellectual property rights from third parties that we identify as necessary for our CRISPR technology and product candidates we develop. For example, certain methods for editing cells, guide RNA modifications and delivery modes, including certain adeno-associated virus vector technologies, that we are evaluating for us for use are covered by patents held by third parties. If we are unable to successfully obtain rights to required third party intellectual rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Issued patents covering our technology and product candidates could be found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad.

If we or one of our licensors or our collaborators were to initiate legal proceedings against a third party to enforce a patent covering a product candidate we develop or our technology, including CRISPR genome editing technology, the defendant could counterclaim that such patent is invalid or unenforceable. Third parties have raised challenges to the validity of certain of our in-licensed patent claims and may in the future raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These and other proceedings could result in the revocation or cancellation of, or amendment to our patents in such a way that they no longer cover our technology or platform, or any product candidates that we develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or platform, or any product candidates that we develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

The intellectual property landscape around genome editing technology, including CRISPR, is highly dynamic, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating, or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

The field of genome editing, especially in the area of CRISPR technology, is still in its infancy, and no such products have reached the market. Due to the intense research and development that is taking place by several companies, including us and our competitors, in this field, the intellectual property landscape is in flux, and it may remain uncertain for the coming years. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed, and other third party, intellectual property and proprietary rights in the future.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture,

market, and sell any product candidates that we develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. We are subject to and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and any product candidates we develop, including interference, re-examination, post-grant review, inter partes review, and derivation proceedings before the USPTO and similar proceedings in foreign jurisdictions such as oppositions before the EPO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. We are aware of certain third party patents and patent applications in this landscape that may be asserted to encompass our CRISPR/Cas9 technology. In particular, we are aware of several separate families of U.S. patents and/or U.S. patent applications and foreign counterparts which relate to CRISPR/Cas9 technology, where the earliest priority dates of each family pre-date the priority dates of our in-licensed patents and patent applications, including patent families filed by Vilnius University, by the University of California, the University of Vienna, and Emmanuelle Charpentier, by ToolGen, and by Sigma-Aldrich. Each of these patent families are owned by a different third party and contain claims that may be construed to cover components and uses of CRISPR/Cas9 technology. If we are not able to obtain or maintain a license on commercially reasonable terms to any third-party patents that cover our product candidates or activities, such third parties could potentially assert infringement claims against us, which could have a material adverse effect on the conduct of our business.

Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we develop and any other product candidates or technologies covered by the asserted third party patents. If we are found to infringe a third party's intellectual property rights, and we are unsuccessful in demonstrating that such patents are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing, and marketing any product candidates we develop and our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing the infringing technology or product candidates. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations, and prospects.

If we do not obtain patent term extension and data exclusivity for any product candidates we may develop, it could have a material adverse effect on our business.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, an extension may not be granted because of, for example, failure to exercise due diligence during the testing phase or regulatory review process, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Further, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or if the term of any such extension is less than we request, we will be unable to rely on our patent position to forestall the marketing of competing products following our patent expiration, and it could have a materially adverse effect on our business, financial condition, results of operations, and prospects.

We may be subject to claims that our employees, consultants, or advisors have wrongfully used or disclosed alleged

trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Many of our employees, consultants, and advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology, and other proprietary information and to maintain our competitive position. With respect to our technology platform, we consider trade secrets and know-how to be one of our primary sources of intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to our technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel from academic to industry scientific positions.

We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, collaborators, CROs, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be materially and adversely harmed.

If we do not obtain patent term extension and data exclusivity for any product candidates we develop, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 (the "Hatch-Waxman Amendments"). The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the

approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and prospects could be materially harmed.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming, and uncertain and may prevent us from obtaining approvals for the commercialization of any of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Any of our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by the FDA and other regulatory authorities in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate in a given jurisdiction. We have not received approval to market any product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any of our product candidates may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities, or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of any of our product candidates, the commercial prospects for those product candidates may be harmed, and our ability to generate revenues will be materially impaired.

We may seek certain designations for our product candidates, including Breakthrough Therapy, Fast Track and Priority Review designations in the US, and PRIME Designation in the EU, but we might not receive such designations, and even if we do, such designations may not lead to a faster development or regulatory review or approval process.

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination

with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

The FDA may also designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective.

We may also seek a priority review designation for one or more of our product candidates. If the FDA determines that a product candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months.

These designations are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for these designations, the FDA may disagree and instead determine not to make such designation. Further, even if we receive a designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for these designations, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

In the EU, we may seek PRIME designation for some of our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the EU or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the EU and the applicant intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims. The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

If approved, our product candidates that are licensed and regulated as biologics may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Biologics Price Competition and Innovation Act of 2009, ("BPCIA"), was enacted as part of the Patient Protection and Affordable Care Act, ("ACA"), to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, a reference biological product is granted 12 years of data

exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product In addition, the licensure of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still develop and receive approval of a competing biologic, so long as its BLA does not reply on the reference product, sponsor's data or submit the application as a biosimilar application. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty, and any new policies or processes adopted by the FDA could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the product candidates we develop as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing. Nonetheless, the approval of a biosimilar to our product candidates would have a material adverse impact on our business due to increased competition and pricing pressure.

We may not be able to obtain orphan drug exclusivity for one or more of our product candidates, and even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition. A similar regulatory scheme governs approval of orphan products by the EMA in the European Union. Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product for the same therapeutic indication for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation, in particular if the product is sufficiently profitable so that market exclusivity is no longer justified.

In order for the FDA to grant orphan drug exclusivity to one of our products, the agency must find that the product is indicated for the treatment of a condition or disease with a patient population of fewer than 200,000 individuals annually in the United States. The FDA may conclude that the condition or disease for which we seek orphan drug exclusivity does not meet this standard. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. In particular, the concept of what constitutes the "same drug" for purposes of orphan drug exclusivity remains in flux in the context of gene therapies. In September 2021, the FDA issued final guidance describing its current thinking on when a gene therapy product is the "same" as another product for purposes of orphan exclusivity. Under the guidance, if either the transgene or vector differs between two gene therapy products in a manner that does not reflect "minor" differences, the two products would be considered different drugs for orphan drug exclusivity purposes. The FDA will determine whether two vectors from the same viral class are the same on a case-by-case basis and may consider additional key features in assessing sameness. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may also be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of the patients with the rare disease or condition.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017 ("FDARA"). FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act

unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. Further, under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017, but have not yet been approved or licensed by the FDA.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, FDA announced that, in matters beyond the scope of that court order, FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Failure to obtain marketing approval in foreign jurisdictions would prevent any of our product candidates from being marketed in such jurisdictions, which, in turn, would materially impair our ability to generate revenue.

In order to market and sell any of our product candidates in the European Union and many other foreign jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any jurisdiction, which would materially impair our ability to generate revenue.

Additionally, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit, and, effective January 1, 2021, the United Kingdom ceased to be part of the European Single Market and European Union Customs Union. A co-operation agreement was signed between the United Kingdom and the European Union in December 2020, which entered into force on May 1, 2021. The agreement addresses trade, economic arrangements, law enforcement, judicial cooperation and a governance framework including procedures for dispute resolution, among other things. As both parties continue to work on the rules for implementation, significant political and economic uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, the consequences of Brexit and the impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom remains unclear. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the

United Kingdom for our product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets (such as the ongoing conflict between Ukraine and Russia); compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

Even if we, or any collaborators we may have, obtain marketing approvals for any of our product candidates, the terms of approvals and ongoing regulation of our products could require the substantial expenditure of resources and may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more of our product candidates, we, and such collaborators, and our and their contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. If we and such collaborators are not able to comply with post-approval regulatory requirements, we and such collaborators could have the marketing approvals for our products withdrawn by regulatory authorities and our, or such collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, operating results, financial condition, and prospects.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future

government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, a number of companies announced in 2020 and 2021 that they had received complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and review timelines could be extended, thus the FDA may be unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may experience delays in their regulatory activities.

If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory agencies impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the Department of Justice. Violation of the Federal Food, Product, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may also lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown problems with our medicines, manufacturers, or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such medicines, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;
- restrictions on the distribution or use of a medicine;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- fines, restitution, or disgorgement of profits or revenue;

- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

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 product candidates we develop and adversely affect our business, financial condition, results of operations, and prospects.

Our relationships with healthcare providers, physicians, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits and future earnings.

Healthcare providers, physicians, and third-party payors play a primary role in the recommendation and prescription of any of our product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving, or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order, or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval from Medicare, Medicaid, or other government payors that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties;
- the federal Health Insurance Portability and Accountability Act of 1996, as further amended by the Health Information Technology for Economic and Clinical Health Act, which imposes certain requirements, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses, and health care providers;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items, or services;
- the federal transparency requirements under the federal Physician Payment Sunshine Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians, other

healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and certain state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from participation in government health care programs, such as Medicare and Medicaid, imprisonment, and the curtailment or restructuring of our operations, any of which could adversely affect our business, financial condition, results of operations, and prospects.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order, or use of medicinal products is prohibited in the European Union. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization, and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Liabilities they incur pursuant to these laws could result in significant costs or an interruption in operations, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Enacted and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively the "ACA"). In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act"). Pursuant to subsequent legislation, however, these Medicare sequester reductions were suspended and reduced through the end of June 2022 , with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our products or product candidates for which we may obtain regulatory approval or the frequency with which any such product is prescribed or used.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts for Jobs Act, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. In June 2021, the U.S. Supreme Court dismissed this action after finding that the plaintiffs did not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents. This Executive Order also directed the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions is subject to considerable legislative and executive actions and could impact the prices we obtain for our products, if and when licensed.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to

incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Infrastructure Investment and Jobs Act to January 1, 2026 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which has been delayed until January 1, 2026 by the Infrastructure Investment and Jobs Act.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs the Department of Health and Human Services, or HHS, to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Our employees, principal investigators, consultants, and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants, and partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations, and prospects, including the imposition of significant fines or other sanctions.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act ("FCPA") prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be

improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies, contractual obligations and failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally-identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information, including comprehensive regulatory systems in the U.S., EU and UK. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In 2018, California passed into law the California Consumer Privacy Act (the "CCPA"), which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation (the "GDPR"), including requiring businesses to provide notice to data subjects regarding the information collected about

them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In November 2020, California voters passed a ballot initiative for the California Privacy Rights Act (the "CPRA"), which went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition, other states, including Virginia, Colorado, Utah, and Connecticut already have passed state privacy laws. Virginia's privacy law also went into effect on January 1, 2023, and the laws in the other three states will go into effect later in the year. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Similar to the laws in the U.S., there are significant privacy and data security laws that apply in Europe and other countries. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area ("EEA"), and the processing of personal data that takes place in the EEA, is regulated by the GDPR, which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR imposes onerous accountability obligations requiring data controllers and processors to maintain a record of their data processing and policies. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill.

The GDPR places restrictions on the cross-border transfer of personal data from the EU to countries that have not been found by the EC to offer adequate data protection legislation, such as the U.S. There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union (the "CJEU") invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the U.S. While we were not self-certified under the Privacy Shield, this CJEU decision may lead to increased scrutiny on data transfers from the EEA to the U.S. generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

Additionally, in October 2022, President Joe Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The EC initiated the process to adopt an adequacy decision for the EU-US Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU.

Following the withdrawal of the UK from the EU, the UK Data Protection Act 2018 applies to the processing of personal data that takes place in the UK and includes parallel obligations to those set forth by GDPR. As with other issues related to Brexit, there are open questions about how personal data will be protected in the UK and whether personal information can transfer from the EU to the UK. It is still unclear whether transfer of data from the European Economic Area, or EEA, to the UK will remain lawful under GDPR. The United Kingdom government has already determined that it considers all European Union and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the European Union/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the UK as being "essentially adequate" for purposes of data transfer from the EU to the UK, although this decision may be re-evaluated in the future.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and the sale and distribution of commercial products, through increased compliance costs, costs associated with contracting and potential enforcement actions.

While we continue to address the implications of the recent changes to data privacy regulations, data privacy remains an evolving landscape at both the domestic and international level, with new regulations coming into effect and continued legal challenges, and our efforts to comply with the evolving data protection rules may be unsuccessful. It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with laws regarding data protection would expose us to risk of enforcement actions taken by data protection authorities in the EEA and elsewhere and carries with it the potential for significant penalties if we are found to be non-compliant. Similarly, failure to comply with federal and state laws in the U.S. regarding privacy and security of personal information could expose us to penalties under such laws. Any such failure to comply with data protection and privacy laws could result in government-imposed fines or orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Risks Related to Employee Matters, Managing Growth, Public Health and Information Technology

Our future success depends on our ability to attract and retain key executives and to attract, retain, and motivate qualified personnel.

We are highly dependent on the principal members of our management and scientific teams. Each of these individuals is employed "at will," meaning we or the individual may terminate the employment relationship at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development, and commercialization objectives. Additionally, we are actively trying to recruit a candidate for the role of Chief Scientific Officer. Any inability to fill this position in an expedient manner may have a material adverse effect on our business.

Recruiting and retaining qualified scientific, clinical, manufacturing, and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. In addition, our ability to recruit and retain qualified personnel could be impacted by other factors, such as remote or hybrid working arrangements, which could impact employees' productivity and morale, as well as any failure to succeed in preclinical or clinical trials. The inability to recruit or the loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

We face risks related to health epidemics, pandemics and other widespread outbreaks of contagious disease, including the COVID-19 pandemic, which could significantly disrupt our operations, impact our financial results or otherwise adversely impact our business.

Significant outbreaks of contagious diseases, and other adverse public health developments, could have a material impact on our business operations and operating results. Any public health crises, including the COVID-19 pandemic, or related healthcare staffing shortages, supply chain restrictions, or other issues, may result in disruptions that could adversely impact our operations, research and development, including preclinical studies, clinical trials and manufacturing activities, including:

- delays or disruptions in clinical trials that we may be conducting, including patient screening, patient enrollment, patient dosing, clinical trial site activation, and study monitoring;

- delays or disruptions in preclinical experiments and IND- and clinical trial application-enabling studies due to restrictions related to our staff being on site;

- interruption or delays in the operations of the FDA, EMA and comparable foreign regulatory agencies;

- interruption of, or delays in, receiving, supplies of drug substance and drug product from our CMOs or delays or disruptions in our pre-clinical experiments or clinical trials performed by CROs due to staffing shortages, production and research slowdowns or stoppages and disruptions in delivery systems or research;

- limitations imposed on our business operations by local, state, or federal authorities to address such pandemics or similar public health crises could impact our ability to conduct preclinical or clinical activities, including conducting IND- and CTA-enabling studies or our ability to select future development candidates; and

- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, staffing shortages, travel limitations, cyber security and data accessibility, or communication or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees, manufacturing sites, research or clinical trial sites and other important agencies and contractors.

Our clinical trials for EDIT-301, as well as timely completion of preclinical activities and initiation of planned clinical trials for other product candidates, is dependent upon the availability of, for example, preclinical and clinical trial sites, researchers and investigators, regulatory agency personnel, and materials, which may be adversely affected by a public health crisis and related government responses. A resurgence or other negative developments relating to the COVID-19 pandemic may require us to restrict access to our offices and laboratories for an extended period of time, or to pause or suspend preclinical research and our clinical trials; and, further, may cause delays or restrictions at healthcare facilities or disrupt our manufacturing and supply chain or those of our third-party suppliers and manufacturers. In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile in part as a result of the COVID-19 pandemic. As a result, we may face difficulties raising additional capital through sales of our common stock or such sales may be on unfavorable terms.

We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage, however, were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business and our results of operation and financial condition.

