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, 2025

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 001-37923

CRISPR THERAPEUTICS AG

(Exact name of registrant as specified in its charter)

Switzerland	**Not Applicable**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
Baarerstrasse 14	
6300 Zug, Switzerland	**Not Applicable**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: +41 (0)41 561 32 77

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 Shares, nominal value CHF 0.03	**CRSP**	**The Nasdaq Global Market**

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 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, smaller reporting company, or an emerging growth company. See the 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 Exchange Act). YES ☐ NO ☒

The aggregate market value of the common shares held by non-affiliates of the Registrant was approximately $4.1 billion, based on the closing price on the Nasdaq Global Market of the Registrant's common shares on June 30, 2025 (the last trading day of the Registrant's second fiscal quarter of 2025).

The number of the Registrant's common shares outstanding as of February 10, 2026 was 95,985,312.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2026 Annual General Meeting of Shareholders, which the Registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days after the end of the Registrant's fiscal year ended December 31, 2025, are incorporated by reference into Part III of this Report.

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Risk Factor Summary

Our business is subject to a number of risks and uncertainties of which you should be aware before making an investment decision in our business. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K. These risks include, but are not limited to, the following:

- We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.
- We will need to raise substantial additional funding, which will dilute our shareholders. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate some of our product development programs or commercialization efforts.
- If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Our CRISPR/Cas9 gene editing product candidates are based on a relatively new gene editing technology, which makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval, if at all. There have only been a limited number of clinical trials of product candidates based on gene editing technology.
- The U.S. Food and Drug Administration, or FDA, the National Institutes of Health, the Medicines and Healthcare products Regulatory Agency, or MHRA and the European Medicines Agency, or EMA, have demonstrated caution in their regulation of gene therapy treatments, and ethical and legal concerns about gene therapy and genetic testing may result in additional regulations or restrictions on the development and commercialization of our product candidates, which may be difficult to predict.
- If any of the product candidates we may develop or administration processes 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.
- 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.
- Positive results from early preclinical studies or preliminary results from clinical trials of our product candidates are not necessarily predictive of the results of later preclinical studies and any future clinical trials of our product candidates. If we cannot replicate the positive results from our earlier preclinical studies of our product candidates in our later preclinical studies, clinical trials and future clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.
- Adverse public perception of gene editing and cellular therapy products may negatively impact demand for, or regulatory approval of, our product candidates.
- The commercial success of any of our products or product candidates will depend upon its degree of market acceptance by physicians, patients, third-party payors and others in the medical community.
- We face significant competition in the biotechnology and pharmaceutical industries.
- We have partnered with Vertex Pharmaceuticals Incorporated, or Vertex, on our lead program CASGEVY; Vertex has significant control over the CASGEVY program.
- Gene editing and gene silencing products are novel and may be complex and difficult to manufacture. We could experience manufacturing problems or regulatory requirements that result in delays in the development, approval or commercialization of our product candidates or otherwise harm our business.
- Our status as a Swiss corporation may limit our flexibility with respect to certain aspects of capital management and may cause us to be unable to make distributions without subjecting our shareholders to Swiss withholding tax.
- If we are unable to obtain, maintain or protect intellectual property rights related to our proprietary gene editing technology and product candidates, we may not be able to compete effectively in our markets.
- The intellectual property landscape around gene editing technology, including CRISPR/Cas9, is highly dynamic, and third parties may initiate and prevail in legal proceedings alleging that the patents that we in-license or own are invalid or 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.

Throughout this Annual Report on Form 10-K, the "Company," "CRISPR," "CRISPR Therapeutics," "we," "us," and "our," except where the context requires otherwise, refer to CRISPR Therapeutics AG and its consolidated subsidiaries; "our board of directors" refers to the board of directors of CRISPR Therapeutics AG; and we generally refer to CASGEVY (exagamglogene autotemcel [exa-cel]), as "CASGEVY."

"CRISPR Therapeutics®" standard character mark and design logo, "CRISPRX™," "CRISPR TX™," "CTX112™," "CTX211™," "CTX213™," "CTX310®," "CTX321™," "CTX340™," "CTX460™", "CTX611™ and "SyNTase™" are trademarks and registered trademarks of CRISPR Therapeutics AG. CASGEVY® and the CASGEVY logo are registered trademarks of Vertex Pharmaceuticals Incorporated, and Vertex Pharmaceuticals Incorporated is the manufacturer and exclusive license holder of CASGEVY. All other trademarks and registered trademarks contained in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, trademarks, service marks and trade names referred to in this Annual Report on Form 10-K may appear without the ® or ™ symbols and any such omission is not intended to indicate waiver of any such rights.

Special Note Regarding Forward-Looking Statements and Industry Data

This Annual Report on Form 10-K contains "forward-looking statements" that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K are forward-looking statements. These statements are often identified by the use of words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "will," "would" or the negative or plural of these words or similar expressions or variations, although not all forward-looking statements contain these identifying words. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our strategic plans to develop and, if approved, subsequently commercialize any product candidates we may develop, including plans and expectations for the commercialization of, and anticipated benefits of, CASGEVY, including plans for patient access to CASGEVY;
- the safety, efficacy and clinical progress of various clinical programs, including those for CASGEVY, zugocabtagene geleucel, CTX213, CTX310, CTX321 and CTX611;
- the status of clinical trials, including development timelines and discussions with regulatory authorities related to product candidates under development by us and our collaborators;
- the results of our preclinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials, and our research and development programs;
- the actual or potential benefits of regulatory designations, such as orphan drug, fast track and regenerative medicine advanced therapy in the United States or such European equivalents, including the PRIority MEdicines designation;
- our ability to advance product candidates into, and successfully complete, clinical trials;
- the size and growth potential of the markets for our product candidates and our ability to serve those markets, including our estimates regarding the addressable patient population and potential market opportunity for our current and future product candidates;
- the rate and degree of market acceptance of our product candidates and the success of competing therapies that are or become available;
- our internal manufacturing capabilities and operation of our cell therapy manufacturing facility;
- our intellectual property coverage and positions, including those of our licensors and third parties as well as the status and potential outcome of proceedings involving any such intellectual property;
- the expected benefits of our collaborations;
- our strategy, goals, and anticipated financial performance;
- our anticipated expenses, ability to obtain funding for our operations and the sufficiency of our cash resources;
- the therapeutic value, development, and commercial potential of gene editing technologies and therapies, including CRISPR/Cas9 and SyNTase, as well as other technologies we develop and use, including delivery and siRNA; and
- the volatility of capital markets and unfavorable macroeconomic conditions resulting from factors including rising inflation, changes in or disruptions of U.S. governmental agencies, new or increased international tariffs and retaliatory tariffs, interest rate and currency rate fluctuations, new laws and regulations or amendments to existing laws and regulations in the U.S. and foreign countries, trade protection measures, economic sanctions and economic slowdowns or recessions, banking instability, monetary policy changes, geopolitical tensions or the outbreak of hostilities or war.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and assumptions that could cause our actual results and the timing of certain events to differ materially from future results expressed or implied by the forward-looking statements.

Factors that could cause or contribute to such differences include, but are not limited to, those identified herein, and those discussed in the section titled "Risk Factors," set forth in Part I, Item 1A of this Annual Report on Form 10-K. You should not rely upon forward-looking statements as predictions of future events. Such forward-looking statements speak only as of the date of this report. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

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, performance or achievements may be materially different from what we expect. Except as required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

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.

PART I

Item 1. Business.

BUSINESS

Overview

Our mission is to create transformative gene-based medicines for serious human diseases. We are a leading biopharmaceutical company focused on the development of CRISPR-based therapeutics, including by using CRISPR/Cas9 technology. CRISPR/Cas9 is a revolutionary technology for gene editing, the process of precisely altering specific sequences of genomic DNA. We have advanced this technology from discovery to an approved medicine with unparalleled speed, culminating in the landmark first approval of a CRISPR-based therapy, CASGEVY (exagamglogene autotemcel [exa-cel]), in 2023 with our collaborators at Vertex Pharmaceuticals Incorporated, or Vertex.

We have established a portfolio of therapeutic programs spanning four core franchises: hemoglobinopathies, *in vivo*, CAR T approaches and regenerative medicine. Depending on the program, we take either an *ex vivo* approach, in which we edit cells outside of the human body before administering them to the patient, or an *in vivo* editing approach, where we deliver the CRISPR-based therapeutic directly to target cells within the human body.

- **Hemoglobinopathies**: Our most advanced program, CASGEVY, has received approval in the United States and other countries for the treatment of eligible patients with severe sickle cell disease, or SCD, or transfusion-dependent beta thalassemia, or TDT, two genetic disorders of hemoglobin, or hemoglobinopathies, with high unmet medical need. In addition, we have further research efforts, also in collaboration with Vertex, on targeted conditioning and *in vivo* editing of hematopoietic stem cells that have the potential to expand the number of patients that could benefit significantly.
- ***In vivo* approaches**: We are advancing a portfolio of programs leveraging *in vivo* editing for both common and rare diseases, as well as using siRNA approaches.
- **CAR T**: We are progressing next-generation gene-edited cell therapy programs, including allogeneic chimeric antigen receptor T cell, or CAR T, candidates for autoimmune indications and oncology.
- **Regenerative medicine**: We are advancing a deviceless beta cell replacement product candidate consisting of unencapsulated precursor islet cells derived from induced pluripotent stem cells for the treatment of Type 1 diabetes, or T1D.

We continue to innovate on our platform to develop next-generation technologies that can enable new therapies. We are developing other technologies, including delivery technologies and other gene editing technologies, like SyNTase. Through our efforts, we aim to unlock the full potential of gene-based therapeutics to create medicines that can transform people's lives. We believe that our innovative research, translational expertise, and clinical development experience, position us as a leader in the development of CRISPR-based therapeutics and may enable us to create an entirely new class of highly effective and potentially curative therapies for patients with both common and rare diseases for whom current biopharmaceutical approaches have had limited success.

Hemoglobinopathies

CASGEVY is a non-viral, *ex vivo* CRISPR/Cas9 gene-edited cell therapy, in which a patient's own hematopoietic stem and progenitor cells are edited at the erythroid specific enhancer region of the *BCL11A* gene through a precise double-strand break. This edit results in the production of high levels of fetal hemoglobin in red blood cells, which can compensate for the defective adult hemoglobin in patients with SCD and TDT. CASGEVY is the first therapy to emerge from our strategic partnership with Vertex and is being advanced under a joint development and commercialization agreement between us and Vertex and certain of its affiliates.

In 2023, CASGEVY became the first-ever approved CRISPR-based gene-editing therapy in the world. To date, CASGEVY has been approved in the United States, European Union, Great Britain, Canada, Switzerland and certain countries in the Middle East for the treatment of eligible patients 12 years and older with SCD or TDT. Efficacy data presented to date support the profile of this therapy as a potential one-time functional cure for people with severe SCD and TDT.

We continue to advance our internally developed targeted conditioning program, as well as *in vivo* hematopoietic stem cell editing approaches utilizing lipid nanoparticle-mediated delivery through preclinical studies. Both initiatives could significantly expand the addressable patient populations for SCD and TDT.

In Vivo Liver Editing

We have established a leading platform for *in vivo* gene editing and are rapidly advancing a pipeline of *in vivo* gene editing

candidates that target the liver, taking advantage of validated lipid nanoparticle, or LNP, delivery technologies, and aim to treat diseases where we can produce a strong therapeutic effect by safely disrupting a gene with well-understood genetic association. We have established a proprietary LNP delivery platform to enable gene editing in the liver using both CRISPR/Cas9 and our novel, proprietary SyNTase editing technologies. Our *in vivo* portfolio includes cardiovascular investigational programs, such as CTX310, directed towards angiopoietin-related protein 3 or ANGPTL3, which is currently in an ongoing Phase 1b clinical trial. Additionally, we have a number of earlier stage investigational *in vivo* programs leveraging gene disruption in the liver for both common and rare diseases, including CTX340, directed towards angiotensinogen for the treatment of refractory hypertension, our next-generation *LPA* program, CTX321, and CTX460, directed towards SERPINA1 using our proprietary SyNTase editing platform, for the treatment of alpha-1 antitrypsin deficiency. We are also pursuing additional delivery technologies, including LNPs, for delivery to tissues beyond the liver, including hematopoietic stem cells and T cells.

siRNA-based Programs

Our siRNA-based portfolio includes clinical-stage programs in cardiovascular and thromboembolic diseases, developed in collaboration with Sirius Therapeutics and certain of its affiliates, or Sirius.