We expect to expand our manufacturing, clinical, development, and regulatory capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect growth in the number of our employees and the scope of our operations, particularly in the areas of manufacturing, clinical development, drug development, and regulatory affairs, and, if any product candidates receive marketing approval, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Security breaches and other disruptions to our information technology structure could compromise our information, disrupt our business and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect, process and store sensitive data, including intellectual property, as well as our proprietary business information and that of our suppliers and business partners, employee data, and we may collect personally identifiable information of clinical trial participants in connection with clinical trials. We also rely to a large extent on information technology systems to operate our business, including our financial systems. We have outsourced elements of our confidential information processing and information technology structure, and as a result, we are managing independent vendor relationships with third parties who may or could have access to our confidential information. Similarly, our business partners and other third-party providers possess certain elements of our sensitive data. The secure maintenance of this information is important to our operations and business strategy. Despite our security measures, our information technology infrastructure (and those of our partners, vendors and third-party providers) may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. We, our partners, vendors, and other third-party providers could be susceptible to third party attacks on our, and their, information security systems, which attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives and expertise, including organized criminal groups, hacktivists, nation states and others. Furthermore, we have implemented a hybrid work model, which may place our information technology infrastructure and data at increased risk as more of our employees work from home utilizing network connections outside our premises. We have invested in information technology security measures and the protection of confidential and sensitive information, but there can be no assurance that our efforts will prevent system failures, accidents or security breaches. While we believe we have not experienced any such material system failure, accident or security breach to date, any such event may substantially impair our ability to operate our business and would compromise our, and their, networks and the information stored could be accessed, publicly disclosed, lost, or stolen. In addition, if a ransomware attack or other cybersecurity incident occurs, either internally or at our vendors or third-party technology service providers, we could be prevented from accessing our data or systems, which may cause interruptions or delays in our business operations, cause us to incur remediation costs, subject us to demands to pay a ransom, or damage our reputation, regardless of whether we pay the ransom amount. Any such event, or other loss of information, could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation, any of which could adversely affect our business.

Although we have general liability and cybersecurity insurance coverage, our insurance may not cover all claims, continue to be available on reasonable terms or be sufficient in amount to compensate us fully for potential significant losses; additionally, the insurer may disclaim coverage as to any claim. The successful assertion of one or more large claims against us that exceed or are not covered by our insurance coverage or changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could materially harm our business, financial condition, results of operations and prospects.

Risks Related to Our Common Stock

The market price of our common stock may be volatile, which could result in substantial losses for our stockholders.

Our stock price has been, and is likely to remain, volatile. For example, since January 1, 2021, the trading price of our common stock on the Nasdaq Global Select Market has ranged from a low of $7.71 to a high of $99.95 through January 31, 2023. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the success of existing or new competitive products or technologies;
- the timing and results of clinical trials for EDIT-301 and any preclinical studies and clinical trials of any other product candidates that we develop;
- commencement or termination of collaborations for our product development and research programs;
- failure or discontinuation of any of our product development and research programs;

- results of preclinical studies, clinical trials, or regulatory approvals of product candidates of our competitors, or announcements about new research programs or product candidates of our competitors;
- developments or changing views regarding the use of genomic medicines, including those that involve genome editing;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents, or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our research programs, clinical development programs, or product candidates that we develop;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders, or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this "Risk Factors" section.

In recent years, the stock market in general, and the market for pharmaceutical and biotechnology companies in particular, has experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to changes in the operating performance of the companies whose stock is experiencing those price and volume fluctuations. Because of the potential volatility of our stock price, we may become the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock and trading volume could decline.

The trading market for our common stock depends, in part, on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock or fail to regularly publish reports on us, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of stockholders and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In addition, sales of a significant number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock.

We have registered substantially all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

We incur costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company we have incurred, and will continue to incur, significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We have had to hire additional accounting, finance, and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company, and our management and other personnel devote a substantial amount of time towards maintaining compliance with these requirements. These requirements increase our legal and financial compliance costs and make some activities more time-consuming and costly.

We have broad discretion in the use of our cash reserves and may not use them effectively.

Our management has broad discretion to use our cash reserves and could use our cash reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline, and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

We do not expect to pay any dividends for the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investments.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be stockholders' sole source of gain for the foreseeable future.

Provisions in our restated certificate of incorporation and amended and restated bylaws or Delaware law might discourage, delay, or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions in our restated certificate of incorporation and amended and restated bylaws or Delaware law may

discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares of our common stock. These provisions may also prevent or frustrate attempts by our stockholders to replace or remove our management. These provisions include:

- limitations on the removal of directors;
- a classified board of directors so that not all members of our board of directors are elected at one time;
- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to act by written consent or to call special meetings;
- the requirement that at least 75% of the votes cast by all our stockholders approve the amendment or repeal of certain provisions of our amended and restated bylaws or restated certificate of incorporation;
- the ability of our board of directors to make, alter, or repeal our amended and restated bylaws; and
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors.

In addition, Section 203 of the General Corporation Law of the State of Delaware prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions could deter potential acquirers of our company, thereby reducing the likelihood that our stockholders could receive a premium for their shares of common stock in an acquisition.

Our restated certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors and officers.

Our restated certificate of incorporation provides that, unless our board of directors otherwise determines, the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to our company or our stockholders, any action asserting a claim against us or any of our directors or officers arising pursuant to any provision of the General Corporation Law of the State of Delaware or our restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us or any of our directors or officers governed by the internal affairs doctrine. This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors or officers, which may discourage such lawsuits against us and our directors and officers. This exclusive forum provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act of 1934, which provides for exclusive jurisdiction of the federal courts. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act of 1933, as amended (the "Securities Act"), inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder; provided, that with respect to claims under the Securities Act, our stockholders will not be deemed to have

waived our compliance with the federal securities laws and the rules and regulations thereunder.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties.

We lease 59,783 square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires in October 2028. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings relating to claims arising from the ordinary course of business. There can be no assurance that any proceedings that result from these third-party actions will be resolved in our favor. In addition, if they are not resolved in our favor, there can be no assurance that the result will not have a material adverse effect on our business, financial condition, results of operations, or prospects. Certain of our intellectual property rights, including ones licensed to us under our licensing agreements, are subject to, and from time to time may be subject to, priority and validity disputes. For additional information regarding these matters, see "Item 1A. Risk Factors—Risks Related to Our Intellectual Property." Regardless of outcome, litigation or other legal proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources, and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock trades on the Nasdaq Global Select Market under the symbol "EDIT."

Holders

As of February 17, 2023, we had approximately 18 holders of record of our common stock. This number does not include beneficial owners whose shares were held in street name.

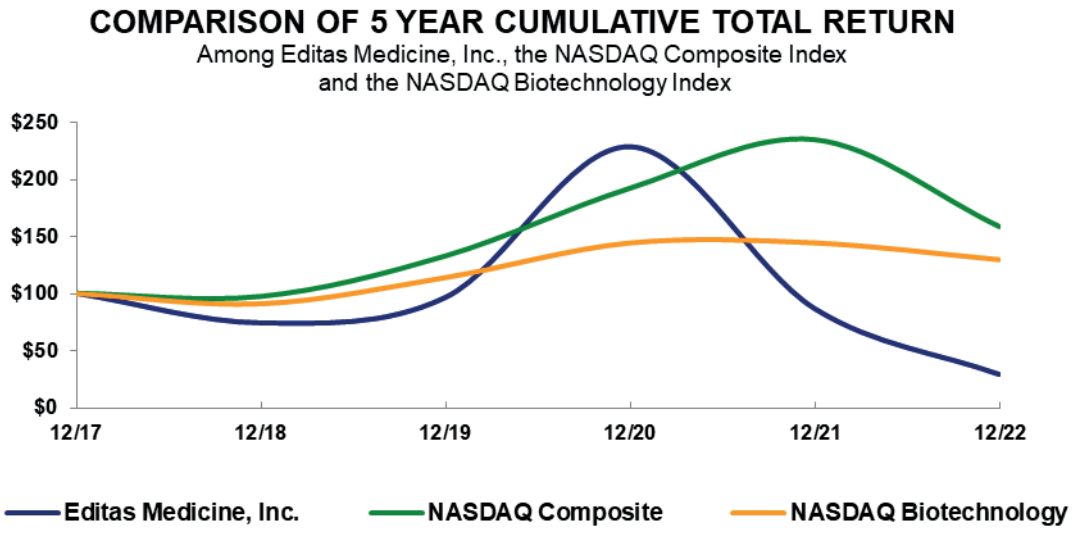
Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain future earnings to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. In addition, the terms of any future debt agreements that we may enter into may preclude us from paying dividends without the lenders' consent or at all.

Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities under that Section, nor shall such information be incorporated by reference into any future filing under the Exchange Act or the Securities Act of 1933, as amended (the "Securities Act"), except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our common stock to The Nasdaq Composite Index and to The Nasdaq Biotechnology Index from December 31, 2017 through December 31, 2022. The comparison assumes $100 was invested after the market closed on December 31, 2017 in our common stock and in each of the foregoing indices, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of future stock price performance.



Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliates Purchasers

Neither we nor any affiliated purchaser or anyone acting on behalf of us or an affiliated purchaser made any purchases of shares of our common stock during the fourth quarter of 2022.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K.

Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section entitled "Risk Factors" in Part I, Item 1A that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K,and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

Overview

We are a clinical stage genome editing company dedicated to developing potentially transformative genomic medicines to treat a broad range of serious diseases. We have developed a proprietary gene editing platform based on CRISPR technology and we continue to expand its capabilities. Our product development strategy is to target diseases where gene editing can be used to enable or enhance therapeutic outcomes for patients, while maximizing probability of technical, regulatory and commercial success. We are focused on advancing gene editing medicines to treat hemoglobinopathies, beginning with the continued development of our current *ex vivo* EDIT-301 program and leveraging the insights gained from this program to pursue next generation *in vivo* gene editing medicines targeting hematopoietic stem cells ("HSCs"). In parallel, we are pursuing the development of *in vivo* gene editing medicines for other organs and tissues that we believe will significantly differentiate our genome editing approach from the current standards of care for serious diseases. As part of these efforts, we are using existing strategic partnerships and collaborations and pursuing further opportunities to extend the reach of our intellectual property portfolio and access complementary technologies to expedite our drug discovery and clinical execution objectives.

Our lead program, EDIT-301, is an experimental *ex vivo* gene-edited medicine to treat sickle cell disease ("SCD"), a severe inherited blood disease that causes premature death, and transfusion-dependent beta thalassemia ("TDT"), the most severe form of beta-thalassemia, another inherited blood disorder characterized by severe anemia. In the second quarter of 2022, we dosed the first patient in our Phase 1/2 clinical trial of EDIT-301, which we refer to as our RUBY trial, for the treatment of severe SCD, and in December 2022, announced initial clinical data from the first two patients treated in the RUBY trial. This clinical data supports human proof of concept by showing that EDIT-301 could safely increase expression of fetal hemoglobin to clinically meaningful levels and correct anemia in SCD patients. For additional information regarding these clinical data, please see "Business—Our Gene Editing Medicine Programs—Hemoglobinopathies." After completing sequential dosing of the first two patients, we have commenced parallel patient dosing in this trial and are on track to dose 20 total patients by the end of 2023. We expect to provide clinical updates from the RUBY trial in mid-2023 and end of 2023.

In December 2021, the FDA cleared our Investigational New Drug ("IND") application for a Phase 1/2 clinical trial of EDIT-301 for the treatment of TDT. This trial, referred to as our EDITHAL trial, is designed to assess the safety, tolerability, and preliminary efficacy of EDIT-301 for the treatment of TDT. We are on track to dose the first patient in this trial in the first quarter of 2023. We expect to provide data on this patient by the end of 2023.

We are also pursuing the development of next generation *in vivo* administered gene editing medicines, in which the medicine is injected or infused into the patient to edit the cells inside their body. We are initially focused on editing HSCs through targeted delivery of our AsCas12a enzyme to our clinically validated HBG1 and HBG2 promotor site. We are also in the discovery stage in developing in vivo gene editing medicines for other organs and tissues.

We previously achieved human proof of concept for our most advanced *in vivo* gene editing medicine for inherited retinal diseases, EDIT-101 to treat Leber congenital amaurosis. In November 2022 we announced updated clinical data from our Phase 1/2 BRILLIANCE trial of EDIT-101. This data demonstrated a favorable safety profile and provided proof of concept. However, we were not able to identify any baseline characteristics of the treatment responder patients that could pre-select a responder patient population other than zygosity. The identified responder patient population was determined to be too small to progress the program independently. We have since paused patient enrollment in this program.

We are pursuing the right combination of gene editing and targeted delivery tools through internal development and the in-licensing of complementary technologies, while also leveraging our intellectual property portfolio to drive potential out-licensing and partnership discussions that can accelerate the achievement of our goal of delivering lifesaving medicines to patients with previously untreatable or under-treated diseases. In cellular therapy medicines, we are leveraging new and existing partnerships to progress engineered cell medicines to treat various cancers. We are advancing alpha-beta T-cell experimental medicines for the treatment of solid and liquid tumors in collaboration with Bristol Myers Squibb Company ("BMS") through its wholly owned subsidiary, Juno Therapeutics, Inc. ("Juno Therapeutics"). This collaboration, which leverages our Cas9 and AsCas12a platform technologies, has resulted in 11 programs. We have also entered into a non-exclusive collaboration and licensing agreement with Immatics N.V. to combine gamma-delta T cell adoptive cell therapies and gene editing to develop medicines for the treatment of cancer.

In January 2023, we announced the sale of our wholly owned oncology assets to Shoreline Biosciences, Inc. ("Shoreline"). Under the agreement, Shoreline acquired EDIT-202, our preclinical multiplexed edited induced human pluripotent stem cell ("iPSC")-derived natural killer ("iNK") cell medicine for the treatment of solid tumors, as well as an additional iNK program under development and certain related manufacturing technologies. We also exclusively licensed to Shoreline our rights to a proprietary knock-in gene editing technology referred to as SLEEK (SeLection by Essential-gene Exon Knock-in) for use in Shoreline's iNK platform and for oncology in Shoreline's iPSC-derived macrophage platform, as well as a non-exclusively licensed our AsCas12a gene editing technology. We believe that this transaction will enable this oncology program to more rapidly move towards clinical applications.

Since our inception in September 2013, our operations have focused on organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio, assembling our core capabilities in gene editing, seeking to identify potential product candidates, and undertaking preclinical studies. Except for EDIT-301, all of our ongoing research programs are still in the preclinical or research stage of development and the risk of failure of all of our research programs is high. We have not generated any revenue from product sales. We have primarily financed our operations through various equity financings and payments received under our research collaboration with BMS and our former strategic alliance with Allergan Pharmaceuticals International Limited (together with its affiliates, "Allergan"), which was terminated in August 2020.

Since inception, we have incurred significant operating losses. Our net losses were $220.4 million, $192.5 million, and $116.0 million for the years ended December 31, 2022, 2021 and 2020 respectively. As of December 31, 2022, we had an accumulated deficit of $1.1 billion. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and from year to year. We anticipate that our expenses will increase substantially as we continue our current research programs and our preclinical development activities; progress the clinical development of EDIT-301; seek to identify additional research programs and additional product candidates; initiate preclinical testing and clinical trials for other product candidates we

identify and develop; maintain, expand, and protect our intellectual property portfolio, including reimbursing our licensors for such expenses related to the intellectual property that we in-license from such licensors; further develop our genome editing platform; hire additional clinical, quality control, and scientific personnel; and incur additional costs associated with operating as a public company. We do not expect to be profitable for the year ending December 31, 2023 or the foreseeable future.

We did not experience any significant impact on our financial condition, results of operations or liquidity due to the COVID-19 pandemic during the year ended December 31, 2022. At its height, the COVID-19 pandemic had a significant negative effect on the global economy, supply chains and labor force participation, and created significant volatility in financial markets. The extent of the future impact of the COVID-19 pandemic on our operational and financial performance, including our ability to timely advance our clinical trials and preclinical actvtivies, will depend on future developments, including the duration, spread and severity of the pandemic, any evolution of the virus, government restrictions imposed in response, and the availability and effectiveness of vaccines and treatment options, all of which are uncertain and cannot be predicted. We will continue to monitor and respond to the changing conditions created by the pandemic, with focus on prioritizing the health and safety of our employees and maintaining safe and reliable operations of our facilities.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and we do not expect to generate any revenue from product sales for the foreseeable future. In connection with our collaboration with BMS, we have received an aggregate of $130.0 million in payments, which have primarily consisted of the initial upfront and amendment payments, development milestone payments and research funding support. We no longer receive research funding support. During the year ended December 31, 2022, we recognized $18.8 million of revenue related to our collaboration with BMS of which $11.3 million was previously deferred revenue. As of December 31, 2022, we had $56.7 million of deferred revenue related to BMS, of which $56.7 million is classified as long-term on our consolidated balance sheet. Under this collaboration, we will recognize revenue upon delivery of option packages to BMS or when milestones are achieved. As such, we expect that our revenue will fluctuate from quarter-to-quarter and year-to-year as a result of the timing of when these events occur.

In connection with our former strategic alliance with Allergan, we received an aggregate of $130.0 million in payments, which consisted of the initial upfront payment, an option exercise payment and a milestone payment. Prior to the termination of our agreements with Allergan, certain of these payments were deferred and were being recognized over the remaining contract term using the proportional performance method. During the third quarter of 2020, as a result of the termination of our agreements with Allergan, we recognized $63.2 million of revenue that consisted of previously deferred revenue net of a payment made to Allergan in connection with the termination.

For additional information about our revenue recognition policy related to the BMS collaboration or the Allergan strategic alliance, see "—Critical Accounting Policies and Estimates—Revenue Recognition" included in this Annual Report on Form 10-K.

For the foreseeable future we expect substantially all of our revenue will be generated from our collaboration with BMS, and any other collaborations or agreements we may enter into.

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research, preclinical development, process and scale-up development, manufacture and clinical development of our product candidates, and

the performance of development activities under our collaboration agreements. These costs are expensed as incurred and include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- costs incurred under clinical trial agreements with investigative sites;
- costs associated with conducting our preclinical, process and scale-up development, manufacturing, clinical and regulatory activities, including fees paid to third-party professional consultants, service providers and suppliers;
- costs of purchasing lab supplies and non-capital equipment used in our preclinical activities and in manufacturing preclinical and clinical study materials;
- costs incurred for the research and development activities under our collaboration agreements;
- facility costs including rent, depreciation, and maintenance expenses; and
- fees for acquiring and maintaining licenses under our third-party licensing agreements, including any sublicensing or success payments made to our licensors.

At this time, we cannot reasonably estimate or know the nature, timing, and estimated costs of the efforts that will be necessary to complete the development of any product candidates we may identify and develop. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful completion of preclinical studies, IND-enabling studies and natural history studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of a product, if and when approved, whether alone or in collaboration with others;
- acceptance of a product, if and when approved, by patients, the medical community, and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

A change in the outcome of any of these variables with respect to the development of any product candidates we develop would significantly change the costs, timing, and viability associated with the development of that product candidate.

Research and development activities are central to our business model. We expect research and development costs to increase significantly for the foreseeable future as our development programs progress, including as we continue to progress our clinical trials as well as support preclinical studies for our other research programs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation for personnel in executive, finance, investor relations, business development, legal, corporate affairs, information technology, facilities and human resource functions. Other significant costs include corporate facility costs not otherwise included in research and development expenses, legal fees related to intellectual property and corporate matters, and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities and potential commercialization of any product candidates we identify and develop. These increases will include increased costs related to the hiring of additional personnel and fees to outside consultants. We also anticipate increased expenses related to reimbursement of third-party patent-related expenses and expenses associated with operating as a public company, including costs for audit, legal, regulatory, and tax-related services, director and officer insurance premiums, and investor relations costs. With respect to reimbursement of third-party intellectual property-related expenses specifically, given the ongoing nature of the opposition and interference proceedings involving the patents licensed to us under our license agreement with The Broad Institute, Inc. ("Broad") and the President and Fellows of Harvard College ("Harvard"), we anticipate general and administrative expenses will continue to be significant.

Other Income (Expense), Net

For the years ended December 31, 2022, and 2021, other income (expense), net consisted primarily of changes in interest income and accretion of discounts associated with other marketable securities.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles. The preparation of our consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues, and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policy used in the preparation of our consolidated financial statements requires the most significant judgments and estimates.

Revenue Recognition

We recognize revenue in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC"), Topic 606, *Revenue Recognition* ("ASC 606"). Accordingly, we recognize revenue following the five step model prescribed under Accounting Standards Updates No. 2014-09, *Revenue from Contracts with Customers*: (i) identify contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenues when (or as) we satisfy the performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we

assess the goods or services promised within each contract and determine those that are performance obligations, and whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. A significant portion of revenue recognized from our strategic alliance with Allergan, prior to termination, was related to research services performed for each clinical development program whereby revenue was recognized as the underlying services were performed using a proportional performance model. Prior to the termination of the arrangement with Allergan, we measured proportional performance based on full time employee hours incurred relative to projected full time employee hours to complete the research services for each clinical development program. We evaluated the measure of progress each reporting period and, if necessary, adjusted the measure of performance and related revenue recognition.

Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in our consolidated balance sheets.

Accrued research and development expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to clinical research organizations, to investigative sites in connection with clinical trials, to sponsored research organizations, to service providers in connection with preclinical development activities and to service providers related to product manufacturing, development and distribution of clinical supplies.

We base our accrued expenses related to clinical trials on our estimates of the services performed and efforts expended pursuant to our contractual arrangements, including those with clinical research organizations. The financial terms of these agreements are sometimes subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our service providers will exceed the level of services performed and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly.

Although we do not expect our estimates to be materially different from expenses actually incurred, if our estimates of the status and timing of services performed differs from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amounts actually incurred.

Results of Operations

Comparison of Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2022	2021	Dollar Change	Percentage Change
Collaboration and other research and development revenues	$ 19,712	$ 25,544	$ (5,832)	(23) %
Operating expenses:				
Research and development	174,958	142,507	32,451	23 %
General and administrative	70,704	76,183	(5,479)	(7) %
Total operating expenses	245,662	218,690	26,972	12 %
Other income, net				
Other income (expense), net	1,293	(1,698)	2,991	n/m
Interest income, net	4,225	2,342	1,883	80 %
Total other income, net	5,518	644	4,874	n/m
Net loss	$ (220,432)	$ (192,502)	$ (27,930)	15 %

For our results of operations, we have included the respective percentage of changes, unless greater than 100% or less than (100)%, in which case we have denoted such changes as not meaningful (n/m).

Collaboration and Other Research and Development Revenues

Collaboration and other research and development revenues decreased by $5.8 million, to $19.7 million for the year ended December 31, 2022, from $25.5 million for the year ended December 31, 2021. The decrease was primarily attributable to fewer programs licensed under our collaboration with BMS in 2022 than in 2021.

Research and Development Expenses

Research and development expenses increased by $32.5 million, to $175.0 million for the year ended December 31, 2022 from $142.5 million for the year ended December 31, 2021. The following table summarizes our research and development expenses for the years ended December 31, 2022 and December 31, 2021, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2022	2021	Dollar Change	Percentage Change
External research and development expenses	$ 79,822	$ 53,964	$ 25,858	48 %
Employee related expenses	47,320	40,474	6,846	17 %
Facility expenses	21,032	16,446	4,586	28 %
Stock-based compensation expenses	12,425	16,553	(4,128)	(25) %
Other expenses	9,025	3,446	5,579	n/m
Sublicense and license fees	5,334	11,624	(6,290)	(54) %
Total research and development expenses	$ 174,958	$ 142,507	$ 32,451	23 %

The increase in research and development expenses for the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily attributable to:

- approximately $25.9 million in increased external research and development expenses primarily attributable to the clinical and manufacturing development of EDIT-301 as well as expenses related to the pause in internal investments in EDIT-101;
- approximately $6.8 million in increased employee related expenses primarily due to an increase in the size of our workforce, including a new Chief Medical Officer, to support clinical programs;
- approximately $5.6 million in increased other expenses related primarily to a COVID-19 employee retention tax credit recognized in the third quarter of 2021, which reduced research and development expenses and did not repeat in 2022, and increased consulting expenses in 2022; and
- approximately $4.6 million in increased facility related expenses primarily related to increased lab and manufacturing space.

These increases were partially offset by the following decreases in research and development expenses:

- approximately $6.3 million in decreased sublicense and license fees primarily related to the triggering of success payments under certain of our license agreements upon the achievement of market capitalization-based milestones in the first quarter of 2021 for which there were no similar fees in 2022, partially offset by license fees owed to certain of our licensors in 2022 in connection with receiving milestone and other payments from our licensees; and
- approximately $4.1 million in decreased stock-based compensation expenses primarily due to equity awards granted in 2021, for which there were no similar awards in 2022, as well as decreased stock-based compensation expense recognized related to the performance-based awards that were granted to certain employees in 2021.

General and Administrative Expenses

General and administrative expenses decreased by approximately $5.5 million, to $70.7 million for the year ended December 31, 2022 from $76.2 million for the year ended December 31, 2021. The following table summarizes our general and administrative expenses for the years ended December 31, 2022 and December 31, 2021, together with the changes in those items in dollars (in thousands) and the respective percentages of change:

	Year Ended December 31,			
	2022	2021	Dollar Change	Percentage Change
Employee related expenses	$ 17,321	$ 16,929	$ 392	2 %
Stock-based compensation expenses	16,869	26,846	(9,977)	(37) %
Intellectual property and patent related fees	14,784	16,542	(1,758)	(11) %
Professional service expenses	11,496	7,590	3,906	51 %
Facility and other expenses	10,234	8,276	1,958	24 %
Total general and administrative expenses	$ 70,704	$ 76,183	$ (5,479)	(7) %

The decrease in general and administrative expenses for the year ended December 31, 2022 compared to the year ended December 31, 2021 was primarily attributable to:

- approximately $10.0 million in decreased stock-based compensation expenses related to the acceleration of vesting of certain equity awards held by our former Chief Executive Officer in connection with her separation from our company in February 2021, as well as stock-based compensation expense recognized related to the performance-based awards that were granted to our succeeding Chief Executive Officer and

other employees in 2021, under which a single performance obligation was achieved in 2021, for which there were no similar expenses recognized in 2022; and

- approximately $1.8 million in decreased intellectual property and patent related fees.

These decreases were partially offset by the following increases in general and administrative expenses:

- approximately $3.9 million in increased professional service expenses to support infrastructure and expanding operations; and

- approximately $1.9 million in increased facility and other expenses.

Total Other Income, Net

For the years ended December 31, 2022, and 2021, total other income, net was $5.5 million and $0.6 million, respectively, which was primarily attributable to interest income and accretion of discounts associated with marketable securities.

Comparison of Years Ended December 31, 2021 and 2020

For a discussion of our results of operations for the year ended December 31, 2021 as compared to the year ended December 31, 2020, see Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations in our annual report on Form 10-K for the year ended December 31, 2021, which was filed with the SEC on February 24, 2022.

Liquidity and Capital Resources

Sources of Liquidity

As of December 31, 2022, we have raised an aggregate of $898.0 million in net proceeds through the sale of shares of our common stock in public offerings and at-the-market offerings. We also have funded our business from payments received under our research collaboration with BMS and our former strategic alliance with Allergan. As of December 31, 2022, we had cash, cash equivalents and marketable securities of $437.4 million.

In May 2021, we entered into a common stock sales agreement with Cowen and Company, LLC (“Cowen”) under which we from time to time can issue and sell shares of our common stock through Cowen in at-the-market offerings for aggregate gross sale proceeds of up to $300.0 million (the “ATM Facility”). We have not sold any shares of our common stock under this ATM Facility as of the date of this Annual Report on Form 10-K.

In addition to our existing cash, cash equivalents and marketable securities, we are eligible to earn milestone and other payments under our collaboration agreement with BMS. Our ability to earn the milestone payments and the timing of earning these amounts are dependent upon the timing and outcome of our development, regulatory and commercial activities and, as such, are uncertain at this time. As of December 31, 2022, our right to contingent payments under our collaboration agreement with BMS is our only significant committed potential external source of funds.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2022 and 2021, respectively (in thousands):

	Year Ended December 31,	
	2022	2021
Net cash (used in) provided by:		
Operating activities	$ (177,349)	$ (163,803)
Investing activities	114,068	(54,466)
Financing activities	1,284	282,106
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (61,997)	$ 63,837

Net Cash Used in Operating Activities

The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was approximately $177.3 million for the year ended December 31, 2022, which primarily consisted of operating expenses that relate to our on-going preclinical and clinical activities, sublicense and license fees, and increased personnel costs to support our expanding operations.

Net cash used in operating activities was approximately $163.8 million for the year ended December 31, 2021, which primarily consisted of operating expenses that relate to our on-going preclinical and clinical activities, a success payment that was settled in cash during the year, patent costs and license fees, rent expenses and increased costs as a result of staffing needs due to our expanding operations. These expenses were partially offset by cash inflows from license fees received in the period.

Net Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was approximately $114.1 million for the year ended December 31, 2022, primarily related to proceeds from maturities of marketable securities of $433.4 million, partially offset by costs used to acquire marketable securities of $315.2 million and purchases of property and equipment of $4.1 million.

Net cash used in investing activities was approximately $54.5 million for the year ended December 31, 2021, primarily related to costs to acquire marketable securities of $409.0 million and purchases of property and equipment of $8.0 million, partially offset by proceeds from maturities of marketable securities of $362.4 million.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was approximately $1.3 million for the year ended December 31, 2022 primarily related to proceeds received from issuance of common stock under our employee stock purchase plan and exercises of options for our common stock.

Net cash provided by financing activities was approximately $282.1 million for the year ended December 31, 2021 and consisted of $249.5 million in net proceeds received from the offering of our common stock in the first quarter 2021 and $31.5 million in proceeds received from exercises of options for our common stock.

For a discussion of our cash flows for the year ended December 31, 2020, see Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations in our annual report on Form 10-K for the year ended December 31, 2021, which was filed with the SEC on February 24, 2022.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we progress the clinical development of EDIT-301; further advance our research programs and our preclinical development activities; seek to identify product candidates and additional research programs; initiate preclinical testing and clinical trials for other product candidates we identify and develop; maintain, expand, and protect our intellectual property portfolio, including reimbursing our licensors for expenses related to the intellectual property that we in-license from such licensors; hire additional clinical, quality control, and scientific personnel; and incur costs associated with operating as a public company. In addition, if we obtain marketing approval for any product candidate that we identify and develop, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution to the extent that such sales, marketing, and distribution are not the responsibility of a collaborator. We do not expect to generate significant recurring revenue unless and until we obtain regulatory approval for and commercialize a product candidate. Furthermore, since 2016 we have incurred, and in future years we expect to continue to incur, significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce, or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents and marketable securities at December 31, 2022 will fund our operating expenses and capital expenditure requirements into 2025. Our forecast of the period of time through which our existing cash and cash equivalents and investments will be adequate to support our operations is a forward-looking statement and involves significant risks and uncertainties. We have based this forecast on assumptions that may prove to be wrong, and actual results could vary materially from our expectations, which may adversely affect our capital resources and liquidity. We could utilize our available capital resources sooner than we currently expect. The amount and timing of future funding requirements, both near- and long-term, will depend on many factors, including, but not limited to:

- the scope, progress, results, and costs of drug discovery, preclinical development, laboratory testing, and clinical or natural history study trials for the product candidates we develop;
- the costs of progressing the clinical development of EDIT-301 to treat sickle cell disease and to treat transfusion-dependent beta-thalassemia;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights, and defending intellectual property-related claims;
- the costs, timing, and outcome of regulatory review of the product candidates we develop;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for any product candidates for which we receive regulatory approval;
- the success of our collaboration with BMS;
- whether BMS exercises any of its options to extend the research program term and/or to additional research programs under our collaboration;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other medicines and technologies;
- the costs of reimbursing our licensors for the prosecution and maintenance of the patent rights in-licensed by us; and

- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive, and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, any product candidate that we identify and develop, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of genomic medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

If we raise funds through additional collaborations, strategic alliances, or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

As of December 31, 2022, we had non-cancelable operating leases with total future minimum lease payments of $54.0 million, of which $14.5 million will be payable in 2023. These minimum lease payments exclude our share of the facility operating expenses, real-estate taxes and other costs that are reimbursable to the landlord under the leases.

Our agreements with certain institutions to license intellectual property include potential milestone and success fees, sublicense fees, royalty fees, licensing maintenance fees, and reimbursement of patent maintenance costs that we may be required to pay. Our agreements to license intellectual property include potential milestone payments that are dependent upon the development of products using the intellectual property licensed under the agreements and contingent upon the achievement of development or regulatory approval milestones, as well as commercial milestones. These potential obligations are contingent upon the occurrence of future events and the timing and likelihood of such potential obligations are not known with certainty. For further information regarding these agreements, please see "Business—Our Collaborations and Licensing Strategy."