CTX611 (formerly known as SRSD107) is a novel double-stranded, long-acting siRNA, designed to target the human coagulation factor XI, or FXI, messenger RNA and inhibit FXI protein expression. Through modulation of the intrinsic coagulation pathway, CTX611 is intended to provide anticoagulant and antithrombotic effects. Supported by clinical experience conducted by Sirius in two Phase 1 clinical trials, CTX611 is being developed as a long-acting FXI inhibitor with the potential to support infrequent, including semi-annual, subcutaneous administration. CTX611 is in an ongoing Phase 2 clinical trial in patients undergoing total knee arthroplasty.

CAR T

We believe CRISPR/Cas9 has the potential to create the next generation of CAR T cell therapies that may have a superior product profile and allow broader patient access compared to current autologous therapies. We are advancing cell therapy programs for autoimmune indications and oncology, including our lead next-generation product candidate zugocabtagene geleucel (zugo-cel; formerly CTX112), which targets Cluster of Differentiation 19, or CD19, and incorporate edits designed to enhance CAR T potency, reduce CAR T exhaustion and evade the immune system. As a result of the next-generation edits, zugo-cel exhibits increased manufacturing robustness, with a higher and more consistent number of CAR T cells produced per batch. We are producing zugo-cel for clinical trials at our internal GMP manufacturing facility in Framingham, Massachusetts.

Zugo-cel continues to advance in both autoimmune disease and hematologic malignancies. In autoimmune disease, it is being investigated in an ongoing clinical trial designed to assess the safety and efficacy of the product candidate in adult patients with systemic lupus erythematosus, or SLE, systemic sclerosis, and inflammatory myositis, and a second clinical trial in immune thrombocytopenia purpura and warm autoimmune hemolytic anemia. In oncology, the Phase 1/2 clinical trial in adult patients with relapsed or refractory B-cell malignancies who have received at least two prior lines of therapy is ongoing. We have also established a collaboration and clinical supply agreement with Eli Lilly to evaluate zugo-cel together with pirtobrutinib in aggressive B-cell lymphomas, further expanding the program's development in oncology. Zugo-cel has been granted RMAT designation by the U.S. Food and Drug Administration for the treatment of relapsed or refractory follicular lymphoma and marginal zone lymphoma.

Our CRISPR/Cas9 platform enables us to innovate continuously by incorporating incremental edits into next-generation products. We are advancing several additional investigational CAR T programs.

Regenerative Medicine

We continue to advance our regenerative medicine portfolio, including in diabetes. We are advancing CTX213, a deviceless beta cell replacement product candidate consisting of unencapsulated precursor islet cells derived from induced pluripotent stem cells for the treatment of T1D. To date, CTX213 has demonstrated preclinical efficacy data via direct administration. In addition, we have granted a non-exclusive license to certain of our CRISPR/Cas9 intellectual property to Vertex to accelerate Vertex's development of hypoimmune cell therapies for T1D in exchange for certain milestones and royalties.

Partnerships

Given the numerous potential therapeutic applications for CRISPR/Cas9, we have partnered strategically to broaden the indications we can pursue and accelerate development of programs by accessing specific technologies and/or disease-area expertise. We maintain broad partnerships to develop gene-based therapeutics in specific disease areas. For additional information regarding certain of these partnerships, please see "*Business—Strategic Partnerships and Collaborations*."

Hemoglobinopathies. In 2015, we partnered with Vertex and entered into a strategic collaboration, option and license agreement, which focused on the discovery and development of gene-based treatments for hemoglobinopathies and cystic fibrosis using CRISPR/Cas9 gene-editing technology. In 2017, Vertex exercised its option to co-develop and co-commercialize the

hemoglobinopathies program and we entered into a joint development and commercialization agreement with Vertex, which we amended and restated in 2021, pursuant to which, among other things, we are co-developing and co-commercializing CASGEVY for TDT and SCD.

siRNA. In May 2025, we partnered with Sirius and entered into the Sirius Agreement pursuant to which, among other things, we and Sirius will collaborate on the research, development, manufacture, commercialization and use of the Sirius Collaboration Products, including co-development and co-commercialization of CTX611; and (2) Sirius granted us options to exclusively license Sirius siRNA technology to target up to two licensed targets from a list of reserved targets for the research, develop, manufacture and commercialization of siRNA Licensed Products, For the first Sirius Collaboration Product successfully developed, we will be the lead party responsible for Phase 3 global development and commercialization efforts in the United States and Sirius will be the lead party responsible for Phase 3 development (subject to the global development plan) and commercialization efforts in Greater China.

Other Partnerships. We have entered into a number of additional collaborations, research and license agreements in other therapeutic areas, including an additional agreements with Vertex including for the treatment of Duchenne muscular dystrophy, or DMD, and myotonic dystrophy type 1, or DM1, as well as diabetes, and others, including to support and complement our hematopoietic stem cell, CAR T, *in vivo* and diabetes programs and platform.

Gene Editing Background

There are thousands of diseases caused by aberrant DNA sequences. Traditional small molecule and biologic therapies have had limited success in treating many of these diseases because they fail to address the underlying genetic causes. Newer approaches, such as RNA therapeutics and viral gene therapy, more directly target the genes related to disease, but each has clear limitations. RNA-based therapies, such as mRNA and siRNA may provide clinical benefit in certain diseases, however, these approaches face challenges with repeat dosing and related toxicities. Non-integrating viral gene therapy platforms, such as adenovirus-associated vectors, or AAV, may have limited durability because they do not permanently change the genome and have limited efficacy upon re-administration due to resulting immune responses. Integrating viral gene therapy platforms, such as lentivirus, permanently alter the genome but do so randomly, which leads to the potential for undesirable mutations. Additionally, cells may recognize the transduced genes as foreign and respond by reducing their expression, limiting their efficacy. Thus, while our understanding of genetic diseases has increased since the mapping of the human genome, our ability to treat them effectively has been limited.

We believe gene editing has the potential to enable a next generation of therapeutics and provide potentially curative therapies to many genetic diseases through precise gene modification. Furthermore, the ability to alter DNA sequences precisely has applications beyond the treatment of genetic diseases. CRISPR/Cas9 gene editing could also enable the engineering of cell-based therapies to make them more efficacious, safer and available to a broader group of patients. Cell therapies have already begun to make a meaningful impact in certain diseases and gene editing could help accelerate that progress across diverse disease areas, including oncology, autoimmune diseases and diabetes.

The process of gene editing involves precisely altering DNA sequences within the genomes of cells using enzymes to cut the DNA at specific locations. After a cut is made, natural cellular processes repair the DNA to either silence or correct undesirable sequences, potentially reversing their negative effects. Importantly, because the genome itself is modified in this process, the change is permanent in the patient. Earlier generations of gene editing technologies, such as zinc finger nucleases, or ZFNs, transcription-activator like effector nucleases, or TALENs, and meganucleases, rely on engineered protein-DNA interactions to govern the location of editing. While these systems were an important first step to demonstrate the potential of gene editing, their development has been challenging in practice due to the complexity of engineering protein-DNA interactions. In contrast, CRISPR/Cas nucleases are guided by RNA-DNA interactions, which are more predictable and straightforward to engineer and apply.

The CRISPR/Cas9 Technology

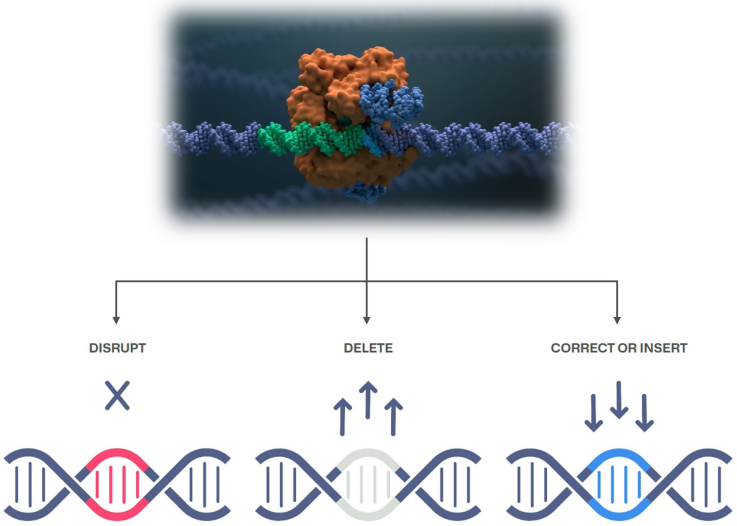
CRISPR/Cas9 stands for Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/CRISPR-associated protein 9 (Cas9) and evolved as a naturally occurring defense mechanism that protects bacteria against viral infections. Dr. Emmanuelle Charpentier and her collaborators elucidated this mechanism and developed ways to adapt and simplify it for use in gene editing. In recognition of this groundbreaking work, Dr. Charpentier was awarded the 2020 Nobel Prize in Chemistry along with her collaborator, Dr. Jennifer Doudna of the University of California, Berkeley. The CRISPR/Cas9 technology they described consists of three basic components: Cas9, CRISPR RNA, or crRNA, and trans-activating CRISPR RNA, or tracrRNA. Cas9, in combination with these two RNA molecules, is described as “molecular scissors” that can make specific cuts and edits in selected double-stranded DNA.

Dr. Charpentier and her collaborators further simplified the system for use in gene editing by combining the crRNA and tracrRNA into a single RNA molecule called a guide RNA, or gRNA. The gRNA binds to Cas9 and can be programmed to direct the Cas9 enzyme to a specific DNA sequence based on Watson-Crick base pairing rules. The CRISPR/Cas9 technology can be used to make cuts in DNA at specific sites of targeted genes, providing a powerful tool for developing gene editing-based therapeutics.

Once the DNA is cut, the cell uses naturally occurring DNA repair mechanisms to rejoin the cut ends. If a single cut is made, a

process called non-homologous end joining can result in the addition or deletion of base pairs, disrupting the original DNA sequence and causing gene inactivation. A larger fragment of DNA can also be deleted by using two gRNAs that target separate sites. After cleavage at each site, non-homologous end joining unites the separate ends, deleting the intervening sequence. Alternatively, if a DNA template is added alongside the CRISPR/Cas9 machinery, the cell can correct a gene or even insert a new gene through a process called homology-directed repair.

CRISPR/Cas9 gene editing



Given the versatility of CRISPR/Cas systems, multiple groups have developed new technologies based on CRISPR/Cas9, such as base editing and reverse transcriptase editing. While still nascent, such new CRISPR-based technologies could have advantages in select disease applications. As a result, we have continued to invest in broadening our CRISPR platform so we can employ a variety of technologies as appropriate.

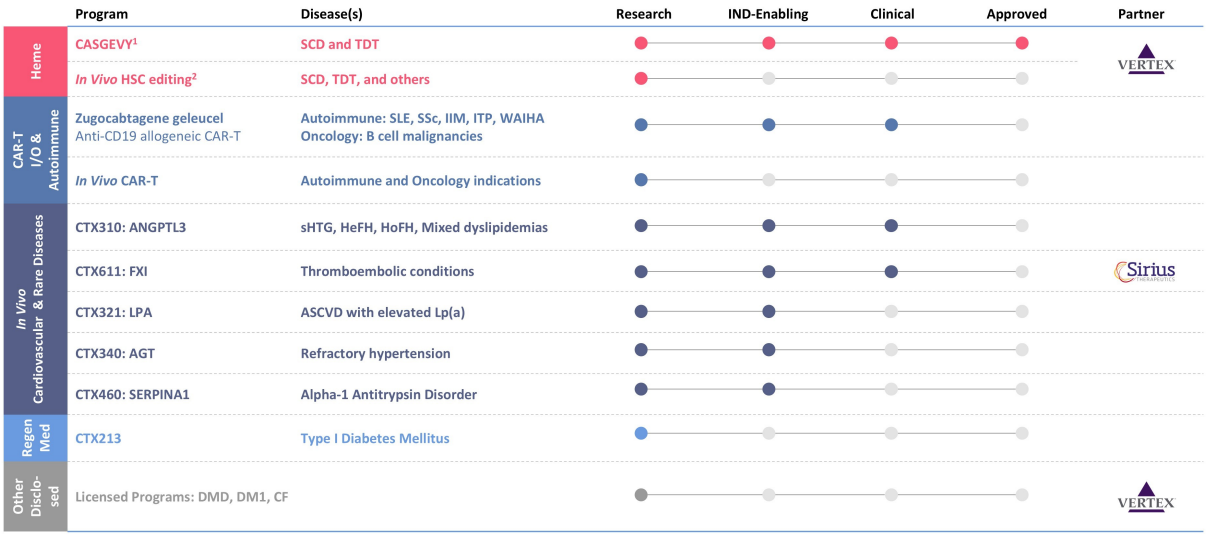
Next-generation Editing Modalities

While we have made significant progress with our current portfolio of programs, we recognize that we may be able to bring transformative therapies to even more patients by continuing to innovate to unlock the full potential of gene editing. We are focused on innovating next-generation editing modalities. For example, we have developed a proprietary, next-generation, site-specific gene correction platform called SyNTase editing. SyNTase editors represent a significant advance over currently described prime editing systems by combining compact Cas9 proteins with a novel class of engineered polymerases. Together, these components enable gene correction with greater efficiency and precision, while also supporting scalable manufacturing. Using AI-guided structural modeling and large-scale screening, the polymerase was optimized to support gene correction activity based on synthetic nucleotide templates. When integrated with optimized Cas9, SyNTase editors can utilize engineered templates with improved serum stability, enabling higher target correction efficiency. In addition, we are also developing technologies to enable whole gene correction and insertion via non-viral DNA delivery and all-RNA systems.