We also enter into contracts in the normal course of business with contract research organizations, contract manufacturing organizations and other vendors to assist in the performance of our research and development activities and other services and products for operating purposes. These contracts generally provide for termination at any time upon prior notice.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of December 31, 2022, we had cash and cash equivalents of $141.5 million, primarily held in money market mutual funds consisting of U.S. government-backed securities, and marketable securities of $295.8 million, primarily consisting of U.S. government-backed securities, commercial paper and corporate debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form, or may be in the form of, money market funds or marketable securities and are or may be

invested in U.S. Treasury and U.S. government agency obligations. Due to the short-term maturities and low risk profiles of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our investments.

While we contract with certain vendors and institutions internationally, substantially all of our total liabilities as of December 31, 2022 were denominated in the United States dollar and we believe that we do not have any material exposure to foreign currency exchange rate risk.

Item 8. Financial Statement and Other Supplementary Information.

EDITAS MEDICINE, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Editas Medicine, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Editas Medicine, Inc. (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 22, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

	Accrued Research and Development Expense
Description of the Matter	The Company's accrual for research and development expenses totaled $15.3 million at December 31, 2022. As discussed in Note 2 to the consolidated financial statements, the Company expenses research and development costs as incurred. The Company's determination of costs incurred to conduct research and development on the Company's product candidates, as well as the related accrued expenses at each reporting period incorporates judgment and utilizes various assumptions, including an evaluation of the information provided to the Company by third parties on actual costs incurred but not yet

billed, estimated project timelines and patient enrollment. Payments for these activities are based on the terms of the individual arrangements, which often differ from the pattern of costs incurred.

Auditing the Company's research and development accruals is especially complex due to the judgments and estimations of the research and development expenses. The Company uses judgment and estimation to estimate costs incurred and not yet billed at each reporting period as a result of the volume of pre-clinical and clinical trials and the related manufacturing activities, as well as the extent of third-party vendors utilized. Additionally, due to the timing of invoices received from third parties, actual amounts incurred are not always known as of the audit report date.

We obtained an understanding of the Company's process, evaluated and tested the design and operating effectiveness of internal controls that address the risks related to the completeness and valuation of accrued research and development expenses.

How We Addressed the Matter in Our Audit

To test the research and development accrual, our audit procedures included, among others, testing the accuracy and completeness of the underlying data used in the estimates and evaluating and testing the significant assumptions that are used by management to estimate the accruals. To test the significant assumptions, we inspected the contracts and any amendments to the contracts with third-party service providers, corroborated the progress of pre-clinical and clinical trials and other research and development projects with the Company's research and development personnel that oversee the clinical trials and the related manufacturing activities, and obtained information received from third parties, which included the third parties' estimate of costs incurred to date. We also tested subsequent invoicing received from third parties.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.

Boston, Massachusetts
February 22, 2023

Editas Medicine, Inc.
Consolidated Balance Sheets
(amounts in thousands, except share and per share data)

	December 31,	
	2022	2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 141,522	$ 203,519
Marketable securities	202,752	296,326
Accounts receivable	5,145	267
Prepaid expenses and other current assets	7,335	7,198
Total current assets	356,754	507,310
Marketable securities	93,097	120,071
Property and equipment, net	15,569	17,118
Right-of-use assets	43,648	26,173
Restricted cash and other non-current assets	5,253	6,811
Total assets	$ 514,321	$ 677,483
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 9,511	$ 5,050
Accrued expenses	31,296	20,192
Deferred revenue, current	8,221	11,333
Operating lease liabilities	11,082	10,309
Total current liabilities	60,110	46,884
Operating lease liabilities, net of current portion	32,864	16,069
Deferred revenue, net of current portion	60,667	60,888
Total liabilities	153,641	123,841
Stockholders' equity		
Preferred stock, $0.0001 par value per share: 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, $0.0001 par value per share: 195,000,000 shares authorized; 68,847,382 and 68,489,257 shares issued, and 68,847,382 and 68,435,257 shares outstanding at December 31, 2022 and December 31, 2021, respectively	7	7
Additional paid-in capital	1,442,405	1,411,827
Accumulated other comprehensive loss	(3,601)	(493)
Accumulated deficit	(1,078,131)	(857,699)
Total stockholders' equity	360,680	553,642
Total liabilities and stockholders' equity	$ 514,321	$ 677,483

The accompanying notes are an integral part of the consolidated financial statements.

Editas Medicine, Inc.
Consolidated Statements of Operations
(amounts in thousands, except per share and share data)

	Year Ended December 31,		
	2022	2021	2020
Collaboration and other research and development revenues	$ 19,712	$ 25,544	$ 90,732
Operating expenses:			
Research and development	174,958	142,507	157,996
General and administrative	70,704	76,183	67,576
Total operating expenses	245,662	218,690	225,572
Operating loss	(225,950)	(193,146)	(134,840)
Other income, net:			
Other income (expense), net	1,293	(1,698)	16,259
Interest income, net	4,225	2,342	2,605
Total other income, net	5,518	644	18,864
Net loss	$ (220,432)	$ (192,502)	$ (115,976)
Reconciliation of net loss to net loss attributable to common stockholders:			
Net loss	$ (220,432)	$ (192,502)	$ (115,976)
Net loss per share, basic and diluted	$ (3.21)	$ (2.85)	$ (1.98)
Weighted-average common shares outstanding, basic and diluted	68,664,822	67,619,388	58,609,389

The accompanying notes are an integral part of the consolidated financial statements.

Editas Medicine, Inc.
Consolidated Statements of Comprehensive Loss
(amounts in thousands)

	Year Ended December 31,		
	2022	2021	2020
Net loss	$ (220,432)	$ (192,502)	$ (115,976)
Other comprehensive loss:			
Unrealized loss on marketable debt securities	(3,108)	(447)	(153)
Comprehensive loss	$ (223,540)	$ (192,949)	$ (116,129)

The accompanying notes are an integral part of the consolidated financial statements.

Editas Medicine, Inc.
Consolidated Statements of Stockholders' Equity
(amounts in thousands except share data)

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2019	54,355,798	$ 5	$ 811,546	$ (549,221)	$ 107	$ 262,437
Issuance of common stock from public offering, net of issuance costs of $0.3 million	6,900,000	1	203,725	—	—	203,726
Exercise of stock options	964,412	—	19,500	—	—	19,500
Stock-based compensation expense	—	—	23,156	—	—	23,156
Vesting of restricted common stock awards	304,638	—	—	—	—	—
Purchase of common stock under benefits plans	38,609	—	896	—	—	896
Unrealized loss on marketable debt securities	—	—	—	—	(153)	(153)
Net loss	—	—	—	(115,976)	—	(115,976)
Balance at December 31, 2020	62,563,457	$ 6	$ 1,058,823	$ (665,197)	$ (46)	$ 393,586
Issuance of common stock from public offering, net of issuance costs of $0.3 million	4,025,000	1	249,458	—	—	249,459
Issuance of common stock for repayment of notes payable	303,599	—	27,500	—	—	27,500
Exercise of stock options	1,233,958	—	31,495	—	—	31,495
Stock-based compensation expense	—	—	43,399	—	—	43,399
Vesting of restricted common stock awards	267,268	—	—	—	—	—
Purchase of common stock under benefit plan	41,975	—	1,152	—	—	1,152
Unrealized loss on marketable debt securities	—	—	—	—	(447)	(447)
Net loss	—	—	—	(192,502)	—	(192,502)
Balance at December 31, 2021	68,435,257	$ 7	$ 1,411,827	$ (857,699)	$ (493)	$ 553,642
Exercise of stock options	19,769	—	305	—	—	305
Stock-based compensation expense	—	—	29,294	—	—	29,294
Vesting of restricted common stock awards	286,642	—	—	—	—	—
Purchase of common stock under benefit plans	105,714	—	979	—	—	979
Unrealized loss on marketable debt securities	—	—	—	—	(3,108)	(3,108)
Net loss	—	—	—	(220,432)	—	(220,432)
Balance at December 31, 2022	68,847,382	$ 7	$ 1,442,405	$ (1,078,131)	$ (3,601)	$ 360,680

The accompanying notes are an integral part of the consolidated financial statements.

Editas Medicine, Inc.
Consolidated Statements of Cash Flows
(amounts in thousands)

	Year Ended December 31,		
	2022	2021	2020
Cash flow from operating activities			
Net loss	$ (220,432)	$ (192,502)	$ (115,976)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	29,294	43,399	23,156
Depreciation	6,337	5,053	3,959
Realized gain on corporate equity securities	—	—	(16,366)
Non-cash research and development expenses	—	—	27,500
Other non-cash items, net	(724)	1,657	104
Changes in operating assets and liabilities:			
Accounts receivable	(4,878)	5,781	(5,630)
Prepaid expenses and other current assets	(137)	3,731	(4,643)
Right-of-use assets	(17,475)	9,691	3,633
Other non-current assets	1,558	(2,108)	(719)
Accounts payable	4,368	(1,139)	855
Accrued expenses	10,505	(4,166)	1,707
Deferred revenue	(3,333)	(22,706)	(91,794)
Operating lease liabilities	17,568	(10,494)	(2,946)
Other current and non-current liabilities	—	—	(2,683)
Net cash used in operating activities	(177,349)	(163,803)	(179,843)
Cash flow from investing activities			
Purchases of property and equipment	(4,118)	(7,977)	(7,162)
Proceeds from the sale of equipment	18	—	12
Purchases of marketable securities	(315,186)	(408,891)	(458,404)
Proceeds from maturities of marketable securities	433,354	362,402	305,000
Proceeds from sale of corporate equity securities	—	—	20,032
Net cash provided by (used in) investing activities	114,068	(54,466)	(140,522)
Cash flow from financing activities			
Proceeds from offering of common stock, net of issuance costs	—	249,459	203,726
Proceeds from exercise of stock options	305	31,495	19,501
Issuance of common stock under benefit plans	979	1,152	895
Net cash provided by financing activities	1,284	282,106	224,122
Net (decrease) increase in cash, cash equivalents, and restricted cash	(61,997)	63,837	(96,243)
Cash, cash equivalents, and restricted cash, beginning of period	207,396	143,559	239,802
Cash, cash equivalents, and restricted cash, end of period	$ 145,399	$ 207,396	$ 143,559
Supplemental disclosure of cash and non-cash activities:			
Fixed asset additions included in accounts payable and accrued expenses	$ 1,440	$ 749	$ 656
Cash paid in connection with operating lease liabilities	14,851	13,094	9,760
Right-of-use assets obtained in exchange of operating lease obligations	29,861	10,736	—
Issuance of common stock for settlement of success payments (see Note 8)	—	—	27,500

The accompanying notes are an integral part of the consolidated financial statements.

Editas Medicine, Inc.
Notes to Consolidated Financial Statements

1. Nature of Business

Editas Medicine, Inc. (the "Company") is a clinical stage genome editing company dedicated to developing potentially transformative genomic medicines to treat a broad range of serious diseases. The Company was incorporated in the state of Delaware in September 2013. Its principal offices are in Cambridge, Massachusetts.

Since its inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital. The Company has primarily financed its operations through various equity financings, payments received under a research collaboration with Juno Therapeutics, a wholly-owned subsidiary of the Bristol-Myers Squibb Company ("BMS"), and payments received under a strategic alliance and option agreement with Allergan Pharmaceuticals International Limited (together with its affiliates, "Allergan").

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any drug product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from pilot-scale manufacturing to large-scale production of products.

Liquidity

As of December 31, 2022, we have raised an aggregate of $898.0 million in net proceeds through the sale of shares of our common stock in public offerings and at-the-market offerings. We also have funded our business from payments received under our research collaboration with BMS and our former strategic alliance with Allergan. As of December 31, 2022, we had cash, cash equivalents and marketable securities of $437.4 million.

In May 2021, the Company entered into a common stock sales agreement with Cowen and Company, LLC ("Cowen"), under which the Company from time to time can issue and sell shares of its common stock through Cowen in at-the-market offerings for aggregate gross sale proceeds of up to $300.0 million (the "ATM Facility"). As of December 31, 2022 the Company has not sold any shares of its common stock under the ATM Facility.

The Company has incurred annual net operating losses in every year since its inception. The Company has an accumulated deficit of $1.1 billion at December 31, 2022. The Company expects that its existing cash, cash equivalents and marketable securities on December 31, 2022 fund its operating expenses and capital expenditure requirements into 2025.The Company will require substantial additional capital to fund its operations. The Company has never generated any product revenue. There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations, and financial condition.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Editas Medicine, Inc. and its wholly owned subsidiary, Editas Securities Corporation, which is a Delaware subsidiary created to buy, sell and hold securities. All intercompany transactions and balances have been eliminated.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, stock-based compensation expense, the accrual for research and development expenses, valuations of in-process research and development assets and deferred tax valuation allowances. The Company bases its estimates on historical experience and other market-specific or relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Fair Value of Financial Instruments

ASC Topic 820, *Fair Value Measurement* ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- *Level 1* – Quoted market prices in active markets for identical assets or liabilities.
- *Level 2* – Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates, and yield curves.
- *Level 3* – Unobservable inputs developed using estimates of assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the consolidated balance sheets for cash and cash equivalents, restricted cash, marketable securities, accounts receivable, prepaid expenses and other current assets, accounts payable, accrued expenses, and other current liabilities approximate their fair values, due to their short-term nature.

Cash, Cash Equivalents, and Restricted Cash

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds.

The Company has restricted cash of $3.9 million held as collateral for the Company's office and lab facilities and credit card program. The restricted funds are maintained in a traditional bank account.

The following table presents cash, cash equivalents, and restricted cash as reported on the consolidated balance sheets that equal the total amounts on the consolidated statements of cash flows (in thousands):

	Year Ended December 31,	
	2022	2021
Cash and cash equivalents	$ 141,522	$ 203,519
Restricted cash included in "Restricted cash and other non-current assets"	3,877	3,877
Total cash, cash equivalents, and restricted cash	$ 145,399	$ 207,396

Marketable Securities

The Company classifies marketable securities with a remaining maturity when purchased of greater than three months and less than one year from the balance sheet date as current. Marketable securities are classified as long-term assets on the consolidated balance sheets if the contractual maturity exceeds one year and the Company does not intend to utilize the marketable securities to fund current operations. For the years ended December 31, 2022 and 2021, the Company's marketable securities consisted of investments in available-for-sale debt securities.

Available-for-sale debt securities are carried at fair value with the unrealized gains and losses included in other comprehensive loss as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the of the underlying security. Realized gains and losses are included in other income (expense).

At each reporting date, the Company records an allowance for credit losses and reports it as credit loss expense which is included in "Other income (expense), net" in the Company's consolidated statement of operations. The estimate for credit losses includes a measure of the expected risk of credit loss even if the risk is remote. When assessing financial assets for credit losses, the Company pools financial assets with similar risk characteristics and performs a collective evaluation. A credit loss on an available-for-sale debt security is limited to the difference in fair value and the amortized cost. A previously recognized credit loss may be increased or decreased in subsequent periods if the Company's estimate of fair value changes. To determine whether to record a credit loss, the Company considers issuer or vendor specific credit ratings and historical losses as well as current economic conditions and its expectations for future economic conditions. To date, the Company has not had any credit losses, and the Company did not have an allowance for credit losses as of December 31, 2022 and 2021.

During 2021, the Company's marketable securities also included corporate equity securities. The Company classified investments in equity securities that had a readily determinable fair value as marketable securities in the Company's consolidated balance sheets. The fair value of these securities were based on a quoted price for an identical equity security. If the equity security had a restriction that was determined to be an attribute of the security that would transfer to a market participant, the fair value of the security was measured based on the quoted price for an otherwise identical unrestricted equity security, adjusted for the effect of the restriction. The adjustment reflects the discount that a market participant would demand for the risk relating to the inability to dispose of the security for a specified period of time. The Company recorded changes in the fair value of its equity securities in "Other income (expense), net" in the Company's consolidated statement of operations.

Accounts Receivable

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. The Company's receivables primarily relate to amounts reimbursed under its collaboration agreements. The Company believes that credit risk associated with its collaborations partners is not significant. To date, the Company has not had any write-offs of bad debt, and the Company did not have an allowance for doubtful accounts as of December 31, 2022 and 2021.