We believe that gene-based medicines will form the basis of an entirely new class of therapeutics with the potential to treat both common and rare diseases. To turn this promise into reality, we have built a broad and diversified pipeline of product candidates leveraging gene-based technologies, including CRISPR/Cas9 gene editing technology.

Our Pipeline

The following table summarizes the status of our product development pipeline:



SCD: Severe sickle cell disease; TDT: Transfusion-dependent β-thalassemia; HeFH: Heterozygous familial hypercholesterolemia; HoFH: Homozygous familial hypercholesterolemia; sHTG: Severe hypertriglyceridemia; SLE: Systemic lupus erythematosus; IIM: Idiopathic inflammatory myopathies; ITP: Immune Thrombocytopenic Purpura; WAIHA: Warm Autoimmune Hemolytic Anemia; DMD: Duchenne's muscular dystrophy; DM1: Myotonic dystrophy type I; CF: Cystic Fibrosis; SSc: Systemic sclerosis; RegenMed: Regenerative Medicine

1. Currently approved in some countries for certain eligible patients with SCD or TDT (40-60 cost / profit split); 2. Collaboration with Vertex for applications in SCD and TDT (50-50 cost / profit split)

Hemoglobinopathies

Hemoglobinopathies are a diverse group of inherited blood disorders that result from variations in the synthesis or structure of hemoglobin. Our lead program in hemoglobinopathies, CASGEVY, is the first-ever approved CRISPR-based gene-editing therapy in the world. It is the first therapy to emerge from our strategic partnership with Vertex and is being advanced under a joint development and commercialization agreement, with Vertex leading commercialization. CASGEVY has received approvals in the United States and multiple other countries worldwide for the treatment of eligible patients with SCD or TDT. SCD and TDT are caused by mutations in the gene encoding the beta globin protein. Beta globin is an essential component of hemoglobin, a protein in red blood cells that delivers oxygen and removes carbon dioxide throughout the body.

CASGEVY (exagamglogene autotemcel [exa-cel])

CASGEVY is a non-viral, *ex vivo* CRISPR/Cas9 gene-edited cell therapy, in which a patient's own hematopoietic stem and progenitor cells, or HSPCs, are edited at the erythroid specific enhancer region of the *BCL11A* gene through a precise double-strand break. This edit results in the production of high levels of fetal hemoglobin, or HbF; hemoglobin F, in red blood cells. HbF is the form of the oxygen-carrying hemoglobin that is naturally present during fetal development, which then switches to the adult form of hemoglobin after birth.

This HbF upregulation approach mimics a phenomenon observed in natural human genetics. In most patients with SCD or TDT, HbF disappears in infancy, at which point the symptoms of the disease begin to manifest. However, some patients have elevated levels of HbF that persist into adulthood, a condition known as hereditary persistence of fetal hemoglobin, or HPFH. These patients are often asymptomatic or experience much milder forms of disease because elevated HbF compensates for the defective adult hemoglobin. This protective HPFH condition has been shown to result from specific changes to these individuals' genomic DNA, including in regions associated with genetic regulatory elements that control the expression levels of the globin genes, such as BCL11A. We chose to pursue this HbF upregulation strategy—rather than directly correcting the mutated beta globin gene—given the efficiency and consistency of the editing approach involved, the ability of this approach to counteract a wide variety of different beta globin mutations, including patients with TDT, and the natural history data supporting absence of symptoms in patients with HPFH.

Patients treated with CASGEVY first undergo a treatment that mobilizes a population of HSPCs, from the bone marrow into the bloodstream. Blood cells are collected from the patient's bloodstream and transferred to a manufacturing facility where the HSPCs are sorted and CRISPR/Cas9 gene-editing is performed. Following manufacturing, the edited cells, now called CASGEVY, are transferred back to the clinical site. Patients are preconditioned with a treatment that ablates their bone marrow prior to infusion of CASGEVY.

We and Vertex continue to investigate CASGEVY, including in clinical trials designed to assess the safety and efficacy of a

single dose of CASGEVY in patients ages 12 to 35 with severe SCD and TDT, respectively, two pivotal trials in patients 5 to 11 years of age, one in severe SCD and a second in TDT, and long-term follow-up clinical trials designed to follow participants for up to 15 years after CASGEVY infusion. Overall, CASGEVY safety data presented to date is generally consistent with an autologous stem cell transplant and myeloablative conditioning. Efficacy data presented to date support the profile of CASGEVY as a potential one-time functional cure for people with severe SCD and TDT.

At the American Society of Hematology annual meeting, or ASH, in December 2025, positive data from the pivotal studies of CASGEVY in children ages 5 to 11 years old with SCD or TDT were presented. In children with SCD, 11 patients have been dosed with CASGEVY in the Phase 3 CLIMB-151 clinical study, and all (4/4) patients with sufficient follow-up (4/4) achieved the primary endpoint of being free from vaso-occlusive crises, or VOCs, for at least 12 consecutive months, or VF12. In children with TDT, 13 patients have been dosed with CASGEVY in the Phase 3 CLIMB-141 clinical study, and all patients with sufficient follow-up (6/6) achieved the primary endpoint of transfusion independence for at least 12 consecutive months while maintaining a weighted average hemoglobin of at least 9 g/dL (TI12). The safety profile of CASGEVY in younger patients is consistent with myeloablative conditioning and autologous transplant in both SCD and TDT, as established in clinical studies in older patients. Consistent with studies in older patients, children treated with CASGEVY have durable increases in HbF and stable allelic editing.

In addition, longer-term data for people with SCD and TDT ages 12 years and older treated with CASGEVY were also presented at ASH. These data, as of April 2025, continue to demonstrate the transformative, durable clinical benefits that CASGEVY provides to people living with SCD or TDT. In SCD, 100% of patients (45/45) achieved VF12 in either CLIMB-121 or the long-term follow-up study CLIMB-131, with a mean duration of VOC-free for 35.3 months (range 12.9–67.7 months). In TDT, 98.2% of patients (55/56) achieved TI12 in either CLIMB-111 or CLIMB-131 with a mean duration of transfusion independence of 41.4 months (range 13–72.3 months). The safety profile remained consistent with myeloablative conditioning and autologous transplant in both SCD and TDT.

To date, CASGEVY has been approved by regulatory authorities in the United States, European Union, Great Britain, Canada, Switzerland, Kingdom of Saudi Arabia, Kingdom of Bahrain, Qatar, the United Arab Emirates and Kuwait for the treatment of eligible patients 12 years and older with SCD or TDT. We estimate that in the United States, Canada, Europe and parts of the Middle East, the total addressable patient population with severe SCD or TDT is approximately 60,000 individuals.

Beta Thalassemia

Beta thalassemia is a blood disorder that is associated with a reduction in the production of hemoglobin. This disease is caused by mutations that give rise to the insufficient expression of the beta globin protein, which can lead to symptoms related not only to the lack of hemoglobin, but also to the buildup of unpaired alpha globin proteins in red blood cells. The severity of symptoms associated with beta thalassemia varies depending on the levels of functional beta globin present in the blood cells. The unpaired alpha globin chains are toxic to red blood cells and reduce red blood cell lifespan. In the most severe cases, described as beta thalassemia major, functional beta globin is either completely absent or reduced, resulting in severe anemia. In these patients, the bone marrow cannot keep pace with the destruction of red blood cells, and thus these patients require regular blood transfusions. While chronic blood transfusions can be effective at addressing symptoms, they often lead to iron overload, progressive heart and liver failure, and eventually early death. Patients with mild forms of beta thalassemia may experience some mild anemia or even be asymptomatic. The total worldwide incidence of beta thalassemia is estimated to be 60,000 births annually and there are over 200,000 people worldwide who are alive and registered as receiving treatment for the disease.

The most common treatment for beta thalassemia is chronic blood transfusions. Transfusion-dependent patients typically receive transfusions every two to four weeks and chronic administration of blood often leads to elevated levels of iron in the body, which can cause organ damage over a relatively short period of time. Patients often undergo phlebotomy or are given iron chelators, or medicines to reduce iron levels in the blood, which are associated with their own significant toxicities. In developing countries, where chronic transfusions are not available, most patients die in early childhood. Also, a disease-modifying therapy for beta thalassemia, Reblozyl (luspatercept-aamt), received FDA approval in 2019.

A potentially curative therapy for beta thalassemia is allogeneic hematopoietic stem cell transplant, or allo-HSCT, but few patients elect to have this procedure given its associated morbidity and mortality and the lack of matched and willing donors. Another option is Zynteglo (betibeglogene autotemcel), an *ex vivo* autologous lentiviral gene therapy developed by Genetix Biotherapeutics (formerly bluebird bio), which the FDA approved for the treatment of certain patients with TDT in August 2022.

Sickle Cell Disease

SCD is an inherited disorder of red blood cells resulting from a specific mutation in the beta globin gene that causes abnormal red blood cell function. Under conditions of low oxygen concentration, the abnormal hemoglobin proteins aggregate within the red blood cells causing them to become sickled in shape and inflexible. These sickled cells obstruct blood vessels, restricting blood flow to organs, ultimately resulting in severe pain, infections, stroke, overall poor quality of life and early death. Patients also experience increased hemolysis, leading to anemia. The worldwide incidence of SCD is estimated to be 300,000 births annually and there are 20-25 million people worldwide with the disease.

As with beta thalassemia, in regions where medical infrastructure can support it, standard treatment for patients with SCD who have high levels of hemolysis involves chronic blood transfusions, which has the same associated risks of iron overload and toxicities associated with chelation therapy. The FDA and/or EMA have approved several disease-modifying therapies for SCD as well, such as hydroxyurea. Prior to December 2023, the only curative option was Allo-HSCT which is often avoided given the significant risk of transplant-related morbidity and mortality in these patients and the lack of matched and willing donors. In December 2023, the FDA approved Lyfgenia (lovotibeglogene autotemcel), an *ex vivo* autologous lentiviral gene therapy developed by Genetix Biotherapeutics (formerly bluebird bio), which carries a boxed warning for hematologic malignancy.

Next-generation Efforts

Building upon CASGEVY, we and Vertex are pursuing next-generation efforts in targeted conditioning regimens, which could offer benefits over the myeloablative conditioning regimen currently used with CASGEVY. In addition, we and Vertex are pursuing *in vivo* editing of hematopoietic stem cells in SCD and TDT. Either of these efforts could broaden the number of patients that can benefit from our therapies.

In Vivo Approaches - Liver Editing

We have established a leading platform for *in vivo* gene editing and are rapidly advancing a broad portfolio of *in vivo* programs. *In vivo* gene editing, or delivery of a CRISPR/Cas9-based therapeutic directly to tissues within the human body, could enable the treatment of many common and rare diseases, including those difficult to address with *ex vivo* approaches.