Concentrations of Credit Risk and Off-Balance Sheet Risk

The Company has no financial instruments with off-balance sheet risk such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially subject the Company to a concentration of credit risk are cash, cash equivalents, marketable securities and receivables owed to the Company from collaboration partners. The Company's cash, cash equivalents and marketable securities are held in accounts at a financial institution that may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds.

Property and Equipment

Property and equipment consists of computers, laboratory equipment, furniture and office equipment, and leasehold improvements and is stated at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred, while costs of major additions and betterments are capitalized. Depreciation is calculated over the estimated useful lives of the assets using the straight-line method. The Company capitalizes laboratory equipment used for research and development if it has alternative future use in research and development or otherwise.

Asset:	Estimated Useful life
Lab equipment	5 years
Computer equipment and software	3 years
Furniture and equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term

Impairment of Long-lived Assets

The Company evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses from inception through December 31, 2022.

Profit-Sharing Arrangements

The Company considers the nature and contractual terms of the arrangements and assesses whether such arrangements involve a joint operating activity pursuant to which the Company is an active participant and is exposed to significant risks and rewards with respect to such arrangement. If the Company is an active participant and is exposed to significant risks and rewards with respect to such arrangement, the Company accounts for such arrangement as a collaboration under ASC Topic 808, *Collaborative Arrangements* ("ASC 808"). ASC 808 describes arrangements within its scope and considerations surrounding presentation and disclosure, with recognition matters subjected to other authoritative guidance, in certain cases by analogy.

Payments received from a collaboration partner to which this policy applies are recorded as contra-expense in the applicable period and may include development costs or patent expense reimbursements. The Company classifies payments made under the cost sharing provisions of such arrangements as a component of research and development expenses to reflect the joint risk sharing nature of such profit-sharing arrangements. The Company classifies payments owed or receivables recorded as other current liabilities or prepaid expenses and other current assets, respectively, in the Company's consolidated balance sheets. The Company had one agreement that was accounted for in accordance with ASC 808 prior to the termination of the arrangement during the year ended 2020. The arrangements and payments are described more fully in Note 9.

Revenue Recognition

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company enters into collaboration agreements and certain other agreements that are within the scope of ASC 606, under which the Company licenses, may license or grants an option to license rights to certain of the Company's product candidates and performs research and development services in connection with such arrangements. The terms of these arrangements typically include payment of one or more of the following: non-refundable, up-front fees; reimbursement of research and development costs; development, clinical, regulatory and commercial sales milestone payments; and royalties on net sales of licensed products.

Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine the appropriate amount of revenue to be recognized for arrangements determined to be within the scope of ASC 606, the Company performs the following five steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect consideration it is entitled to in exchange for the goods or services it transfers to the customer.

The promised goods or services in the Company's arrangements typically consist of a license, or option to license, rights to the Company's intellectual property or research and development services. The Company provides options to additional items in such arrangements, which are accounted for as separate contracts when the customer elects to exercise such options, unless the option provides a material right to the customer. Performance obligations are promised goods or services in a contract to transfer a distinct good or service to the customer and are considered distinct when (i) the customer can benefit from the good or service on its own or together with other readily available resources and (ii) the promised good or service is separately identifiable from other promises in the contract. In assessing whether promised good or services are distinct, the Company considers factors such as the stage of development of the underlying intellectual property, the capabilities of the customer to develop the intellectual property on its own or whether the required expertise is readily available and whether the goods or services are integral or dependent to other goods or services in the contract.

The Company estimates the transaction price based on the amount expected to be received for transferring the promised goods or services in the contract. The consideration may include fixed consideration or variable consideration. At the inception of each arrangement that includes variable consideration, the Company evaluates the amount of potential payment and the likelihood that the payments will be received. The Company utilizes either the most likely amount method or expected value method to estimate the amount expected to be received based on which method best predicts the amount expected to be received. The amount of variable consideration that is included in the transaction price may be constrained and is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period.

The Company's contracts often include development and regulatory milestone payments that are as assessed under the most likely amount method and constrained if it is probable that a significant revenue reversal would occur. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of achievement of such development and clinical milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and other research and development revenues in the period of adjustment.

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty

has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of the Company's collaboration or strategic alliance arrangements.

The Company allocates the transaction price based on the estimated standalone selling price. The Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company utilizes key assumptions to determine the stand-alone selling price, which may include other comparable transactions, pricing considered in negotiating the transaction and the estimated costs. Variable consideration is allocated specifically to one or more performance obligations in a contract when the terms of the variable consideration relate to the satisfaction of the performance obligation and the resulting amounts allocated are consistent with the amounts the Company would expect to receive for the satisfaction of each performance obligation.

The consideration allocated to each performance obligation is recognized as revenue when control is transferred for the related goods or services. For performance obligations which consist of licenses and other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company receives payments from its customers based on billing schedules established in each contract. Up-front payments and fees are recorded as deferred revenue upon receipt or when due until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

Research and Development Expenses

Research and development expenses are charged to expense as incurred in performing research and development activities. The costs include employee-related expenses including salaries, benefits, and stock-based compensation expense, costs of funding research performed by third parties that conduct research and development and preclinical and clinical activities on the Company's behalf, the cost of purchasing lab supplies and non-capital equipment used in preclinical and clinical activities and in manufacturing preclinical and clinical study materials, consultant fees, facility costs including rent, depreciation, and maintenance expenses, and fees for acquiring and maintaining licenses under third party licensing agreements which are typically expensed when incurred if the technology licensed has no alternate future uses, including any sublicensing or success payments made to the Company's licensors. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the accrual or prepaid is adjusted accordingly. The Company defers and capitalizes non-refundable advance payments made by the Company for research and development activities until the related goods are received or the related services are performed. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

In-process Research and Development Assets

In-process research and development assets that are acquired in a transaction that does not qualify as a business combination under GAAP and that do not have an alternative future use are expensed in the period in which the assets are acquired.

Patent Costs

The Company expenses patent and patent application costs and related legal costs for the prosecution and maintenance of such patents and patent applications, including patents and patent applications the Company in-licenses, as incurred, and classifies such costs as general and administrative expenses in the accompanying consolidated statements of operations.

Leases

The Company accounts for leases in accordance with ASC 842. At the inception of an arrangement the Company determines whether the arrangement contains a lease. If a lease is identified in an arrangement, the Company recognizes a right-of-use asset and liability on its balance sheet and determines whether the lease should be classified as a finance or operating lease. The Company does not recognize assets or liabilities for leases with lease terms of less than 12 months. Lease payments for short-term leases are recorded to operating expense on a straight-line basis over the lease term and variable lease payments are recorded in the period in which the obligation for those payments is incurred.

A lease qualifies as a finance lease if any of the following criteria are met at the inception of the lease: (i) there is a transfer of ownership of the leased asset to the Company by the end of the lease term, (ii) the Company holds an option to purchase the leased asset that it is reasonably certain to exercise, (iii) the lease term is for a major part of the remaining economic life of the leased asset, (iv) the present value of the sum of lease payments equals or exceeds substantially all of the fair value of the leased asset, and (v) the nature of the leased asset is specialized to the point that it is expected to provide the lessor no alternative use at the end of the lease term. All other leases are recorded as operating leases.

Finance and operating lease assets and liabilities are recognized at the lease commencement date based on the present value of the lease payments over the lease term using the discount rate implicit in the lease. If the rate is not readily determinable, the Company utilizes its incremental borrowing rate at the lease commencement date. Operating lease assets are further adjusted for prepaid or accrued lease payments. Operating lease payments are expensed using the straight-line method as an operating expense over the lease term. Finance lease assets are amortized to depreciation expense using the straight-line method over the shorter of the useful life of the related asset or the lease term. Finance lease payments are bifurcated into (i) a portion that is recorded as imputed interest expense and (ii) a portion that reduces the finance liability associated with the lease.

The Company does not separate lease and non-lease components when determining which lease payments to include in the calculation of its lease assets and liabilities. Variable lease payments are expensed as incurred. If a lease includes an option to extend or terminate the lease, the Company reflects the option in the lease term if it is reasonably certain it will exercise the option.

Stock-based Compensation Expense

The Company accounts for all stock-based awards granted to employees and non-employees as stock-based compensation expense at fair value in accordance with FASB ASC Topic 718 Compensation—Stock Compensation ("ASC 718"). The Company estimates the grant date fair value of restricted stock based on the market value of the Company's common stock on the date of the grant. The Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (1) the expected stock price volatility, (2) the calculation of expected term of the award, (3) the risk-free interest rate, and (4) the expected dividend yield. Because there had been no public market for the Company's common stock prior to its initial public offering, there was a lack of company-specific historical and implied volatility data. Accordingly, the Company based its estimates of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The Company calculates historical volatility based on a period of time commensurate with the expected term. The Company computes expected volatility based on the historical volatility of a representative group of companies with similar characteristics to the Company, including their stages of product development and focus on the life science

industry. The Company uses the simplified method as prescribed by the Securities and Exchange Commission's Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term. The Company determines the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. The Company uses an assumed dividend yield of zero as the Company has never paid dividends and does not have current plans to pay any dividends on its common stock.

Restricted stock awards ("RSAs") are subject to repurchase rights. Accordingly, the Company has recorded the proceeds from the issuance of RSAs as a liability in the consolidated balance sheets. The restricted stock liability is reclassified into stockholders' equity as the restricted stock vests.

Service-Based Awards

For stock-based awards issued to employees, non-employee service providers and members of the Company's board of directors (the "Board"), the Company recognizes the grant date fair value of the service-based options, RSAs or restricted stock unit awards ("RSUs") on a straight-line basis over the requisite service period, which is generally the vesting period of the respective award. If an employee or non-employee service requirement is concluded to be non-substantive, the stock-based compensation expense would be expensed immediately.

Market-Based Awards

For market-based awards, the Company recognizes the grant date fair value of the market-based options over the earlier of the derived service period, pursuant to a Monte-Carlo simulation model, or when the market-based vesting conditions are met. The Company estimates an award's derived service period based on the best estimate of the period over which an award's vesting condition(s) will be achieved. If the market-based vesting conditions are met ahead of the derived service period, the expense will be accelerated. If the market-based vesting conditions are not met and the market-based award is cancelled, the expense will not be reversed unless the market-based award is forfeited.

Performance-Based Awards

For performance-based awards, the Company recognizes the grant date fair value of the performance-based options or RSUs over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable. Certain awards are subject to both performance and continued service conditions.

The Company classifies stock-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's salary or service payments are classified. Forfeitures are recorded as they occur. If factors change or different assumptions are used, the Company's stock-based compensation expense could be materially different in the future.

Success Payments, Research Funding Payments and Notes Payables

Certain arrangements require the Company to make payments, if and when, the Company's market capitalization reaches specified thresholds for a specific period of time or upon a sale of the Company for consideration in excess of those thresholds or above a specific amount. The payments are accounted for under the provisions of ASC 718, whereby the Company recognizes the expense and liability when it becomes probable that the amounts will become due. The Company records this expense as a research and development expense in its consolidated statements of operations. The arrangements and payments are described more fully in Note 8.

The payments are payable in either cash, common stock or promissory notes payable, depending upon the licensor and the Company's election. If the Company elects to issue a promissory note relating to contractual obligations, the promissory note bears interest at 4.8% per annum. Outstanding principal and accrued interest on the promissory notes are typically payable on the earlier of five months or a specified period of time following a Company sale or change of control event, subject to certain exceptions.

Income taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the weight of available evidence, it is more likely than not that the deferred tax assets will be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances.

The Company assesses the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where they have operations to determine the potential effect on the Company's business and any assumptions they have made about their future taxable income. The Company cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on the Company if they were to be enacted.

Beginning in 2022, the Tax Cut and Jobs Act of 2017 eliminates the currently available option to deduct research and development expenditures and requires taxpayers to amortize them over five years. The U.S. Congress is considering legislation that would defer the amortization requirement to future periods, however, the Company has no assurance that the provision will be repealed or otherwise modified.

Comprehensive Loss

Comprehensive loss currently consists of net loss and changes in unrealized gains and losses on marketable securities.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision maker, the Company's Chief Executive Officer, view the Company's operations and manage the Company's business as a single operating segment, which is the business of developing and commercializing genome editing technology.

3. Cash Equivalents and Marketable Securities

Cash equivalents and marketable securities consisted of the following at December 31, 2022 (in thousands):

December 31, 2022	Amortized Cost	Allowance for Credit Losses	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents and marketable securities:					
Government agency securities	$ 161,902	$ —	$ 11	$ (2,556)	$ 159,357
Money market funds	141,522	—	—	—	141,522
Corporate notes/bonds	57,575	—	2	(694)	56,883
U.S. Treasuries	50,019	—	3	(229)	49,793
Commercial paper	29,954	—	3	(141)	29,816
Total	$ 440,972	$ —	$ 19	$ (3,620)	$ 437,371

Cash equivalents and marketable securities consisted of the following at December 31, 2021 (in thousands):

December 31, 2021	Amortized Cost	Allowance for Credit Losses	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents and marketable securities:					
Money market funds	$ 203,519	$ —	$ —	$ —	$ 203,519
U.S. Treasuries	124,016	—	1	(84)	123,933
Government agency securities	126,927	—	—	(228)	126,699
Commercial paper	89,699	—	1	(13)	89,687
Corporate notes/bonds	76,248	—	—	(170)	76,078
Total	$ 620,409	$ —	$ 2	$ (495)	$ 619,916

As of December 31, 2022, the Company did not hold any marketable securities that had been in an unrealized loss position for more than twelve months. Furthermore, the Company has determined that there were no material changes in the credit risk of the debt securities. As of December 31, 2022, the Company holds 32 securities with an aggregate fair value of $93.1 million that had remaining maturities between one and two years.

4. Fair Value Measurements

Assets measured at fair value on a recurring basis as of December 31, 2022 were as follows (in thousands):

Financial Assets	December 31, 2022	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 141,522	$ 141,522	$ —	$ —
Marketable securities:				
Government agency securities	159,357	—	159,357	—
Corporate bonds	56,883	—	56,883	—
U.S. Treasuries	49,793	49,793	—	—
Commercial paper	29,816	—	29,816	—
Restricted cash and other non-current assets:				
Money market funds	3,877	3,877	—	—
Total financial assets	$ 441,248	$ 195,192	$ 246,056	$ —

Assets measured at fair value on a recurring basis as of December 31, 2021 were as follows (in thousands):

Financial Assets	December 31, 2021	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 203,519	$ 203,519	$ —	$ —
Marketable securities:				
U.S. Treasuries	123,933	123,933	—	—
Government agency securities	126,699	—	126,699	—
Commercial paper	89,687	—	89,687	—
Corporate bonds	76,078	—	76,078	—
Restricted cash and other non-current assets:				
Money market funds	3,877	3,877	—	—
Total financial assets	$ 623,793	$ 331,329	$ 292,464	$ —

During the year ended December 31, 2020, the Company held an investment in Beam Therapeutics Inc. ("Beam Therapeutics") consisting of shares of Beam Therapeutics' common stock. Prior to Beam Therapeutics' initial public offering in February 2020, the Company valued such investment based on the cost of the equity securities adjusted for any observable market transactions. Following the initial public offering, the equity securities had a readily determinable fair value, and were included in marketable securities on the consolidated balance sheet. The Company sold this investment in October 2020, resulting in a realized gain of $16.4 million recorded in other income (expense), net on the consolidated statements of operations.

5. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	As of	
	December 31, 2022	December 31, 2021
Laboratory equipment	$ 24,407	$ 21,579
Leasehold improvements	9,761	8,162
Construction-in-progress	1,573	1,529
Computer equipment	875	876
Furniture and office equipment	264	264
Software	215	215
Total property and equipment	37,095	32,625
Less: accumulated depreciation	(21,526)	(15,507)
Property and equipment, net	$ 15,569	$ 17,118

The Company recorded $6.3 million, $5.1 million, and $4.0 million in depreciation expense during the years ended December 31, 2022, 2021 and 2020, respectively.

6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	As of December 31,	
	2022	2021
External research and development expenses	$ 16,452	$ 5,614
Employee related expenses	10,140	10,159
Intellectual property and patent related fees	1,809	1,408
Other expenses	1,635	666
Professional service expenses	1,260	2,345
Total accrued expenses	$ 31,296	$ 20,192

7. Leases

The Company has multiple lease agreements for office, laboratory and manufacturing space with varying contractual terms set to expire between 2023 and 2028. Typically, base rent payments commence at the beginning of each lease term and continue through the term of the respective lease. The Company's lease agreements have escalating rent clauses, which require higher rent payments in future years. The Company has two significant leases for office and laboratory space located in Cambridge, Massachusetts that are summarized below.