Our lead *in vivo* programs target the liver and take advantage of clinically established and validated lipid nanoparticle, or LNP, delivery technologies. LNPs have several advantages that make them well-suited for delivering CRISPR/Cas9 *in vivo*, including efficient and safe delivery to the liver, large cargo size and transient cargo expression. Our first programs in the liver aim to treat diseases where we can produce a strong therapeutic effect by safely disrupting a gene with well-understood genetic association. For example, our most advanced clinical program, CTX310, aims to address cardiovascular disease by disrupting the validated target ANGPTL3.

Beyond the liver, for delivery to hematopoietic stem cells, T cells and other extrahepatic tissues, we are pursuing multiple delivery technologies, including LNPs. Through internal efforts and external collaborations, we are developing new delivery modalities to support future *in vivo* therapeutics.

Cardiovascular and Dyslipidemia Programs

Cardiovascular disease, or CVD, is the leading cause of death globally, accounting for close to one third of all deaths, or nearly 20.5 million people, in 2021. CVD includes heart failure, stroke, atherosclerotic cardiovascular disease, or ASCVD, aortic valve calcification and more. Dyslipidemias are a leading cause of CVD. Dyslipidemias are characterized by abnormally high levels of lipids, including cholesterol, lipoproteins and triglycerides, in the bloodstream. Three of the most common dyslipidemias are hypercholesterolemia, hypertriglyceridemia and elevated lipoprotein (a), or Lp(a). Today's chronic care treatment model of CVD involves daily medication, weekly injection, multiple infusions annually and/or surgical interventions. This model places a heavy burden on patients and the healthcare system. Adherence to lipid-lowering therapy remains a major challenge, and over 80% of people with very high cardiovascular risk do not reach low density lipoprotein, cholesterol, or LDL-C target goal.

We aim to transform the treatment paradigm for CVD by developing one-time *in vivo* editing therapies that can durably lower levels of atherogenic lipoproteins for a patient's lifetime. To do so, we aim to disrupt genes like ANGPTL3 that when dysfunctional or inhibited result in lower levels of key lipoproteins and improved cardiovascular outcomes based on studies of natural human genetics and other therapeutic modalities. By recapitulating this benefit, we believe that our therapies have the potential to minimize or eliminate the need for additional treatments and improve long-term cardiovascular outcomes for both patients with severe genetic dyslipidemias and much larger ASCVD patient populations.

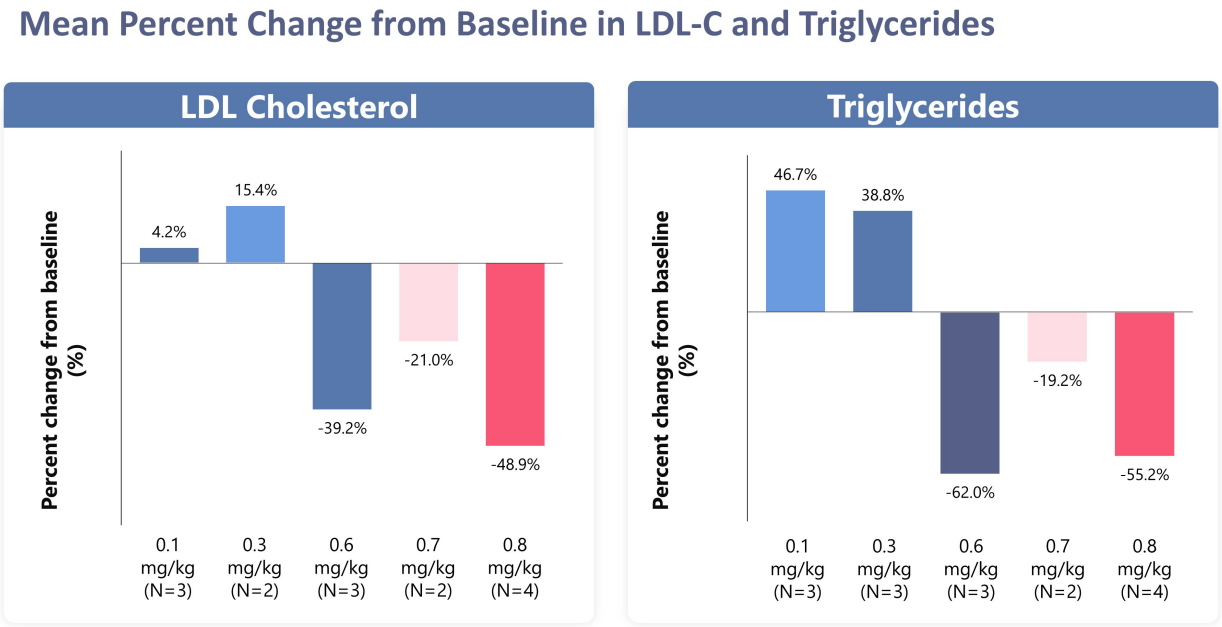
CTX310

Our most advanced *in vivo* product candidate, CTX310, targets the gene encoding angiopoietin-related protein 3, or ANGPTL3, for the treatment and prevention of CVD. ANGPTL3 plays an important role in lipid metabolism by inhibiting an enzyme called lipoprotein lipase, or LPL. LPL is the main enzyme that breaks down triglyceride-enriched lipoproteins like chylomicrons, very low density lipoprotein, or VLDL, and LDL. By preventing LPL from hydrolyzing these lipoproteins, ANGPTL3 activity increases the level of circulating triglycerides. Reducing ANGPTL3 expression by disrupting the ANGPTL3 gene increases LPL expression and thereby reduces triglyceride-rich lipoproteins, as well as LDL-C. This mechanism has been validated through natural history studies, as individuals with natural loss-of-function variants of ANGPTL3 have lower triglyceride levels, lower LDL-C levels, and a lower risk of coronary artery disease. CTX310, which consists of messenger RNA encoding Cas9 and a gRNA targeting ANGPTL3 delivered via LNP, aims to recapitulate this effect by disrupting the ANGPTL3 gene. CTX310 has been shown to decrease ANGPTL3 protein levels by nearly 90% in non-human primates, or NHPs, leading to a greater than 50% reduction in serum triglycerides. CTX310 is currently

being investigated in an ongoing Phase 1b clinical trial in patients with heterozygous familial hypercholesterolemia, homozygous familial hypercholesterolemia, mixed dyslipidemias, or severe hypertriglyceridemia.

In November 2025, we presented positive Phase 1 data from our ongoing clinical trial evaluating CTX310 during a late-breaking session at the American Heart Association Scientific Sessions and published simultaneously in The New England Journal of Medicine in a peer-reviewed article entitled "*Phase 1 Trial of CRISPR-Cas9 Gene Editing Targeting ANGPTL3.*" A single-course treatment with CTX310 produced dose-dependent, durable reductions in circulating ANGPTL3 with a mean reduction from baseline of -73% (maximum -89%), a mean reduction in triglycerides, or TG, of -55% (maximum -84%) and a mean reduction of low-density lipoprotein, or LDL, of -49% (maximum -87%) at the highest dose. The Phase 1, open label, dose-escalation trial evaluated single-course intravenous doses of CTX310 ranging from 0.1 to 0.8 mg/kg (lean body weight) targeting ANGPTL3 in four patient groups: homozygous familial hypercholesterolemia, severe hypertriglyceridemia, or sHTG, heterozygous familial hypercholesterolemia, or mixed dyslipidemias (elevated TG and LDL). Eligible participants had uncontrolled TG levels >150 mg/dL and/or LDL cholesterol >100 mg/dL (or >70 mg/dL for those with established atherosclerotic cardiovascular disease) despite background standard of care per local guidelines. The majority of participants were receiving statins and/or ezetimibe, while 40% were taking PCSK9 inhibitors. The trial was designed to evaluate safety and tolerability as primary endpoints, with changes in circulating ANGPTL3 protein, TG, and LDL as secondary endpoints. Single-course ascending doses of CTX310 were administered to 15 participants across sequential cohorts, and all participants completed at least 28 days of follow-up as of the data cutoff. CTX310 was generally well tolerated, and no dose-limiting toxicities or serious adverse events related to treatment. Adverse events were generally mild to moderate. One participant experienced an allergic reaction that resolved the following day with supportive care. Infusion-related reactions occurred in three participants (two at 0.6 mg/kg and one at 0.8 mg/kg dose), all Grade 2. All events resolved, and all participants completed their infusions. One participant with elevated transaminases level at baseline had a Grade 2 elevation of transaminases that peaked by Day 4 and resolved completely by Day 14 without any rise in bilirubin. Overall, CTX310 demonstrated a well-tolerated safety and tolerability profile that supports continued advancement of the program.

CTX310 Phase 1a Demonstrated Clinically Meaningful Reductions in LDL-C and Triglycerides



Mean percent change from baseline are reported at 90 days following 0.1, 0.3, 0.6 mg/kg CTX310 doses and at 60 days following 0.7 and 0.8 mg/kg CTX310 doses.

Based on the positive Phase 1 results we have advanced CTX310 into Phase 1b clinical trials, prioritizing development in severe hypertriglyceridemia and refractory hypercholesterolemia.

Severe Hypertriglyceridemia (sHTG)

Hypertriglyceridemia is clinically defined as having triglyceride levels above l50 mg/dL. The most severe patients can have levels exceeding 2000 mg/dl. Hypertriglyceridemia is associated with CVD and acute pancreatitis. Like LDL-C, triglyceride levels can be affected by diet and lifestyle choices and treated with common therapies. However, over three million adults in the United

States still have severe hypertriglyceridemia, or sHTG. Known genetic conditions can cause sHTG, including familial chylomicronemia syndrome, or FCS, and multifactorial chylomicronemia syndrome, or MCS. There are parallels between FCS/MCS and homozygous familial hypercholesterolemia / heterozygous familial hypercholesterolemia, or HoFH/HeFH. FCS is the only true monogenic form of hypertriglyceridemia and is associated with extreme levels of triglycerides exceeding 885 mg/dL. The prevalence of FCS is 1 in 200,000 to 300,000 individuals in the United States and EU. MCS is polygenic in nature, meaning that the genetic underpinnings causing the disease to vary among individuals, and is clinically defined as having triglyceride levels between 150 and 885 mg/dL. MCS has a prevalence of 1 in 250 to 600 individuals.

Refractory Hypercholesterolemia

Hypercholesterolemia is defined by levels of LDL-C above 130 mg/dL and is associated with increased risk of heart disease and stroke. In hypercholesterolemia, high levels of LDL-C accumulate in blood vessels, leading to atherosclerosis. Treatment aims to reduce LDL-C levels to below 100 mg/dL with 70 mg/dL as the ultimate goal, but some patients cannot achieve this level of reduction through existing means. Patients with LDL-C levels above 200 mg/dL are considered to have familial hypercholesterolemia, or FH. Patients with FH have one or more genetic mutations that contribute to the disease in addition to diet and lifestyle. Patients with FH cannot metabolize LDL-C effectively, leading to high levels of circulating LDL-C, in some cases exceeding 1000 mg/dL. FH can be subcategorized by mutation status into HeFH, and HoFH. HoFH patients have the most severe phenotype, with LDL-C levels usually exceeding 400 mg/dL. HoFH patients often suffer from CVD early in life and have an average life expectancy of 33 years if untreated. HoFH has a prevalence of 1 in 200,000 to 1,000,000 adults. Refractory hypercholesterolemia is a condition defined by persistently high LDL-C levels despite maximum tolerated lipid-lowering therapies, including patients with and without FH.

Additional In Vivo Programs

In addition to CTX310, we have a number of earlier stage investigational *in vivo* programs, including: CTX340, CTX460 and CTX321. CTX340 is currently in Investigational New Drug application enabling, or IND-enabling, studies and is directed towards angiotensinogen for the treatment of refractory hypertension. CTX460 is the first investigational candidate to emerge utilizing our SyNTase editing platform and is directed towards SERPINA1 for the treatment of alpha-1 antitrypsin deficiency. CTX460 is currently in preclinical studies. Building on insights from CTX320, our next-generation product candidate, CTX321, is directed towards *LPA*, the gene encoding apolipoprotein(a), a major component of Lp(a). Like CTX320, CTX321 consists of a gRNA targeting *LPA* and messenger RNA encoding Cas9 delivered via LNP. CTX321 incorporates an updated guide RNA that demonstrates approximately two-fold greater potency in preclinical testing while utilizing the same LNP delivery system. CTX321 is currently in IND-enabling studies in patients with elevated Lp(a), which has shown to have an independent association with major adverse cardiovascular events.