The Company's leases are included on its consolidated balance sheet as follows (in thousands):

	As of	
	December 31, 2022	December 31, 2021
Right-of-use assets	$ 43,648	$ 26,173
Operating lease liabilities, current	$ (11,082)	$ (10,309)
Operating lease liabilities, noncurrent	$ (32,864)	$ (16,069)

During the years ended December 31, 2022, 2021 and 2020, the Company recorded $13.6 million, $10.9 million and $10.5 million related to operating lease costs and $3.0 million, $2.1 million and $1.1 million related to variable costs associated with the Company's operating leases.

Maturities of the Company's lease liabilities as of December 31, 2022 were as follows (in thousands):

Maturity of lease liabilities:	Year Ended December 31, 2022
2023	$ 14,553
2024	$ 12,414
2025	$ 7,128
2026	$ 6,930
2027	$ 7,024
Thereafter	$ 6,000
Total minimum lease payments	$ 54,049
Less: imputed interest	$ (10,103)
Total operating lease liabilities at December 31, 2022	$ 43,946

The weighted-average remaining lease term is 4.1 years and the weighted-average discount rate is 9.0%.

Hurley Street

In 2016, the Company entered into a lease agreement for 59,783 square feet of office and laboratory space located on Hurley Street in Cambridge, Massachusetts. The term of the lease began on October 1, 2016 and continues until October 2028.

In November 2022, the Company entered into an amendment to the lease agreement to extend the term of its existing facility space to October 31, 2028 under the same terms as its existing agreement except for the terms of payment. As a result of this amendment, the Company recognized an additional right-of-use asset and corresponding lease liability of $24.6 million.

In connection with the lease and as a security deposit, the Company holds, with the landlord, a letter of credit in the amount of approximately $1.6 million. Subject to the terms of the lease and certain reduction requirements specified therein, the $1.6 million security deposit may decrease over time. The letter of credit, which is collateralized by the Company, is recorded in restricted cash and other non-current assets in the accompanying consolidated balance sheets as of December 31, 2022 and December 31, 2021.

One Main Street

In 2019, the Company entered into a lease agreement for 31,571 square feet of office space located on One Main Street in Cambridge, Massachusetts. The term of the lease began on January 15, 2020 and continues until January 2025. In connection with the lease and as a security deposit, the Company issued a letter of credit in the amount of approximately $0.8 million.

The Company has the option to extend the lease for an additional five-year term at market-based rates. The base

rent payments commenced in January 2020 and continue through the term of the lease and are subject to increases over the term of the lease.

8. Commitments and Contingencies

The Company is a party to a number of license agreements under which the Company licenses patents, patent applications and other intellectual property from third parties. As such, the Company is obligated to reimburse licensors for various costs including upfront licenses fees, annual license fees, certain licensor expense reimbursements, success payments, research funding payments, and milestones triggerable upon certain development, regulatory, and commercial events as well as royalties on future products. These contracts are generally cancellable, with notice, at the Company's option and do not have significant cancellation penalties.

Broad Sponsored Research Agreement

In 2018, the Company entered into a sponsored research agreement (the "Sponsored Research Agreement") with The Broad Institute, Inc. ("Broad"). The Sponsored Research Agreement provides for Broad to conduct research useful or relevant to genome editing in the field of genomic medicines for the prevention or treatment of human disease with funding from the Company. Under the Sponsored Research Agreement, Broad granted to the Company an exclusive right of first negotiation for licenses from Broad with respect to patentable inventions developed by Broad in the course of the sponsored research, subject to certain limitations and retained rights ("Sponsored Invention Licenses").

Under the Sponsored Research Agreement, the Company is obligated to make payments ("Market Cap Research Funding") in the event the Company's market capitalization reaches certain amounts for a specified period of time. Unless the Company has undergone a change in control, Market Cap Research Funding is payable by the Company in cash, in shares of common stock, or in the form of promissory notes, which may be settled in shares of common stock at the election of the Company. In aggregate, the Company has triggered $25.0 million in Market Cap Research Funding and has primarily settled these amounts through the issuance of shares of its common stock. The remaining $100.0 million in Market Cap Research Funding may be triggered when the Company's market capitalization reaches various low-ten to eleven dollar amounts or in the event of a Company sale. The Company is not required to make additional Market Cap Research Funding payments if the Company, whether directly or through its affiliates or sublicensees, is not researching, developing, or commercializing products based on or incorporating inventions exclusively licensed to the Company from Broad subject to certain exclusions.

The Sponsored Research Agreement is terminable by each party upon the occurrence of specified bankruptcy events of the other party and otherwise will continue in effect until the remaining Market Cap Research Funding payments are received by Broad and such time as the Company has no further rights of first negotiation for Sponsored Invention Licenses, unless otherwise mutually agreed between the parties.

Broad & Harvard License Agreements

The Company has entered into agreements with Broad and the President and Fellows of Harvard College ("Harvard") to license certain patent rights owned or co-owned by the institutions. The foundational patent rights that were in-licensed by the Company include Cas9-I ("Cas9-I License Agreement"), Cas12a (formerly known as Cpf1) ("Cpf1 License Agreement"), and Cas9-II ("Cas9-II License Agreement") (collectively referred to herein as the "License Agreements"). The Company received exclusive, worldwide, royalty-bearing, sublicensable licenses to certain patent rights to develop and commercialize licensed product and a non-exclusive, worldwide, royalty-bearing sublicensable license under the same patent rights for all other purposes, subject to certain limitations and retained rights. The Company is obligated to use commercially reasonable efforts to research, develop, and commercialize licensed products. The Company is also required to achieve certain development milestones within specified time periods for products covered by the License Agreements, with Broad or Harvard, as applicable, having the right to terminate the License Agreements, on a license agreement-by-license agreement basis, if the Company fails to achieve these milestones within the required time periods. Broad or Harvard may grant licenses under specified circumstances to third parties that wish to develop and commercialize products that target a particular gene that otherwise would fall within the scope of the exclusive licenses granted to the Company, provided that the Company is not, directly or through any of its affiliates, sublicensees, or collaborators, researching, developing, or commercializing a product directed toward the same gene target, or can demonstrate to Broad's and/or Harvard's, as applicable, reasonable satisfaction that the Company is interested in researching, developing, and commercializing a product directed toward the same gene target, that the Company has a commercially reasonable research, development, and commercialization plan to do so, and the Company commences and continues reasonable commercial efforts under such plan. The Company has the right to terminate each of the License Agreements at will with four months written notice to Broad. Unless terminated earlier, the term of each of the License Agreements will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the licensed patent rights in such country.

Milestones

In aggregate, the Company may pay up to $14.8 million, $20.0 million, and $3.7 million in clinical and regulatory milestones under the Cas9-I License Agreement, Cpf1 License Agreement, and Cas9-II License Agreement, respectively. In addition, the Company owes aggregate sales milestones totaling $54.0 million, $54.0 million, and $13.5 million under the Cas9-I License Agreement, Cpf1 License Agreement, and Cas9-II License Agreement, respectively. If the licensed product or service prevents or treats a human disease that afflicts fewer than a specified number of patients in the aggregate in the United States ("U.S.") or a specified number of patients per year in the U.S., the clinical and regulatory milestones reduce to $4.1 million, $5.5 million, and $1.1 million under the Cas9-I License Agreement, Cpf1 License Agreement, and Cas9-II License Agreement, respectively. In addition, the aggregated sales milestones reduce to $36.0 million, $36.0 million, and $9.0 million under the Cas9-I License Agreement, Cpf1 License Agreement, and Cas9-II License Agreement, respectively. Certain clinical and regulatory milestones are subject to a multiplier payout equivalent to a double-digit percentage in the event of a change of control.

Royalties

The Company is required to pay on a product-by-product and country-by-country basis, a mid single-digit percentage royalty on net sales of licensed products made by the Company, its affiliates, or its sublicensees. The royalty percentage depends on the product and service, and whether such licensed product or licensed service is covered by a valid claim. If the Company is legally required to pay royalties to a third party on net sales of the Company's products because such third party holds patent rights that cover such licensed product, then the Company can credit up to a specified percentage of the amount paid to such third party against the royalties due to the institutions. Such credit may not exceed 50% of the applicable royalties paid by the Company to the applicable third party. The Company's obligation to pay royalties will expire on a product-by-product and country-by-country basis upon the later of the expiration of the last to expire valid claim of the patent rights that covers each licensed product or service in each country or the tenth anniversary of the date of the first commercial sale of the licensed product or licensed service.

Licensor Expense Reimbursements

The Company is obligated to reimburse to Broad and Harvard for expenses incurred by each of them associated with the prosecution and maintenance of the patent rights that the Company licenses from them pursuant to the license agreement by and among the Company, Broad and Harvard, including the interference and opposition proceedings involving patents licensed to the Company under the license agreement, and other license agreements between the Company and Broad. As such, the Company anticipates that it has a substantial commitment in connection with these proceedings until such time as these proceedings have been resolved, but the amount of such commitment is not determinable. The Company incurred an aggregate of $8.8 million, $10.6 million, and $13.1 million in expense during the years ended December 31, 2022, 2021 and 2020, respectively, for such reimbursement.

Success Payments

Under the Cpf1 License Agreement and Cas9-II License Agreement, the Company is obligated to make payments ("Success Payments") in the event the Company's market capitalization reaches certain thresholds for a specified period of time, or in the event of a change in control of the Company, if the consideration is in excess of those thresholds. Unless the Company has undergone a change in control, Success Payments are payable by the Company in cash or in the form of promissory notes, which may be settled in shares of common stock at the election of the Company. In the event of a change in control of the Company, the Success Payments are required to be paid in cash. The Success Payments under the Cpf1 License Agreement are triggered when the Company's market capitalization reaches certain amounts ranging from $750.0 million to $10.0 billion for a specified period of time. The Success Payments under the Cas9-II License Agreement are triggered when the Company's market capitalization reaches certain amounts ranging from $1.0 billion to $9.0 billion for a specified period of time. In aggregate, the Company has triggered $25.0 million and $7.5 million of Success Payments under the Cpf1 License Agreement and Cas9-II License Agreement, respectively. The Company has primarily settled these amounts through the issuance of shares of its common stock.

The remaining $100.0 million and $22.5 million in Success Payments under the Cpf1 License Agreement and Cas9-II License Agreement, respectively are only payable if the market capitalization threshold are met and the Company or any affiliate or sublicensee has at least one product candidate covered by a claim of a patent right licensed to the Company that is or was subject of a clinical trial.

Other Payments

The Company pays nominal annual license fees to the institutions. If the Company sublicenses any of the patent rights to a third party, the institutions have the right to receive sublicense income, which may be offset by the licensor expense reimbursement payments that the Company has made to the institution subject to certain limitations.

Litigation

The Company is not a party to any litigation and did not have contingency reserves established for any litigation liabilities as of December 31, 2022 or 2021.

9. Collaboration Agreements

The Company has entered into multiple collaborations, out-licenses and strategic alliances with third parties that typically involve payments to or from the Company, including up-front payments, payments for research and development services, option payments, milestone payments and royalty payments to or from the Company.

Collaboration Revenue

As of December 31, 2022, the Company's contract liabilities were primarily related to the Company's collaboration with BMS. The following table presents changes in the Company's accounts receivable and contract liabilities for the year ended December 31, 2022 (in thousands):

For the year ended December 31, 2022	Balance at December 31, 2021	Additions	Deductions	Balance at December 31, 2022
Accounts receivable	$ 267	$ 6,722	$ (1,844)	$ 5,145
Contract liabilities:				
Deferred revenue	$ 72,221	$ 8,150	$ (11,483)	$ 68,888

During the three and twelve months ended December 31, 2022, the Company recognized the following collaboration revenue (in thousands):

Revenue recognized in the period from:	Three Months Ended December 31, 2022	Year Ended December 31, 2022
Amounts included in deferred revenue at the beginning of the period	$ —	$ 11,483
Performance obligations satisfied in previous periods	$ —	$ —

BMS Collaboration Agreement

In 2019, the Company entered into an amended and restated collaboration agreement ("BMS Collaboration Agreement") and license agreement ("BMS License Agreement") with BMS to focus on the research, development, and commercialization of autologous and allogenic alpha-beta T cell medicines for the treatment of all diseases, subject to certain exceptions. The Company and BMS started their collaboration in 2015 and have amended the agreement twice. The Company received a $70.0 million up-front, non-refundable, non-creditable cash payment ("Amendment Fee") in connection with the execution of the 2019 amendment. The Company may develop genome editing tools, specific to a gene target and enzyme combination (or a "Program") that, following the exercise of its option and the Company's grant of a license, BMS may use in its development of gene edited alpha-beta T-cell therapies and certain other T-cell derived from pluripotent stem cells or any other precursor cell for the treatment of all diseases, subject to certain exceptions (the "BMS Field"). To assess the Programs prior to opt-in, the Company granted BMS a non-exclusive perpetual research license in the BMS Field. If BMS exercises their option to the Program, they receive an exclusive, worldwide, development and commercialization license in the BMS Field for a nominal option exercise fee. The BMS License Agreement provided that the Company would manufacture clinical grade materials through a Phase 1 clinical trial if requested by BMS at an incremental cost to be negotiated by the parties. However, BMS has sole responsibility, at its own cost, for the worldwide research, development, manufacturing, and commercialization of its products. They must use commercially reasonable efforts and meet certain regulatory and commercial diligence requirements. The first development and commercialization license was delivered to BMS at the onset of the amended arrangement for which the Company received $0.5 million in consideration for the license (the "First Development and Commercialization License).

On a product-by-product basis, the Company is eligible to receive up to $27.5 million in development milestones and $107.5 million in regulatory milestones. The Company is also eligible to receive up to an aggregate of $60.0 million for the first two licensed products to reach certain sales milestones. The Company is entitled to a high-single digit to low double-digit percentage of royalties on net sales of licensed products, subject to reductions in certain circumstances, through the later of the expiration of the patent(s) related to the licensed products or six years post-first commercial sale of such licensed products.

The amended term of the BMS Collaboration Agreement is five years, which is subject to two one-year extension periods. During the term, including the extension periods, the Company may not alone, or with a third party, research, develop, manufacture, or commercialize a product in the BMS Field. BMS has the right to terminate the BMS Collaboration Agreement at any time upon no less than six months prior written notice. Per the termination provisions of the BMS License Agreement, BMS has the right to terminate the License Agreement either on a licensed product-by-product basis or in its entirety for any reason at any time upon ninety days prior written notice. If BMS terminates the license agreement without cause, the exclusive licenses granted to BMS automatically revert back to the Company.

Accounting Assessment

The Company concluded that the BMS Collaboration Agreement and the BMS License Agreement qualify as a contract with a customer under ASC 606 as one combined arrangement. The contract modification was accounted for on a prospective basis as if it were a termination of the existing contract and the creation of a new contract since the promised goods and services were distinct from the goods and services that were transferred on or before the effective date of the amendment.

The Company identified the following performance obligations: (i) First Development and Commercialization License and (ii) seventeen material rights for additional development and commercialization licenses for other Programs. The Company also evaluated the (i) the research license, (ii) contract term extensions, (iii) clinical supply arrangement, (iv) participation by employees on the oversight committee, alliance and technology transfer teams and (v) certain intellectual property rights and concluded that none of these met the definition of a performance obligation as a result of the promise being quantitively and qualitatively immaterial in the context of the arrangement or the promise did not convey a material right to BMS. The Company also concluded that there was not an implicit promise to perform research and development services.