Elevated Lp(a)

Lp(a) is a lipoprotein consisting of an LDL-like particle covalently bound to a protein called apolipoprotein(a), or apo(a). Lp(a) transports cholesterol in the blood and is highly atherogenic. It can infiltrate and bind to components of the extracellular matrix in the inner layers of the aortic valve and other areas of the circulatory system, resulting in increases in inflammation and fatty deposits that over time lead to a weakened aortic valve and other serious symptoms contributing to CVD. Lp(a) is its own independent risk factor for CVD. High concentrations of Lp(a), as well as genetic variants associated with high Lp(a) concentrations, are both associated with CVD. Elevated levels of Lp(a) above 50 mg/dL are directly associated with aortic valve calcification disease, or AVCD. Up to 20% of adults in the United States have Lp(a) levels above 50 mg/dL and over 1 million adults in the United States have AVCD. Additionally, 30% of patients with familial hypercholesterolemia have elevated Lp(a) levels. To date, there are no Lp(a) lowering therapies approved by the FDA.

Refractory hypertension

Hypertension is the leading cause of cardiovascular morbidity and mortality worldwide and adherence is a major limitation. Refractory hypertension is a phenotype of antihypertensive treatment failure, distinct from resistant hypertension and clinically-defined as uncontrolled blood pressure, typically >140/90 mmHg, despite treatment with five or more antihypertensive agents of different classes. To date, there are no FDA approved therapies specifically for refractory hypertension, though several therapies are indicated for resistant hypertension.

Alpha-1 Antitrypsin Disorder

Alpha-1 antitrypsin deficiency, or AATD, is a hereditary genetic disorder caused by mutations in the SERPINA1 gene, which encodes the protein alpha-1 antitrypsin, or AAT. AAT is a protease inhibitor synthesized primarily in the liver that protects the lungs from proteolytic enzymes, specifically neutrophil elastase. AATD mechanism of disease is characterized by a loss-of-function in the lungs and a toxic gain-of-function in the liver. In the lungs, insufficient levels of functional AAT lead to unchecked neutrophil elastase activity, causing the destruction of alveolar tissue and resulting in early-onset emphysema and chronic obstructive pulmonary disease, or COPD. In the liver, the most common disease-causing variant, the Z allele, causes the misfolded AAT protein to polymerize and accumulate within hepatocytes. This intracellular accumulation triggers an inflammatory cascade and cell death, leading to fibrosis, cirrhosis, and an increased risk of hepatocellular carcinoma, or HCC. AATD is the most common genetic cause of liver disease in

children and a significant genetic risk factor for COPD in adults. It is estimated that approximately 100,000 individuals in the United States are living with AATD, yet fewer than 10% of these individuals have been clinically diagnosed. While intravenous augmentation therapies are FDA-approved to slow the progression of lung emphysema by restoring plasma AAT levels, there are currently no approved pharmacotherapies to treat AATD-associated liver disease.

In Vivo Approaches - siRNA-based Programs

Our siRNA-based portfolio includes clinical-stage programs in cardiovascular and thromboembolic diseases, developed in collaboration with Sirius. CTX611 is a novel double-stranded siRNA designed to target the human coagulation factor XI, or FXI, messenger RNA and inhibit FXI protein expression. Through modulation of the intrinsic coagulation pathway, CTX611 is intended to provide anticoagulant and antithrombotic effects. By targeting FXI, CTX611 aims to reduce thrombotic events while minimizing the risk of bleeding, representing a differentiated approach compared to Factor Xa inhibitors. In addition, CTX611 may offer the potential for reversibility not observed with other anti-Factor XI modalities. The addressable population for CTX611 is a range of thromboembolic and clotting-related indications, including atrial fibrillation (AF), venous thromboembolism, or VTE, ischemic stroke, cancer-associated thrombosis, chronic kidney disease, peripheral vascular disease, chronic coronary artery disease.

Two Phase 1 clinical trials of CTX611 have been completed by Sirius, and single doses of CTX611 have been well tolerated. CTX611 demonstrated robust pharmacodynamic effects, including reductions of over 93% in FXI levels and FXI activity, along with more than a twofold increase in activated partial thromboplastin time relative to baseline. These effects were sustained, with responses maintained for up to six months post-dosing.

Supported by clinical experience to date, CTX611 is being developed as a long-acting FXI inhibitor with the potential to support infrequent, including semi-annual, subcutaneous administration. CTX611 is being investigated in an ongoing Phase 2 clinical trial in evaluating the safety and efficacy of the candidate in preventing VTE in patients undergoing total knee arthroplasty.

Thromboembolic and clotting-related indications

Thromboembolic conditions arise from dysregulation of the coagulation cascade, a series of enzymatic reactions that give rise to a fibrin clot. Historic anticoagulation therapies target enzymes, such as Factor Xa and Thrombin, which are essential for hemostasis. While these therapies are effective at preventing clotting complications, they come with inherent bleeding risk. More recent therapeutic strategies aim to target enzymes, such as Factor XI, that are critical for thrombosis, but largely redundant for hemostasis. These approaches aim to decouple hemostasis from thrombosis and, consequently, widen the therapeutic window for silencing approaches toward thromboembolisms.

Venous Thromboembolism, or VTE, describes the formation of blood clots in venous circulation, giving rise to two disparate indications: deep vein thrombosis, or DVT, and pulmonary embolism, or PE. DVT occurs when a thrombus forms in the deep veins, typically of the legs, pelvis, or arms, obstructing venous return and causing local pain and swelling. PE occurs when a portion of this thrombus embolizes and travels to the lungs, blocking pulmonary arteries and impairing oxygenation. VTE represents a massive public health burden, as the Centers for Disease Control and Prevention, or CDC, estimates that up to 900,000 individuals are affected by VTE in the United States annually, resulting in 60,000 to 100,000 deaths. The current standard of care consists of anticoagulation with agents such as Low Molecular Weight Heparin, vitamin K antagonists (e.g., warfarin), or Direct Oral Anticoagulants. While effective, these therapies indiscriminately inhibit the coagulation cascade, creating a dose-limiting risk of major bleeding.

CAR T

We believe CRISPR/Cas9 has the potential to create the next generation of CAR T cell therapies that may have a superior product profile and allow broader patient access compared to current autologous therapies. We are advancing cell therapy programs for autoimmune indications and oncology.

We expect that the cellular engineering strategies that are ultimately successful will involve multiple genetic modifications, an application for which we believe CRISPR/Cas9 will play a central role. While other gene editing platforms could potentially be used for these purposes, CRISPR/Cas9 is particularly well-suited for multiplexed editing, which is the modification and/or insertion of multiple genes within a single cell. Gene editing techniques that require different protein enzymes for each genetic modification may be limited in the number of edits they can make concurrently due to efficiency, cytotoxicity and/or manufacturing challenges. In contrast, CRISPR/Cas9 has the potential to efficiently make multiple edits using a single Cas9 protein and multiple small gRNA molecules.

We are using the multiplexing ability of CRISPR/Cas9 both to enable allogeneic administration and to introduce additional genetic edits that aim to improve the efficacy profile of these product candidates. Furthermore, we are leveraging our CRISPR platform to enable a process of continuous innovation in which we incorporate incremental edits into next-generation products to try to increase treatment benefit further. We continue to expand our multiplexing capabilities to help us realize the full potential of engineered cell therapy in immuno-oncology across all tumor types, including solid tumors.

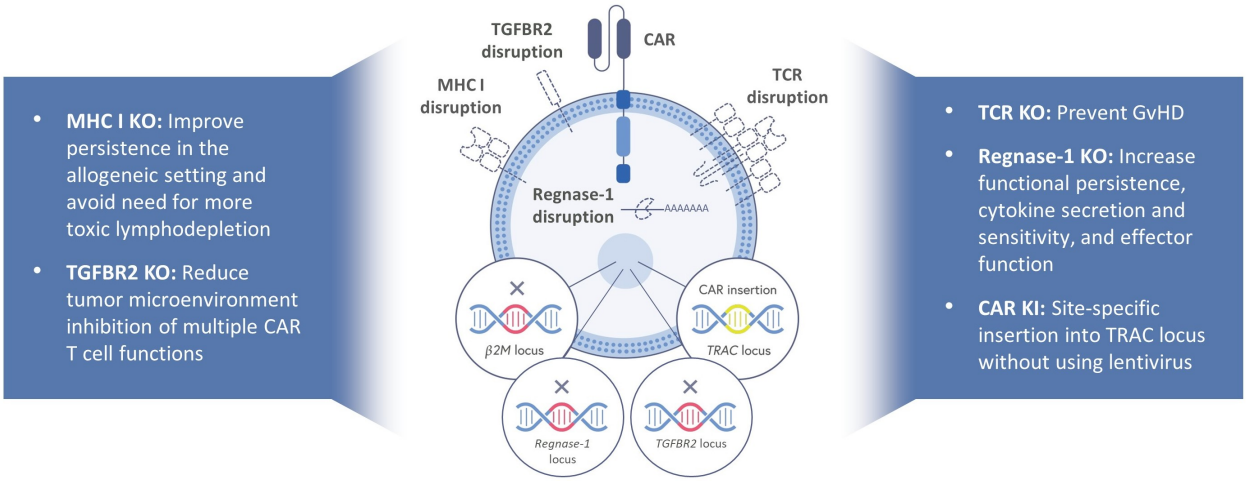
We are advancing cell therapy programs for autoimmune indications and oncology, including a next-generation, investigational, gene-edited, healthy donor-derived allogeneic CAR T product candidate, zugocabtagene geleucel (zugo-cel; formerly CTX112), in clinical trials. Zugo-cel targets CD19 and builds upon our first-generation programs, which provided important proof of concept that allogeneic CAR T cells can produce durable remissions following a standard lymphodepletion regimen and demonstrated a well-tolerated safety profile. Our CRISPR/Cas9 platform has enabled us to incorporate additional edits into our next-generation product candidates, and reflect our mission of innovating continuously to bring potentially transformative medicines to patients as quickly as possible.

Zugo-cel incorporates two novel gene edits. These edits—knock-out of Regnase-1 and knock-out of transforming growth factor-beta receptor type 2, or TGFBR2—are designed to enhance CAR T potency and reduce CAR T exhaustion. Editing Regnase-1 removes an intrinsic "brake" on T cell function while editing TGFBR2 removes a key extrinsic "brake" on T cell anti-tumor activity. We identified this combination of edits through systematic screening of dozens of new and previously described genes.

In total, to generate zugo-cel we make five modifications to T cells taken from healthy donors using our gene editing technology:

1. Elimination of the T-cell receptor, or TCR, to reduce the risk of Graft versus Host Disease, or GvHD.
2. Site-specific insertion of a CD19-directed CAR into the TRAC locus.
3. Removal of the class I major histocompatibility complex, MHC I, from the cell surface to improve the persistence of the CAR T cells in an "off-the-shelf" setting.
4. Disruption of Regnase-1 to increase functional persistence, cytokine secretion and sensitivity, and effector function.
5. Disruption of TGFBR2 to reduce tumor microenvironment inhibition of multiple CAR T cell functions.

Our Next-Generation CRISPR Gene-edited Allogeneic CAR T Chassis



We believe this approach will have advantages over other allogeneic CAR T products in development that semi-randomly insert the CAR using an integrating virus and do not include edits to increase potency. Emerging clinical data from the ongoing clinical trial and pharmacology data, including pharmacokinetics, indicate that the novel potency gene edits in zugo-cel lead to significantly higher CAR T cell expansion and functional persistence in patients compared to first-generation candidates. In addition, zugo-cel exhibits increased manufacturing robustness, with a higher and more consistent number of CAR T cells produced per batch. We are producing zugo-cel for clinical trials at our internal GMP manufacturing facility in Framingham, Massachusetts.

Autoimmune disease

Autoimmune diseases can result from an immune response against the body's own cells, tissues, or organs, also known as autoreactivity. Within autoimmune disease, there is a spectrum of autoreactivity that can manifest in a diverse array of symptoms. One form of autoreactivity is the presence of autoantibodies, which are a product of autoreactive, pathogenic B cells. Targeting these pathogenic B cells has been shown to ameliorate the symptoms of B-cell mediated autoimmune diseases. Several therapies have been approved for B-cell mediated autoimmune diseases, such as rituximab in rheumatoid arthritis; however, such therapies require chronic administration and largely do not achieve complete remission of disease.

Multiple groups have begun to demonstrate the utility of CAR T therapy for the treatment of various B-cell mediated autoimmune diseases, including systemic lupus erythematosus, or SLE, progressive systemic sclerosis and idiopathic immune myositis. Specifically, treatment with CD19-directed autologous CAR T cells after lymphodepletion has produced durable remissions in early clinical studies. Subsequently, several cell therapy approaches are being developed to treat B-cell mediated diseases.

Allogeneic CAR T therapy has the potential to provide meaningful clinical benefit with several potential advantages, including increased scalability, dramatically decreased cost of goods, reduced risk of toxicities and an improved patient experience with no need for apheresis. Removing the requirement for apheresis allows patients to continue to use concurrent medications instead of withdrawing them during the autologous CAR T cell manufacturing process, reducing the risk of disease-related flares. Autoimmune disease could represent a large additional opportunity for our allogeneic CAR T cell therapy platform across multiple indications, including SLE, progressive systemic sclerosis, idiopathic immune myositis, immune thrombocytopenia purpura, and warm autoimmune hemolytic anemia.

Systemic lupus erythematosus

Systemic lupus erythematosus, or SLE, is a chronic autoimmune disease characterized by the production of autoantibodies, particularly against nuclear components, which causes widespread deposition of immune complexes and tissue damage across multiple organ systems. SLE clinical presentation is variable, but can range from mild mucocutaneous symptoms to life-threating organ involvement. According to the CDC, conservative estimates suggest SLE affects approximately 200,000 individuals in the United States. Treatment strategies are stratified by disease severity, with antimalarials serving as the cornerstone of therapy to prevent flares. During active disease, corticosteroids and broad immunosuppressants e.g., methotrexate, mycophenolate mofetil are used to induce remission. Recent years have seen the FDA approval of targeted biologics, including belimumab, and anifrolumab a type I interferon receptor antagonist, as well as voclosporin specifically for lupus nephritis. However, many patients remain refractory to current treatments or suffer from significant steroid-induced toxicity.

Systemic Sclerosis

Systemic sclerosis, or SSC, is a chronic, multi-system autoimmune disease characterized by autoimmunity, vasculopathy, and fibrosis. Initiating endothelial cell injury, production of autoantibodies and activation of fibroblasts leads to production of excessive collagen and extracellular matrix proteins that drive thickening and hardening of skin and connective tissue. Beyond the skin, SSc can affect the lungs, kidneys, heart, and gastrointestinal tract. The prevalence of SSc varies, but is estimated to be approximately 17 per 100,000 individuals. The treatment landscape has evolved to target specific organ manifestations. For SSc-associated interstitial lung disease, Sc-ILD, the FDA has approved nintedanib, a tyrosine kinase inhibitor with antifibrotic activity, and tocilizumab, an IL-6 receptor antagonist. Standard management also includes broad immunosuppression with agents such as mycophenolate mofetil or cyclophosphamide. Despite these advances, significant unmet need remains for therapies that can halt or reverse the underlying fibrotic and vascular progression of the disease.

Idiopathic Inflammatory Myopathies

Idiopathic Inflammatory Myopathies, or IIM, otherwise known as myositis, are a group of systemic autoimmune disorders characterized by chronic muscle inflammation, progressive muscle weakness, and complicating extra-muscle manifestations. The pathophysiology of IIMs is immunologically complex, but, in part, is driven by autoantibody production. The annual incidence of IIM is estimated at approximately 1 to 20 cases per 1,000,000 individuals, with a prevalence of roughly 2 to 34 per 100,000. Treatment strategies rely heavily on broad immunosuppression, including high-dose corticosteroids often combined with steroid-sparing agents such as methotrexate or azathioprine. IVIG is FDA-approved for the treatment of dermatomyositis. For refractory cases, B-cell depleting agents, rituximab, or Janus Kinase inhibitors are increasingly utilized. However, a significant proportion of patients experience chronic disability, interstitial lung disease, and treatment-related toxicity.

Immune thrombocytopenia purpura

Immune thrombocytopenia purpura, or ITP, is an acquired autoimmune disorder characterized by isolated low platelet count (<100,000/μL) in the absence of other causes. The primary mechanism of disease includes production of autoantibodies that target glycoproteins on the surface of platelets, resulting in destruction by the immune system. Concurrently, these autoantibodies impair the ability of de novo platelet generation in the bone marrow. ITP manifests clinically as increased risk for bleeding, which can be life-threatening in cases of events such as intracranial hemorrhage, and significant fatigue. ITP occurs in approximately 31,000 patients in the U.S; the current therapeutic landscape include corticosteroids, intravenous immunoglobulin, or IVIG, and therapies that aim to increase platelet production or address autoantibody production e.g., B-cell depletion; however, a subset of these patients remain refractory.

Autoimmune hemolytic anemia (wAIHA)

Warm autoimmune hemolytic anemia (wAIHA) is a rare, life-threatening autoimmune disorder characterized by the production of polyclonal IgG autoantibodies that bind to antigens on the surface of red blood cells at physiological body temperatures, leading to recognition by macrophages and premature destruction. This accelerated destruction outpaces the bone marrow's compensatory

production of new red blood cells, resulting in severe anemia. wAIHA presents with symptoms of profound fatigue, dyspnea, jaundice, and dark urine, and carries a substantial risk of life-threatening thrombotic events. The annual incidence of wAIHA in the United States is estimated at approximately 1 to 6 cases per 100,000 individuals, with a prevalence of approximately 1 in 8,000 to 12,000 individuals. Currently, there are no FDA-approved pharmacotherapies specifically indicated for the treatment of wAIHA, but standard of care relies on broad immunosuppression, beginning with stabilization using high-dose corticosteroids and progressing to off-label use of B-cell depleting therapies for patients aiming to taper or who are refractory to high-dose steroids.

Immuno-oncology

Interest in the oncology community has grown rapidly in the field of immuno-oncology, or treatments that harness the immune system to attack cancer cells. Engineered immune cell therapy is one such approach, in which immune system cells such as T cells are genetically modified to enable them to recognize and attack cancerous cells.

Engineered cell therapy has demonstrated encouraging results leading to multiple approvals for autologous, or patient-derived, CAR T products in indications such as diffuse large B-cell lymphoma, multiple myeloma, and follicular lymphoma. These cell therapies require unique products to be created for each patient treated, an approach that has in the past proven challenging and cost prohibitive in the field of oncology. This bespoke manufacturing process takes time during which a patient's disease can progress and sometimes fails to produce a viable product at all. In contrast, allogeneic, or donor-derived, engineered T-cell therapies can be manufactured ahead of time and administered "off-the-shelf," enabling immediate availability, improved access and efficiency, simpler logistics, greater consistency, and re-dosing.

Large B-cell Lymphoma

Large B-Cell Lymphoma, or LBCL, represents a heterogeneous group of aggressive non-Hodgkin lymphomas resulting from the malignant transformation and rapid clonal proliferation of mature B-lymphocytes. While LBCL encompasses several subtypes, Diffuse Large B-Cell Lymphoma, or DLBCL, is the dominant clinical entity, accounting for approximately 80% of LBCL cases and 30-40% of all non-Hodgkin lymphomas globally. Pathologically, LBCL is characterized by the disruption of normal B-cell differentiation within the germinal center of lymph nodes, leading to the accumulation of large, rapidly dividing cells that express B-cell surface antigens such as CD19 and CD20. DLBCL is the most common lymphoid malignancy in adults, with an estimated ~18,000 new cases diagnosed annually in the United States. The standard of care for frontline treatment is the chemoimmunotherapy regimen R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), with which approximately 60-70% of patients achieve CR. However, some patients will have disease that is refractory to initial therapy or relapses after remission, or R/R LBCL. For these patients, the prognosis has historically been poor. While the recent approval of CD19-directed CAR-T cell therapies (e.g., axicabtagene ciloleucel, lisocabtagene maraleucel) and bispecific antibodies (e.g., epcoritamab, glofitamab) has transformed the treatment landscape, these modalities are associated with significant toxicities, such as cytokine release syndrome, or CRS, and neurologic events, or ICANS, and complex manufacturing logistics.

Zugocabtagene geleucel

Autoimmune disease

The autologous CAR T cells used successfully in autoimmune diseases to date appear to cause a B cell "reset" following deep B cell depletion whereby reconstituted B cells do not express high levels of autoantibodies. We believe that zugo-cel has the potential to produce a similar B cell "reset".

Zugo-cel is being investigated in two ongoing clinical trials: a Phase 1 basket trial in autoimmune rheumatologic diseases, including systemic lupus erythematosus, or SLE, systemic sclerosis, or SSc, and inflammatory myositis and a second clinical trial in immune thrombocytopenia purpura and warm autoimmune hemolytic anemia. Zugo-cel has been granted RMAT designation by the FDA for the treatment of relapsed or refractory follicular lymphoma and marginal zone lymphoma.

Preliminary clinical data from the Phase 1 study in autoimmune rheumatologic diseases released in December 2025 and updated in January 2026 has been encouraging, and zugo-cel has been well tolerated to date. As of the original data cut-off on December 17, 2025, four patients (2 SLE and 2 immune-mediated necrotizing myopathy with interstitial lung disease) have been treated at a dose of 100 million cells and followed for at least 28 days post-infusion:

- Zugo-cel cell expansion is comparable to that observed at the same dose in patients in the ongoing B-cell lymphomas trial.
- Rapid and deep B-cell depletion in the periphery was observed within the first 1-2 days and maintained over the first month of treatment, with repopulating B-cells demonstrating a shift toward an unswitched, naïve repertoire.
- All patients demonstrated significant clinical improvement at the Day 28 assessment.
- The first patient with SLE, refractory to 9 prior therapies with a baseline Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score of 8, has maintained drug-free DORIS clinical remission through Month 6 following CAR T therapy.

- Treatment has been well-tolerated, with no high-grade CRS or ICANS observed.

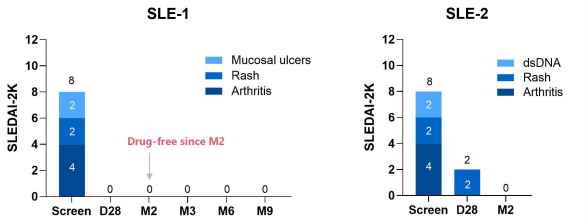
Updated data released in January 2026 indicate the first patient with SLE, refractory to 9 prior therapies with a baseline Systemic Lupus Erythematosus Disease Activity Index 2000, or SLEDAI-2K, score of 8, has maintained drug-free DORIS clinical remission through month 9 following CAR T therapy. Additionally, the second SLE patient with a baseline SLEDAI-2K score of 8, has sustained B cell depletion with SLEDAI-2K score of 0 through month 2 following CAR T therapy.

Summary of Zugo-cel Clinical Efficacy in SLE (N=2)

2 SLE patients in remission; First SLE patient in drug-free remission maintained at Month 9

Baseline Characteristics	SLE-1	SLE-2
Dose	DL1 (100M cells)	DL1 (100M cells)
Age/Sex	33 yo F	30 yo F
Disease Duration (years)	10	11
Organ Involvement	Skin, mucosal ulcers, joints, pleurisy	Skin, alopecia, joints, pleurisy, Raynaud's
Autoantibodies	ANA	ANA, dsDNA
SLEDAI-2K	8 (rash, oral ulcers, arthritis)	8 (rash, arthritis, dsDNA)
# Prior Therapies	8	10
Most Recent Regimen	HCQ, MTX	HCQ, MMF
Corticosteroid Dose	As needed for flares	As needed for flares

Clinical Efficacy Results



Safety: No CRS, ICANS, or serious infections

Immuno-oncology

We are investigating zugo-cel in an ongoing clinical trial designed to assess the safety and efficacy of zugo-cel in adult patients with relapsed or refractory CD19-positive B-cell malignancies who have received at least two prior lines of therapy. In this trial, we use a standard lymphodepletion regimen consisting of cyclophosphamide (500 mg/m^2) and fludarabine (30 mg/m^2) for three days.