As of December 31, 2022 the total transaction price was approximately $117.5 million comprised of the following: (i) $70.0 million Amendment Fee, (ii) $32.0 million in remaining deferred revenue balance that was not recognized pursuant the 2018 amendment agreement (iii) $5.5 million related to option exercise fees for delivered licenses and (iv) $10.0 million related to development milestone payments that were received by the Company. The outstanding milestone payments and extension term fees were fully constrained as of December 31, 2022, as a result of the uncertainty of whether any of the milestones will be achieved or the term would be extended. The assessment of the constraint utilizing the most likely amount method considers the stage of development and the risks associated with the remaining development required to achieve the milestones, as well as whether the achievement of the milestone is outside the control of the Company or BMS. The Company has determined that any commercial milestones and sales-based royalties will be recognized when the related sales occur. The Company reevaluates the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company concluded that rights and attributes of each of the development and commercialization licenses are identical for both the license granted at inception and the licenses that may be issued in the future upon exercise of the associated option. The Company has considered the early stage of the science and the uncertainty of success and concluded that the probability of scientific success and opt-in is equal amongst all Programs. In addition, each Program is multi-functional, and a combination of Programs can be utilized in the development of a product candidate. As such, the Company concluded that the standalone selling price of each material right is the same. The Company will recognize the transaction price allocated to each material right when the material right is exercised, lapsed or expired.

During the years ended December 31, 2022, 2021 and 2020, the Company recognized $18.8 million, $24.7 million and $11.3 million of revenue related to BMS. As of December 31, 2022, the Company recorded $56.7 million of deferred revenue, of which $56.7 million is classified as long-term on our consolidated balance sheet. As of December 31, 2021, the $56.7 million was classified as long-term in the accompanying consolidated balance sheets. There were no material sublicense fees paid to licensors in connection with the consideration received pursuant to the BMS Collaboration Agreement for the years ended December 31, 2022 and 2021.

Allergan Pharmaceuticals Strategic Alliance and Profit-Sharing Agreement

In March 2017, the Company entered into a Strategic Alliance and Option Agreement with Allergan to discover, develop, and commercialize new gene editing medicines for a range of ocular disorders (the "Allergan Agreement"). Under the terms of the Allergan Agreement, the Company received a $90.0 million up-front, non-refundable, non-creditable cash payment to primarily fund the Company's ocular research and development efforts to provide Allergan with the option to exclusively exercise the worldwide development and commercialization rights to five ocular development programs meeting certain criteria. Subsequently Allergan and the Company entered into an agreement (the "Profit-Sharing Agreement") to equally split U.S. profit and losses of EDIT-101, an experimental medicine or leber congenital amaurosis 10 or LCA10 that was the only program licensed to Allergan under the Allergan Agreement. In August 2020, the Company and Allergan agreed to terminate the Allergan Agreement and the Profit-Sharing Agreement (together with the Allergan Agreement, the "Initial Agreements"). In connection with the termination, the Company entered into a transition services agreement with Allergan (together with the termination agreement, the 'Termination Agreements"), primarily to facilitate the transfer of EDIT-101 back to the Company.

Pursuant to the Termination Agreements, the Company regained full global rights to research, develop, manufacture, and commercialize its ocular medicines, including EDIT-101. Allergan has no further obligations pursuant to the Initial Agreements, all unexercised options and contingent payments contemplated under the Initial Agreements have terminated, which includes Allergan's worldwide developmental and commercialization rights to EDIT-101. Under the Termination Agreements, Allergan granted the Company a non-exclusive license to certain know-how that is necessary to develop, manufacture and commercialize EDIT-101 and transferred to the Company certain materials produced under the Initial Agreements. The Company is obligated to use commercially reasonable efforts to develop and commercialize products directed at four collaboration targets, one of which is LCA10.

In connection with the Termination Agreements, the Company agreed to make a $20.0 million payment to Allergan, which was fully paid as of December 31, 2021. In addition, the Company will make certain payments on achievements of clinical and regulatory milestones up to $20.0 million for each target program and aggregated sales milestones for all products covered by the Termination Agreement up to $90.0 million. Allergan is also entitled to royalties in a low-single digit percentage, subject to reduction under specified circumstances, on net sales of specified products. The Company's obligation to pay royalties will expire on a country-by-country and product-by-product basis upon the later of the expiration of regulatory-based exclusivity with respect to such product in such country and the tenth anniversary of the first commercial sale of such product.

Accounting Assessment

The Company evaluated the Termination Agreements in accordance with the provisions ASC 606 and concluded that they resulted in a modification followed by a termination of the Initial Agreements. Upon execution of the Termination Agreements, the Company is no longer obligated to transfer control of any goods or services to Allergan, and therefore there are no remaining performance obligations. As part of this assessment, the Company considered that Allergan relinquished its right to the remaining exclusive license options under the Allergan Agreement and the Company reacquired the development and commercialization rights to EDIT-101. Allergan no longer has any involvement in the development activities of the collaboration targets. Since there are no remaining performance obligations, the Company accounted for the modification as part of the existing contract with a cumulative catch-up adjustment.

The Company concluded that $5.0 million of the $20.0 million payment that was paid to Allergan was for re-acquired rights to EDIT-101 that had no alternative future use, and as such the Company recorded it as in-process research and development expenses as of December 31, 2020. The remainder of the $20.0 million payment was recorded as a reduction to the contract liability and partially offset the recognition of $77.1 million in previously deferred revenue that was received under the Initial Agreements that was recognized on the termination date.

The contingent payments associated with the collaboration targets not previously licensed by Allergan under the Allergan Agreement did not impact the amount of deferred revenue recognized upon termination because it is not

probable that a significant reversal of revenue will occur. The contingent milestone and royalty payments associated with EDIT-101 qualify for scope exceptions from derivative accounting, and therefore there is no accounting for the contingent payments upon termination.

During the year ended December 31, 2020, the Company recognized revenue related to Allergan of approximately $70.6 million. There was no revenue recognized related to Allergan for the years ended December 31, 2021 and 2022.

Beam Therapeutics License Agreement

In 2018, the Company entered into a license agreement with Beam Therapeutics Inc. ("Beam," and such agreement, the "Beam License Agreement"). Pursuant to the Beam License Agreement, the Company granted to Beam a worldwide, exclusive (subject to certain exceptions), sublicensable (subject to certain conditions), development and commercialization license under certain intellectual property controlled by the Company for the use of base editing therapies for the treatment of any field of human diseases and conditions, such to certain exceptions. Additionally, the Company granted Beam a non-exclusive research license. Lastly, the Company provided to Beam with an exclusive option to obtain three development and commercialization licenses to additional groups of intellectual property owned or controlled by the Company, on a group-by-group basis, during the specified option period, subject to certain exceptions.

The Company received preferred stock valued at $3.6 million and received a nominal upfront cash payment. The Company subsequently sold its equity investment in Beam following Beam's initial public offering in 2021. The Company is also eligible to receive additional consideration if Beam exercises its option to obtain additional licenses for a fee ranging from a mid-teen million-dollar amount to a low to mid-eight-digit dollar amount per license, depending on the timing of the option exercise. To the extent that any products are commercialized, the Company would be entitled to receive tiered low single-digit royalty payments, plus any royalties that would be due from the Company to any applicable licensors related to the sale of such licensed products.

Unless earlier terminated by either party pursuant to the terms of the agreement, the Beam License Agreement will continue in full force and effect and will expire on a licensed product-by-licensed product and country-by-country basis upon the expiration of the royalty term with respect to such licensed product in such country. Beam has the right, at its sole discretion, at any time to terminate the Beam License Agreement in its entirety or on a group-by-group of intellectual property basis, upon ninety days written notice to the Company. Upon termination, all rights and licenses granted by the Company will immediately terminate.

Accounting Assessment

The Company identified the following performance obligations (i) the research license and (ii) the initial development and commercialization license. In addition, the Company concluded that the three options for the additional development and commercialization licenses are not discounted and therefore they do not represent material rights.

The total transaction price at the inception of the arrangement was determined to be approximately $3.8 million, consisting of the upfront cash payment and the non-cash value of the preferred shares received by the Company. The consideration associated with the exercise of the option(s) will be accounted for if and when Beam elects to exercise their options. The other forms of consideration, including nominal cost reimbursement for past patent and license fees and sublicense income reimbursement are based on the most-likely amount and were excluded from the initial transaction price as the most likely amount was estimated to be zero or the amount was otherwise fully constrained due to the significant uncertainties surrounding each payment. The commercial-based milestone reimbursement and the sales-based royalty payments will be recognized when the related sales occur as they were determined to relate predominantly to the licenses granted and therefore have also been excluded from the transaction price. Since both of the performance obligations were delivered at the inception of the arrangement and the licenses were made available for Beam's use and benefit, the Company recognized the total transaction price at the inception of the agreement.

During the years ended December 31, 2022 and 2021, the Company recognized revenue under the Beam License Agreement of approximately $0.3 million and $0.3 million, respectively.

10. Preferred Stock

The Company's amended and restated certificate of incorporation authorized 5,000,000 shares of undesignated preferred stock that may be issued from time to time by the Company's board of directors in one or more series. As of December 31, 2022, the Company had no shares of preferred stock issued or outstanding.

11. Common Stock

The voting, dividend, and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers, and preferences of holders of the preferred stock that may be issued from time to time. The common stock had the following characteristics as of December 31, 2022:

Voting

The holders of shares of common stock are entitled to one vote for each share of common stock held at any meeting of stockholders and at the time of any written action in lieu of a meeting.

Dividends

The holders of shares of common stock are entitled to receive dividends, if and when declared by the Company's board of directors. Cash dividends may not be declared or paid to holders of shares of common stock until all unpaid dividends on the redeemable convertible preferred stock have been paid in accordance with their terms. No dividends have been declared or paid by the Company since its inception.

2013 Stock Incentive Plan

In September 2013, the board of directors adopted the 2013 Stock Incentive Plan, which was subsequently amended (as amended, the "2013 Plan"), which provides for the grant of incentive stock options and nonqualified stock options or other awards including restricted stock awards, unrestricted stock awards, and restricted stock units to the Company's employees, officers, directors, advisors, and consultants for the purchase of up to 1,057,692 shares of the Company's common stock, which has been amended several times, and as of July 2015, a total of 6,317,769 shares were reserved.

The terms of stock awards agreements, including vesting requirements, are determined by the board of directors and are subject to the provisions of the 2013 Plan. The stock options granted to employees generally vest over a four-year period and expire ten years from the date of grant. Certain awards contain performance based vesting criteria. There has only been one such award to date. Certain options provide for accelerated vesting in the event of a change in control, as defined in the applicable options. Awards granted to non-employee consultants generally vest monthly over a period

of one to four years. In connection with the Company's initial public offering ("IPO"), the Company's board of directors determined to grant no further awards under the 2013 Plan.

2015 Stock Incentive Plan

The Company's board of directors adopted and the Company's stockholders approved the 2015 stock incentive plan (the "2015 Plan"). The 2015 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2015 Plan.

The number of shares reserved for issuance under the 2015 Plan is subject to further increases for (a) any additional shares of the Company's common stock subject to outstanding awards under the 2013 Plan that expire, terminate, or are otherwise surrendered, cancelled, forfeited, or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right and (b) annual increases, to be added as of the first day of each fiscal year, from January 1, 2017 until, and including, January 1, 2026, equal to the lowest of 2,923,076 shares of common stock, 4% of the number of shares of common stock outstanding on such first day of the fiscal year in question and an amount determined by the Company's board of directors. In January 2023, the shares under the 2015 Plan increased by 2,753,895 shares pursuant to the annual increase described in the prior sentence.

2015 Employee Stock Purchase Plan

The Company's board of directors adopted and the Company's stockholders approved the 2015 employee stock purchase plan (the "2015 ESPP"). The number of shares reserved for issuance under the 2015 ESPP is subject to annual increases, to be added as of the first day of each fiscal year, from January 1, 2017 until, and including, January 1, 2026, in an amount equal to the least of (a) 769,230 shares of common stock, (b) 1% of the total number of shares of common stock outstanding on the first day of the applicable year, and (c) an amount determined by the board of directors. The first offering under the 2015 ESPP opened on December 1, 2017. In January 2023, the board of directors determined that there should be no increase in shares available under the 2015 ESPP for 2023.

Inducement Awards

From time to time the Company's board of directors approves inducement awards to certain employees outside of the existing equity compensation plans in connection with such employees commencing employment with the Company. Inducement awards are typically a service-based option and a restricted stock unit and are subject to the Company's typical vesting terms and the employee's continued service relationship with the Company through the applicable vesting dates. In June 2022 and July 2022, the Company's board of directors approved two inducement grants to the Company's recently hired Chief Executive Officer and Chief Medical Officer, respectively.

Shares Reserved for Future Issuance

	As of December 31,	
	2022	2021
Shares reserved for outstanding stock option awards under the 2013 Stock Incentive Plan, as amended	143,055	145,255
Shares reserved for outstanding stock option awards and restricted stock units under the 2015 Stock Incentive Plan	5,253,299	3,036,797
Shares reserved for outstanding inducement stock option award and restricted stock units	1,378,864	408,765
Remaining shares reserved, but unissued, for future awards under the 2015 Stock Incentive Plan	7,812,540	7,524,431
Remaining shares reserved, but unissued, for future awards under the 2015 Employee Stock Purchase Plan	3,300,853	2,722,040
	17,888,611	13,837,288

12. Stock-Based Compensation

Total compensation cost recognized for all stock-based compensation awards in the consolidated statements of operations was as follows (in thousands):

	Year Ended December 31, 2022	2021
Research and development	$ 12,425	$ 16,553
General and administrative	16,869	26,846
Total stock-based compensation expense	$ 29,294	$ 43,399

Restricted Stock and Restricted Stock Unit Awards

The following table summarizes restricted stock and restricted stock unit awards activity for the instruments discussed above as of December 31, 2022 and 2021 is as follows:

	Shares	Weighted Average Grant Date Fair Value Per Share
Unvested restricted stock and restricted stock unit awards as of December 31, 2021	628,732	$ 41.28
Issued	1,362,658	$ 15.51
Vested	(286,642)	$ 44.18
Forfeited	(205,678)	$ 31.11
Unvested restricted stock and restricted stock unit awards as of December 31, 2022	1,499,070	$ 18.70

The expense related to restricted stock and restricted stock unit awards granted for the years ended December 31, 2022, 2021 and 2020 was $7.9 million, $14.6 million, and $4.4 million, respectively.

The restricted stock and restricted stock units granted in the year ended December 31, 2022 include 563,294 units granted to certain employees that contain performance-based vesting provisions. The expense related to the performance-based vesting restricted stock units was $4.4 million as of December 31, 2022.

As of December 31, 2022, total unrecognized compensation expense related to unvested restricted stock and restricted stock unit awards was $14.5 million, which the Company expects to recognize over a remaining weighted-average period of 2.6 years.

Stock Options

The following is a summary of stock option activity for the year ended December 31, 2022:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2021	3,016,085	$ 34.24	7.5	$ 5,052,469
Granted	2,874,773	$ 14.56		
Exercised	(19,769)	$ 15.45		
Cancelled	(594,941)	$ 30.65		
Outstanding at December 31, 2022	5,276,148	$ 23.99	8.0	$ 401,529
Exercisable at December 31, 2022	2,036,630	$ 30.61	6.7	$ 401,529

The total intrinsic value of options exercised for the years ended December 31, 2022, 2021 and 2020 was $0.09 million, $27.2 million, and $15.6 million, respectively.

Using the Black-Scholes option pricing model, the weighted average fair value of options containing service-based vesting granted during the years ended December 31, 2022, 2021, and 2020 was $15.87, $17.54, and $16.60, respectively. The expense related to options containing service-based vesting was $14.1 million, $18.8 million, and $16.1 million for the years ended December 31, 2022, 2021, and 2020, respectively.

The fair value of each service-based vesting option issued was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Expected volatility	64.2 %	61.2 %	60.0 %
Expected option term (in years)	6.25	6.25	6.25
Risk free interest rate	1.7 %	1.5 %	1.5 %
Expected dividend yield	—	—	—

As of December 31, 2022, total unrecognized compensation expense related to stock options was $33.7 million, which the Company expects to recognize over a remaining weighted-average period of 2.9 years.

13. 401(k) Savings Plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code of 1986, as amended (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. Effective in 2017, the Company will provide a 200% match of employee contributions up to a limit on the Company's contributions of the lesser of $6,000 and 3% of the employee's salary. The Company made $1.4 million, $1.2 million, and $1.1 million in contributions to the 401(k) Plan for the years ended December 31, 2022, 2021 and 2020, respectively.

14. Income Taxes

The Company had no income tax expense due to operating losses incurred for the years ended December 31, 2022 and 2021.