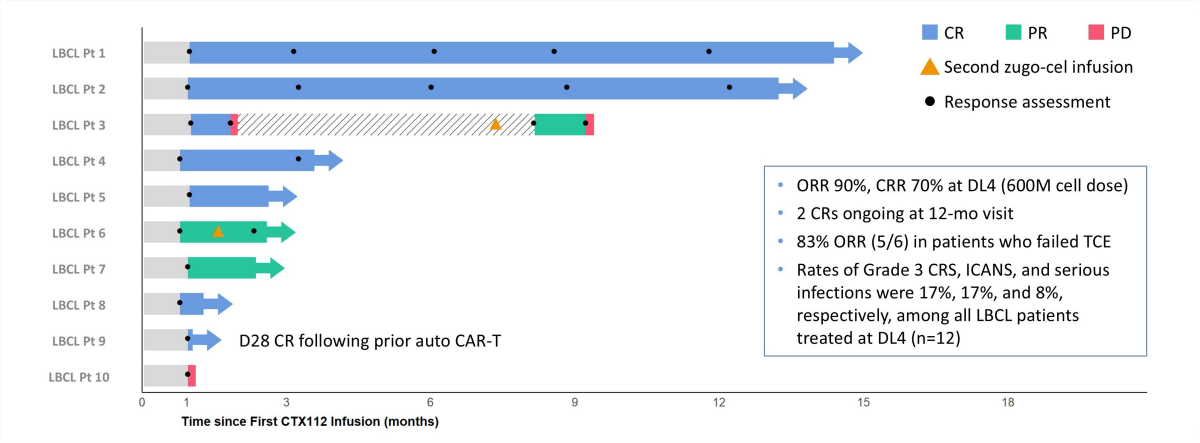
As of December 2025, a total of 39 patients have been treated across all 4 dose levels. The recommended Phase 2 dose, or RP2D, was recently endorsed at the 600 million cell dose for the LBCL cohort. As of the data cut-off of November 20, 2025, 10 patients with R/R LBCL have been treated at the RP2D of 600 million cell dose and have had at least one month of follow-up, with the following observations:

- An overall response rate of 90% (9/10) and a complete response rate of 70% (7/10) were observed, including a complete response, or CR, in a patient who relapsed following autologous CAR T cell therapy.
- Among patients who have completed 12-months of follow-up, 67% (2/3) remained in CR at the 12-month evaluation.
- Peak mean CAR T cell expansion of approximately 1,700 cells/µL was observed at the RP2D, representing approximately a four-fold higher expansion compared with patients receiving 300 million cells.
- Rates of Grade 3 CRS, ICANS and serious infections were 17%, 17%, and 8%, respectively, among all LBCL patients treated at the RP2D (n=12).
- No Grade 3 ICANS or CRS has been observed at the 100 million cell dose, which is the dose currently being studied in the autoimmune basket trials.

As described below, positive clinical data generated through December 2025 support the advancement of zugo-cel into the Phase 2 portion of the ongoing Phase 1/2 clinical trial. Eligible disease subtypes include large B-cell lymphoma, or LBCL, follicular lymphoma grade 1-3a, marginal zone lymphoma, and mantle cell lymphoma.

Interim Zugo-cel Phase 1 Data Suggests Durability in LBCL at RP2D

(N=10 with D28 response assessment[1])



RP2D: Recommended Phase 2 Dose; TCE: T-cell engagers
1. 006-233-015 (DL4, LBCL) passed away before D28; subject with PTLD (DL4) excluded from analysis; Data cutoff Nov 20, 2025

Additional candidates

Our CRISPR/Cas9 platform enables us to innovate continuously by incorporating incremental edits into next-generation products. We are advancing several additional investigational CAR T programs. In addition, we are developing both transient and integrated *in vivo* CAR T therapies by targeting T cells with LNPs and leveraging our delivery, mRNA, and gene editing expertise.

Regenerative Medicine

We continue to advance our regenerative medicine portfolio, including in diabetes. We believe our gene editing capabilities have the potential to enable a beta-cell replacement product candidate that may deliver durable benefit to patients without the need for long-term immunosuppression.

Clinical data with allogeneic islet transplants indicate that beta-cell replacement approaches may offer benefit to patients with insulin-requiring diabetes. However, this approach requires collecting islets from cadavers, which is not a scalable process. In addition, because a patient's immune system will identify these cadaveric cells as foreign, patients require long-term immunosuppression to avoid rejection. The first challenge can be solved by using beta cells derived from stem cells. Multiple groups have advanced stem cell-derived beta-cell replacement product candidates into clinical studies, but these product candidates still require chronic immunosuppression.

Our gene editing technology offers the potential to protect the transplanted cells from the patient's immune system by *ex vivo* editing of immuno-modulatory genes within the stem cell line used to produce the pancreatic-lineage cells. We believe that the speed, specificity and multiplexing efficiency of CRISPR/Cas9 make our technology well suited to this task. Furthermore, our CRISPR platform enables a process of continuous innovation, with additional edits incorporated into next-generation product candidates with the aim of increasing treatment benefit further.

We are advancing CTX213, a deviceless beta cell replacement product candidate consisting of unencapsulated precursor islet cells derived from induced pluripotent stem cells for the treatment of T1D. CTX213 utilizes six gene edits designed to promote immune evasion and cell fitness: knock-out of B2M and TXNIP and knock-in of PD-L1, HLA-E, MANF and A20. CTX213 benefits from work on a precursor product candidate, CTX211, where a Phase 1 trial observed sustained c-peptide production 12 months post implantation and histology-confirmed survival of transplanted insulin producing islet cells, despite the fibrosis of the encapsulation device and infiltration of immune cells. Preclinical studies have shown direct administration of CTX213 leads to improved glycemic control and C-peptide production in a diabetic rat model.

In addition, in March 2023, we entered into a non-exclusive license agreement with Vertex for Vertex to utilize certain of our gene-editing intellectual property to exploit certain products for the diagnosis, treatment or prevention of diabetes type 1, diabetes type 2 or insulin dependent/requiring diabetes throughout the world. To date, we have recognized revenue of $205.0 million in upfront and milestone payments and remain eligible to receive additional research and development milestones and royalties on future products under the license.

Enabling Technologies

We have entered into a number of additional collaborations and license agreements to support and complement our *ex vivo* and *in vivo* programs, including agreements related to: technologies to deliver CRISPR/Cas9 *ex vivo* and *in vivo*; additions to our hematopoietic stem cell and *in vivo* programs, including two grants to advance gene editing therapies for HIV; and enhancements to our CAR T and regenerative medicine cell therapy programs and platform.

Other Vertex Partnered Programs

We have partnered with Vertex, a global leader in rare diseases, in several other disease areas beyond SCD and TDT. We have entered into license agreements with Vertex with respect to cystic fibrosis, or CF, where Vertex has extensive expertise, and DMD. In addition, we have entered into a collaboration agreement on DM1, in which we retain the option to co-develop and co-commercialize products. We believe that our CRISPR/Cas9 gene editing technology is well suited to address CF, DMD and DM1, all of which have significant patient populations with high unmet medical need.

Duchenne Muscular Dystrophy

DMD is an X-linked recessive genetic disease caused by mutations in the dystrophin gene, which results in a lack of the dystrophin protein. Because dystrophin plays a key structural role in muscle fiber function, the absence of this protein in muscle cells leads to significant cell damage and ultimately causes muscle cell death and fibrosis. Patients with the disease experience muscle degeneration, loss of mobility and premature death. DMD is among the most prevalent severe genetic diseases, occurring in one in 3,300 male births worldwide. There are currently several approved disease-modifying therapies in the United States for the treatment of DMD, including one for patients who have confirmed mutations of the dystrophin gene amenable to exon 51 skipping, two for patients who have confirmed mutations of the dystrophin gene amenable to exon 53 skipping, and one for patients who have confirmed mutations of the dystrophin gene amenable to exon 45 skipping. These mutations affect about 13%, 8% and 8% of the DMD population, respectively. In addition, in June 2023, the FDA granted accelerated approval for Elevidys (delandistrogene moxeparvovec), an AAV gene therapy carrying a micro-dystrophin gene for the treatment of ambulatory pediatric patients aged 4 through 5 years with DMD with a confirmed mutation in the DMD gene.

Myotonic Dystrophy Type 1

DM1 is an autosomal genetic disease caused by the expansion of a CTG trinucleotide repeat in the noncoding region of the *DMPK* gene. The disease affects the skeletal and smooth muscle, as well as other organ systems, such as the eye, heart, endocrine system, and central nervous system. The clinical manifestations of DM1 span a continuum from mild to severe. Based on these phenotypes, DM1 is classified into three somewhat overlapping forms: mild, classic, and congenital. Patients with mild DM1 have normal lifespans and typically develop cataracts, and experience mild sustained muscle contractions, or myotonia. Those with classic DM1 tend to have muscle weakness and wasting, myotonia, cataracts and often abnormalities in cardiac conduction, and may become physically disabled and have shortened lifespans. Patients with congenital DM1 commonly have intellectual disability and typically have hypotonia and severe generalized weakness at birth, often with respiratory insufficiency and early death. DM1 affects around 1 in 8,000 people worldwide. No approved therapies exist to treat the underlying disease; instead, most interventions to date aim to address specific symptoms of the disease.

Cystic Fibrosis

CF is a progressive disease caused by mutations in the cystic fibrosis transmembrane regulator, or CFTR, gene resulting in the loss or reduced function of the CFTR protein. Patients with CF develop thick mucus in vital organs, particularly in the lungs, pancreas and gastrointestinal tract. As a result, CF patients experience chronic severe respiratory infections, chronic lung inflammation, poor absorption of nutrients, progressive respiratory failure and early mortality. The median age of death from CF in the United States was 31 years in 2017, with most deaths resulting from respiratory failure. CF is an orphan disease that is estimated to affect more than 70,000 patients in the United States and Europe. CF patients require lifelong treatment with multiple daily medications and hours of self-care. They often require frequent hospitalizations and sometimes even lung transplantation, which can prolong survival but is not curative.

Strategic Partnerships and Collaborations

We view strategic partnerships as a core component of our strategy, allowing us to access capabilities and resources in support of our therapeutic programs. We maintain broad strategic partnerships to develop gene editing-based therapeutics in specific disease areas.

Vertex

We, and certain of our affiliates, have entered into a series of agreements with Vertex, and or affiliates of Vertex, that contemplate certain research, development, manufacturing and commercialization activities involving various targets. Since October

2015, we have entered into a Strategic Collaboration, Option and License Agreement, as amended in 2017 and 2019, or the 2015 Collaboration Agreement; a Joint Development and Commercialization Agreement, or the Vertex JDA, which was amended and restated in April 2021, or the A&R Vertex JDCA, as amended in December 2023, or the Amended A&R Vertex JDCA. In addition, we and Vertex entered into a non-exclusive license agreement in March 2023, or the Non-Ex License Agreement, pursuant to which we agreed to license to Vertex, on a non-exclusive basis, certain of our gene editing intellectual property.

2015 Collaboration Agreement

Pursuant to the 2015 Collaboration Agreement, we agreed to provide technology and options to obtain licenses relating to our CRISPR/Cas technology to Vertex in exchange for a $75.0 million upfront payment. In 2015, in connection with the initial entry into the 2015 Collaboration Agreement, Vertex also made a $30.0 million equity investment in us.

The initial focus of the 2015 Vertex collaboration was to use CRISPR/Cas9 technology to discover and develop gene-based treatments for hemoglobinopathies and cystic fibrosis. In 2017, Vertex exercised its option to co-develop and co-commercialize the hemoglobinopathies program. Matters relating to hemoglobinopathies targets are governed by the Amended A&R Vertex JDCA, as summarized below. Further discovery efforts focused on a specified number of other genetic targets. Under the 2015 Collaboration Agreement, Vertex had the option to exclusively license treatments for a specified number of collaboration targets that emerged from the four-year research collaboration under certain of our platform and background intellectual property to develop, manufacture, commercialize, sell and use therapeutics directed to each such collaboration target. We were responsible for discovery activities, and the related expenses were fully funded by Vertex.

In October 2019, Vertex exercised the remaining options granted to it under the 2015 Collaboration Agreement to exclusively in-license three additional targets for the development of gene-based treatments using CRISPR-based gene editing. The targets include the cystic fibrosis transmembrane conductance regulator gene and two undisclosed targets. Under the terms of the 2015 Collaboration Agreement, we received an upfront payment of $30.0 million in connection with the option exercise and have the potential to receive up to $410.0 million in development, regulatory and commercial milestones, as well as royalty payments in the single digits to low teens on net product sales for each of the three targets. The milestone and royalty payments are each subject to reduction under certain specified conditions set forth in the 2015 Collaboration Agreement. For these targets, Vertex is solely responsible for all research, development, manufacturing and global commercialization activities and Vertex received exclusive rights to develop and commercialize products related to these targets globally. The research term of the 2015 Collaboration Agreement has expired, and Vertex no longer holds rights to in-license additional targets under the 2015 Collaboration Agreement.