A reconciliation of the income tax expense computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2022	2021
Income tax computed at federal statutory tax rate	21 %	21 %
State taxes, net of federal benefit	6.87 %	8.89 %
General business credit carryovers	(1.97)%	2.95 %
162m Limitation	(0.01)%	(1.44)%
Stock Options	(2.31)%	1.12 %
Non-deductible expenses	(0.08)%	0.24 %
Tax Rate Changes	(3.26)%	5.03 %
Change in valuation allowance	(20.04)%	(37.80)%
Other	(0.21)%	— %
	(0)%	(0)%

The principal components of the Company's deferred tax assets and liabilities consist of the following at December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 144,849	$ 127,092
Tax credit carryforwards	20,077	25,028
Accrued expenses	2,869	3,991
Capitalized patent costs	58,387	63,093
Capitalized research	41,915	—
Lease Liabilities	12,627	7,929
Deferred revenue	17,495	21,709
Depreciation and amortization	299	—
Other	10,119	10,431
Total deferred tax assets	308,637	259,273
Less valuation allowance	(296,095)	(251,071)
Net deferred tax assets	12,542	8,202
Deferred tax liabilities	(12,542)	(8,202)
Depreciation and amortization	—	(335)
Right-of-use assets	(12,542)	(7,867)
Net deferred taxes	$ —	$ —

For taxable years beginning after December 31, 2021, the Tax Cuts and Jobs Act (the "Tax Act") eliminated the option to deduct research and development expenditures in the current year and requires taxpayers to capitalize such expenses pursuant to Internal Revenue Code ("IRC") Section 174. As a result of this provision of the Tax Act, deferred tax assets related to capitalized research expenses pursuant to IRC Section 174 increased to $41.9 million for the year ended December 31, 2022.

The Company has incurred net operating losses ("NOL") since inception. At December 31, 2022 and 2021, the Company had federal net operating loss carryforwards of $517.5 million and $447.4 million, respectively. Of the amount

as of December 31, 2022, $442.7 million will carryforward indefinitely while $74.8 million will expire beginning in 2035 and will continue to expire through 2037. As of December 31, 2022, and 2021, the Company also had state net operating loss carryforwards of approximately $609.5 million and $507.1 million, respectively, which may be available to offset future income tax liabilities and will expire beginning in 2035 and will continue to expire through 2042.

Under the provisions of the Internal Revenue Code of 1986, as amended (the "Code"), the NOL and tax credit carryforward are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Code, respectively, as well as other similar state provisions. The Company conducted an analysis under Section 382 to determine if historical changes in ownership through December 31, 2019 would limit or otherwise restrict its ability to utilize its NOL and research and development credit carryforwards. As a result of this analysis, the Company does not believe there are any significant limitations on its ability to utilize these carryforwards. However, future changes in ownership occurring after December 31, 2019 could affect the limitation in future years, and any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization.

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which principally comprise of NOL carryforwards, research and development credit carryforwards and capitalized license and patent costs. The Company's management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, and as a result, a valuation allowance of $296.1 million and $251.1 million has been established at December 31, 2022 and 2021, respectively. The increase in the valuation allowance of $45.0 million for the year ended December 31, 2022 was primarily due to current period pre-tax losses incurred and research tax credits generated.

The Company applies ASC 740 related to accounting for uncertainty in income taxes. The Company's reserves related to income taxes are based on a determination of whether, and how much of, a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit.

The following table summarizes the activity related to the Company's gross unrecognized tax benefits at the beginning and end of the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31, 2022
Balance as of December 31, 2021	$ —
Gross increases for tax positions related to current year	1,708
Gross increases for tax positions related to prior year	10,089
Gross decreases for tax positions related to prior year	—
Balance as of December 31, 2022	$ 11,797

At December 31, 2022 and 2021, the Company had unrecognized tax benefits of $11.8 million and $0 million, respectively. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2022 and 2021, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statement of operations. The company does not anticipate a material change to unrecognized tax benefits in the next twelve months.

The Company has not as of yet conducted a study of its research and development credit carry forwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits, and if an adjustment is

required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheets or statements of operations if an adjustment were required.

The Company files income tax returns in the U.S. federal tax jurisdiction, the Massachusetts state jurisdiction, the California state jurisdiction and the Colorado state jurisdiction. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available. The Company did not have any international operations as of December 31, 2022. An examination by the Internal Revenue Service ("IRS") for the period ended December 31, 2018 related to its R&D tax credits concluded in December 31, 2022 and resulted in a reduction to the Company's deferred tax assets.

15. Net Loss per Share

Basic net loss per common share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock and potentially dilutive securities outstanding for the period determined using the treasury stock and if converted methods. Contingently issuable shares are included in the calculation of basic loss per share as of the beginning of the period in which all the necessary conditions have been satisfied. Contingently issuable shares are included in diluted loss per share based on the number of shares, if any, that would be issuable under the terms of the arrangement if the end of the reporting period was the end of the contingency period, if the results are dilutive.

For purposes of the diluted net loss per share calculation, stock options are considered to be common stock equivalents, but they were excluded from the Company's calculation of diluted net loss per share allocable to common stockholders because their inclusion would have been anti-dilutive. Therefore, basic and diluted net loss per share applicable to common stockholders was the same for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share allocable to common stockholders because their inclusion would have been anti-dilutive:

	As of December 31,	
	2022	2021
Unvested restricted stock and restricted stock unit awards	1,499,070	628,732
Outstanding stock options	5,276,148	3,016,085
Total	6,775,218	3,644,817

The table above reflects restricted stock issued upon exercise of unvested stock options as exercised on the dates that the shares are no longer subject to repurchase.

16. Subsequent Events

None.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (the "Exchange Act") means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with general accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in Internal Control–Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under that framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

The effectiveness of our internal control over financial reporting as of December 31, 2022, has been audited by Ernst & Young LLP, an independent registered public accounting firm, and has issued an attestation report on such audit, which is included herein.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during our fiscal quarter ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Editas Medicine, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Editas Medicine Inc.'s internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Editas Medicine Inc. (the "Company") maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of Editas Medicine Inc. as of December 31, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2022, and the related notes, and our report dated February 22, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission of the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 22, 2023

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Except to the extent provided below, the information required by this Item 10 will be included in the section captioned "Corporate Governance" and the subsections thereof, "Nominees for Election as Class I Directors," "Directors Continuing in Office," "Executive Officers Who Are Not Directors," and "Delinquent Section 16(a) Reports," if applicable, in our definitive proxy statement to be filed with the Securities and Exchange Commission ("SEC") with respect to our 2023 Annual Meeting of Stockholders, which information is incorporated herein by reference.

We have adopted a written code of business conduct and ethics that applies to our directors, officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code is posted on the Corporate Governance section of our website, which is located at www.editasmedicine.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K. We will provide any person, without charge, a copy of such Code of Business Conduct and Ethics upon written request, which may be mailed to 11 Hurley Street, Cambridge, MA 02141, Attn: Corporate Secretary.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in the section captioned "Executive Compensation" in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders, which information (other than the information required by Item 402(v) of Regulation S-K) is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be included in the sections captioned "Principal Stockholders" and "Securities Authorized for Issuance under Equity Compensation Plans" in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders, which information is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be included in the sections captioned "Transactions with Related Persons" and "Director Independence" in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders, which information is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in the sections captioned "Audit Fees" and "Audit Committee Pre-Approval Policy and Procedures" in our definitive proxy statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders, which information is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(1) Financial Statements

Our consolidated financial statements are set forth in Part II, Item 8 of this Annual Report on Form 10-K and are incorporated herein by reference.

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

The exhibits filed as part of this Annual Report on Form 10-K are listed in the following Exhibit Index.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation of the Registrant	8-K	001-37687	2/8/2016	3.1	
3.2	Amended and Restated By-laws of the Registrant	8-K	001-37687	2/8/2016	3.2	
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1	333-208856	1/4/2016	4.1	
4.2	Description of Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934	10-K	001-37687	2/26/2020	4.2	
10.1+	2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.5	
10.2+	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.6	
10.3+	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.7	
10.4+	Form of Early Exercise Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.8	
10.5+	Form of Restricted Stock Agreement under 2013 Stock Incentive Plan, as amended	S-1	333-208856	1/4/2016	10.9	
10.6+	2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.10	
10.7+	Form of Incentive Stock Option Agreement under 2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.11	
10.8+	Form of Nonstatutory Stock Option Agreement under 2015 Stock Incentive Plan	S-1	333-208856	1/4/2016	10.12	
10.9+	Form of Restricted Stock Agreement under 2015 Stock Incentive Plan	10-Q	001-37687	11/8/2017	10.1	
10.10+	Form of Restricted Stock Unit Award Agreement under the 2015 Stock Incentive Plan	8-K	001-37687	1/22/2019	10.1	
10.11+	Employment Offer Letter, dated April 13, 2022, between the Registrant and Gilmore O'Neill	10-Q	001-37687	8/3/2022	10.1	
10.12+	Employment Offer Letter, dated February 14, 2021, between the Registrant and James C. Mullen	10-K	001-37687	2/26/2021	10.14	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit Number	
10.13+	Amendment to Employment Offer Letter, dated April 13, 2022, between the Registrant and James C. Mullen	10-Q	001-37687	8/3/2022	10.2	
10.14+	Amendment to RSU Agreement, dated May 24, 2022, between the Registrant and James C. Mullen	10-Q	001-37687	8/3/2022	10.4	
10.15+	Employment Offer Letter, dated December 27, 2019, between the Registrant and Michelle Robertson	10-K	001-37687	2/26/2020	10.14	
10.16+	Employment Offer Letter, dated June 14, 2022, between the Registrant and Baisong Mei	10-K	001-37687	8/3/2022	10.3	
10.17+	Employment Offer Letter, dated April 19, 2021, between the Registrant and Mark S. Shearman	10-Q	001-37687	8/5/2021	10.2	
10.18+	Employment Offer Letter, dated September 22, 2021, between the Registrant and Bruce Eaton	10-Q	001-37687	11/9/2021	10.1	
10.19+	Form of Inducement Stock Option Agreement for the Registrant's executive officers	10-K	001-37687	2/26/2020	10.15	
10.20+	Form of Inducement Restricted Stock Unit Award Agreement for the Registrant's executive officers	10-K	001-37687	2/26/2020	10.16	
10.21†	Amended and Restated Cas9-I License Agreement, dated December 16, 2016, among the Registrant, the President and Fellows of Harvard College ("Harvard"), and the Broad Institute, Inc. (the "Broad")	8-K	001-37687	1/23/2017	99.2	
10.22	Amendment No.1 to Amended and Restated Cas9-I License Agreement, by and among Editas Medicine, Inc., Harvard, and Broad, dated March 3, 2017	8-K	001-37687	3/7/2017	99.1	
10.23*	Second Amended and Restated License and Collaboration Agreement, dated November 11, 2019, between the Registrant and Juno Therapeutics, Inc. ("Juno")	10-K	001-37687	2/26/2020	10.20	
10.24*	License and Agreement, dated November 11, 2019, between the Registrant and Juno	10-K	001-37687	2/26/2020	10.21	
10.25†	Sponsored Research Agreement, dated June 7, 2018, between the Registrant and Broad	10-Q/A	001-37687	10/23/2018	10.2	
10.26*	First Amendment to Sponsored Research Agreement, dated January 11, 2021, between the Registrant and Broad	10-K	001-37687	2/26/2021	10.24	
10.27+	Summary of Director Compensation Program	10-Q	001-37687	8/5/2021	10.3	
10.28+	2015 Employee Stock Purchase Plan	S-1	333-208856	1/4/2016	10.25	
10.29+	Amended Severance Benefits Plan	10-K	001-37687	2/24/2022	10.28	
10.30	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers	S-1	333-208856	1/4/2016	10.28	
10.31	Lease Agreement, dated February 12, 2016, between Registrant and ARE-MA Region No. 55 Exchange Holding LLC	8-K	001-37687	2/19/2016	99.1	
10.32	First Amendment to Lease Agreement, dated November 15, 2022 between Registrant and ARE-MA Region No. 55, LLC					X
10.33†	Cpf1 License Agreement, dated as of December 16, 2016, by and between the Registrant and Broad	8-K	001-37687	1/23/2017	99.1	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File No.	Date of Filing	Exhibit Number	
10.34†	Cas9-II License Agreement, dated as of December 16, 2016, by and between the Registrant and Broad	8-K	001-37687	1/23/2017	99.3	
10.35*	Omnibus Amendment, dated as of January 11, 2021, by and between the Registrant and Broad	10-K	001-37687	2/26/2021	10.32	
10.36*	Letter Agreement, dated as of November 18, 2019, by and among, the Registrant, Broad and Harvard	10-K	001-37687	2/26/2020	10.30	
10.37*	Letter Agreement, dated as of December 16, 2019, by and among, the Registrant, Broad and Harvard	10-K	001-37687	2/26/2020	10.31	
10.38	Common Stock Sales Agreement, dated as of May 14, 2021, by and between the Company and Cowen and Company, LLC	8-K	001-37687	5/14/2021	1.1	
10.39*	Termination Agreement, dated August 5, 2020, by and between the Registrant and Allergan Sales, LLC	10-Q	001-37687	11/6/2020	10.1	
21.1	Subsidiaries of the Registrant					X
23.1	Consent of Ernst & Young					X
31.1	Rule 13a-14(a) Certification of Principal Executive Officer					X
31.2	Rule 13a-14(a) Certification of Principal Financial Officer					X
32.1	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. §1350					X
101	The following financial statements from the Company's Annual Report on Form 10-K for the year ended December 31, 2022, formatted in Inline XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Comprehensive Loss, (iv) Consolidated Statement of Stockholders' Equity, (v) Consolidated Statements of Cash Flows and (vi) Notes to Condensed Consolidated Financial Statements, tagged as blocks of text and including detailed tags.					
104	The cover page from the Company's Annual Report on Form 10-K for the year ended December 31, 2022, formatted in Inline XBRL.					

† Confidential treatment has been granted as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

* Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K. Certain portions of this exhibit have been omitted because they are not material and are information of the type that the registrant customarily and actually treats as private or confidential.

+ Management contract or compensatory plan or arrangement.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

EDITAS MEDICINE, INC.

Dated: February 22, 2023

By: /s/ Gilmore O'Neill
Gilmore O'Neill
Principal Executive Officer

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Gilmore O'Neill Gilmore O'Neill, M.B., M.M.Sc.	President and Chief Executive Officer, Director (principal executive officer)	February 22, 2023
/s/ Michelle Robertson Michelle Robertson	Chief Financial Officer (principal financial and accounting officer)	February 22, 2023
/s/ James C. Mullen James C. Mullen	Executive Chairman of the Board	February 22, 2023
/s/ Meeta Chatterjee Meeta Chatterjee, Ph.D.	Director	February 22, 2023
/s/ Bernadette Connaughton Bernadette Connaughton	Director	February 22, 2023
/s/ Andrew Hirsch Andrew Hirsch	Director	February 22, 2023
/s/ Jessica Hopfield Jessica Hopfield, Ph.D.	Director	February 22, 2023
/s/ Emma Reeve Emma Reeve	Director	February 22, 2023
/s/ David Scadden David Scadden, M.D.	Director	February 22, 2023

/s/ Akshay K. Vaishnaw	Director	February 22, 2023
Akshay K. Vaishnaw, M.D., Ph.D.		

Directors and Executive Officers (as of April 18, 2023)

Directors

Meeta Chatterjee, Former Senior Vice President of Global Business Development, Legend Biotech Corp.

Bernadette Connaughton, Former President Intercontinental, Bristol Myers Squibb Company

Andrew Hirsch, President and Chief Executive Officer, C4 Therapeutics, Inc.

Jessica Hopfield, Principal, J Hopfield Consulting

Elliott Levy, Venture Partner at 5AM Venture Management, LLC

James Mullen, Executive Chair of the Board of Directors of Editas Medicine, Inc.

Gilmore O'Neill, President and Chief Executive Officer

Emma Reeve, Former Chief Financial Officer of Constellation Pharmaceuticals, Inc.

David Scadden, Gerald and Darlene Jordan Professor of Medicine at Harvard University

Akshay Vaishnaw, President of Alnylam Pharmaceuticals, Inc.

Executive Officers

Gilmore O'Neill, President and Chief Executive Officer

Michelle Robertson, Chief Financial Officer

Bruce Eaton, Chief Business Officer and Chief Technology Officer

Baisong Mei, Chief Medical Officer