Either party can terminate the 2015 Collaboration Agreement upon the other party's material breach, subject to specified notice and cure provisions. Vertex also has the right to terminate the 2015 Collaboration Agreement for convenience at any time upon 90 days' written notice prior to any product receiving marketing approval and upon 270 days' notice after a product has received marketing approval. We may also terminate the 2015 Collaboration Agreement in the event Vertex challenges any of our patent rights.

Absent early termination, the 2015 Collaboration Agreement will continue until the expiration of Vertex's payment obligations under the 2015 Collaboration Agreement.

Joint Development Agreement

In December 2017, we entered into the Vertex JDA with Vertex pursuant to which the parties agreed to, among other things, co-develop and co-commercialize CASGEVY and other product candidates specified in the Vertex JDA. In April 2021, we and Vertex agreed to amend and restate the Vertex JDA and entered into the A&R Vertex JDCA, pursuant to which the parties agreed to, among other things, (a) adjust the governance structure for the collaboration and adjust the responsibilities of each party thereunder; (b) adjust the allocation of net profits and net losses between the parties with respect to CASGEVY only; and (c) exclusively license (subject to our reserved rights to conduct certain activities) certain intellectual property rights to Vertex relating to the specified product candidates and products (including CASGEVY) that may be researched, developed, manufactured and commercialized under such agreement. We and Vertex amended the A&R Vertex JDCA in December 2023.

The A&R Vertex JDCA, as amended, includes, among other things, provisions relating to the following:

Governance; Activities. We and Vertex disbanded the previously established collaboration strategy team and all working groups established by such team and established a joint oversight committee to provide high-level oversight of the ongoing collaboration comprised of an equal number of representatives from each of CRISPR and Vertex. We and Vertex also formed a transition committee to provide for forum planning, discussing and sharing information regarding certain transition activities, which was disbanded following completion of such activities. The agreement provides that, subject to the terms and conditions of such agreement, Vertex has the right to conduct all research, development, manufacturing and commercialization activities relating to the specified product candidates and products (including CASGEVY) throughout the world subject to our reserved right to conduct certain activities. We will continue to participate in certain aspects of such activities in an observer capacity unless and to the extent otherwise agreed to by the parties.

Financial Terms. In the second quarter of 2021, in connection with the closing of the transaction contemplated by the

amendment and restatement of the Vertex JDA, we received a $900 million up-front payment from Vertex. Additionally, in connection with the FDA's approval of CASGEVY on December 8, 2023 for the treatment of sickle cell disease in patients 12 years and older with recurrent vaso-occlusive crises, we received a $200.0 million milestone payment from Vertex in the first quarter of 2024. The net profits and net losses, as applicable, incurred under the Amended A&R Vertex JDCA with respect to all product candidates and products specified in such agreement, other than CASGEVY, shall be shared equally between us and Vertex. With respect to CASGEVY only, the net profits and net losses, as applicable, incurred under the agreement through July 1, 2021 in connection with the initial shared product (i.e., CASGEVY) were shared equally between us and Vertex, and beginning July 1, 2021, the net profits and net losses, as applicable, incurred under the agreement are allocated 40% to CRISPR and 60% to Vertex. In addition, for the years ended December 31, 2022, 2023 and 2024, the agreement allowed us to defer a portion of our share of costs under the arrangement if spending on the CASGEVY program exceeds $110.3 million annually. In December 2023, pursuant to the amendment, the parties agreed to (a) allocate certain costs arising from a license agreement with a third party, resulting in a current payment due to Vertex by CRISPR of $20 million upon an event specified in such amendment; and (b) adjust, under certain specified circumstances, the timing of and portion of CRISPR's share of costs it is permitted to defer under the agreement. Any deferred amounts under the Amended A&R Vertex JDCA are payable to Vertex only as an offset against future profitability of the CASGEVY program and the amounts payable are capped at a specified maximum amount per year.

Termination. Either party can terminate the agreement upon the other party's material breach, subject to specified notice and cure provisions, or, in the case of Vertex, in the event that we become subject to specified bankruptcy, winding up or similar circumstances. Either party may terminate the agreement in the event the other party commences or participates in any action or proceeding challenging the validity or enforceability of any patent that is licensed to such challenging party pursuant to the agreement. Vertex also has the right to terminate the agreement for convenience at any time after giving prior written notice.

If circumstances arise pursuant to which a party would have the right to terminate the agreement on account of an uncured material breach, such party may elect to keep the agreement in effect and cause such breaching party to be treated as if it had exercised its opt-out rights with respect to the products associated with such uncured material breach (described below) and the royalties payable to the breaching party would be reduced by a specified percentage.

Opt-Out Rights. Either party may opt out of the development of a product candidate under the agreement after predetermined points in the development of the product candidate, on a candidate-by-candidate basis. In the event of such opt-out, the party opting out will no longer share in the net profits and net losses associated with such product candidate and, instead, the opting-out party will be entitled to high single to mid-teen percentage royalties on the net sales of such product, if commercialized.

Non-Exclusive License Agreement

In March 2023, we and Vertex entered the Non-Ex License Agreement, pursuant to which we agreed to license to Vertex, on a non-exclusive basis, certain of our gene editing intellectual property to exploit certain products for the diagnosis, treatment or prevention of diabetes type 1, diabetes type 2 or insulin dependent/requiring diabetes throughout the world.

The Non-Ex License Agreement includes, among other things, provisions relating to the following:

Financial Terms. In connection with entering into the Non-Ex License, we received a $100.0 million upfront payment from Vertex and have subsequently received $105.0 million in research and development milestones achieved by Vertex through December 31, 2025. We are eligible to receive additional milestone payments from Vertex of up to $125.0 million in the aggregate. The milestones are dependent on the achievement of pre-determined research, development and commercial milestones for certain products utilizing the licensed intellectual property. We are also eligible to receive tiered royalties on the sales of certain products in the low to mid-single digits. In the event of any termination or expiration of the Non-Ex License Agreement, tiered royalties on the sales of certain products will continue in the low to mid-single digits.

Termination. Either party may terminate the Non-Ex License Agreement upon the other party's material breach, subject to specified notice and cure provisions. We may also terminate the Non-Ex License Agreement in the event Vertex commences or participates in any action or proceeding challenging the validity or enforceability of any patent that is licensed to Vertex pursuant to the Non-Ex License Agreement. Vertex may also terminate the Non-Ex License Agreement upon our bankruptcy or insolvency, or for convenience upon the earlier of the achievement of certain milestone events or a specified period of time, after giving written notice.

Sirius Therapeutics

In May 2025, we entered into a Collaboration, Option and License Agreement, or the Sirius Agreement, with Sirius Therapeutics, or Sirius-CY, and Sirius Therapeutics, Inc., or Sirius-US, and together with Sirius-CY, Sirius, pursuant to which, among other things, (1) we and Sirius-US will collaborate on the research, development, manufacture, commercialization and use of certain collaboration products utilizing Sirius' siRNA technology for targeting Factor XI, including CTX611 (formerly known as SRSD107), collectively, the Sirius Collaboration Products; and (2) Sirius granted to us options to exclusively license Sirius siRNA technology to target up to two licensed targets for the research, develop, manufacture and commercialization of licensed products, collectively the siRNA Licensed Products, in exchange for the potential to receive certain option fees, milestone payments and royalties.

Upfront Consideration. In connection with entering into the Sirius Agreement, we agreed to issue to Sirius-CY an aggregate of (i) approximately $70.0 million of our common shares, and (ii) a cash payment of $25.0 million. In connection with the issuance of our common shares, we and Sirius-CY entered into a share issuance agreement relating to the issuance of 1,842,105 registered common shares at an issue price of $38.00 per common share and which were subject to a customary lock-up.

Governance. We and Sirius established a joint steering committee to provide high-level oversight, decision-making and periodic updates regarding activities under the Sirius Agreement, including formation of additional committees, as applicable. Such committee is comprised of an equal number of representatives from each party and meets at least quarterly to review the progress of collaboration program activities and oversee the research program for licensed products. The committee endeavors to make all decisions by consensus. In the event it is unable to reach consensus, we have final decision-making authority on certain matters, including all matters related to siRNA Licensed Products after option exercise.

Termination Generally. Either party can terminate the Sirius Agreement upon the other party's material breach, subject to specified notice and cure provisions, or upon the insolvency of the other party. To the extent permissible by applicable law, Sirius may also terminate the Sirius Agreement in the event we commence or participate in any action or proceeding challenging the validity or enforceability of any patent that is licensed to us pursuant to the Sirius Agreement. We also have the right to terminate the Sirius Agreement with respect to a siRNA Licensed Product, on a product-by-product basis, for convenience at any time upon 90 days' written notice prior to first commercial sale of any siRNA Licensed Product and upon 180 days' notice after first commercial sales of an siRNA Licensed Product.

Absent early termination or opt-out (and subject to the additional rights in lieu of termination described below), the Sirius Agreement will continue, (a) with respect to Sirius Collaboration Products, until the date on which such product is no longer commercialized, on a country-by-country and product-by-product basis; (b) with respect to siRNA Licensed Products, until expiration of all payment obligations under the Sirius Agreement, on a country-by-country and product-by-product basis.

Sirius Collaboration Products

With respect to Sirius Collaboration Products, the Sirius Agreement includes, among other things, provisions relating to the following:

- *Financial Terms*. With respect to Sirius Collaboration Products, we and Sirius will equally share all development and commercialization costs. For the first collaboration product candidate successfully developed, we will be the lead party responsible for commercialization efforts in the United States and Sirius-US will be the lead party responsible for commercialization efforts in Greater China. The parties will determine the lead party responsible for commercialization in the rest of the world at a future date. The net profits and net losses, as applicable, incurred under the Sirius Agreement with respect to all Sirius Collaboration Products shall be shared equally between us and Sirius.

  In addition, we will pay Sirius future development and regulatory milestones of up to an aggregate of $87.5 million one time regardless of the number of Sirius Collaboration Products that achieve the milestones, and, at our sole election, can be paid in cash, our common shares or a combination thereof.

- *Exclusivity*. Under the Sirius Agreement, from the effective date of the Sirius Agreement and for so long as Sirius Collaboration Products are commercialized, neither party nor any of its affiliates may, alone or in conjunction with a third party, engage in activities to advance any siRNA-based pharmaceutical product, medical therapy, treatment, preparation, substance or formulation targeting factor XI or activities in a specified field.

- *Termination*. If circumstances arise pursuant to which a party would have the right to terminate the Sirius Agreement with respect to a Sirius Collaboration Product for any reason, such party may elect to keep the Sirius Agreement in effect and cause such other party to be treated as if it had exercised its opt-out rights with respect to the products associated with such uncured material breach or other action leading to the termination right and, if there was an uncured material breach, the milestones and royalties payable to the breaching party would be reduced by a specified percentage and the breaching party may no longer participate in any joint committee, subcommittee or working group with respect to the collaboration products program.

- *Opt-Out Rights*. Either party may opt out of the development of a Sirius Collaboration Product under the Sirius Agreement after the later of a period of time or a predetermined point in the development of such Sirius Collaboration Product, on a product-by-product basis. In the event of such opt-out, the party opting-out will no longer share in the net profits and net losses associated with such Sirius Collaboration Product and, instead, the opting-out party will be entitled to mid-single to low-double digit percentage tiered royalties on the net sales of such product, if commercialized. In addition, if the opting-out party is Sirius, Sirius will be entitled to certain milestone payments up to an aggregate of $340.0 million. If we are the opting-out Party, depending on the timing of the opt-out, we will be entitled to certain milestone payments up to an aggregate of $340.0 million, and if the opt-out is prior to the first commercial sale of the opt-out product, the opt-out milestone payments will be capped at a certain percentage of our cumulative development costs for such opt-out product.

siRNA Licensed Products

Under the Sirius Agreement, we have options to exclusively license Sirius siRNA technology to target up to two licensed targets from a list of seven reserved targets for the research, development, manufacture and commercialization of siRNA Licensed Products. Each option is exercisable during a specified exercise period defined by future events for each such licensed target. If we elect to exercise our option to a licensed target to research, develop, manufacture and commercialize siRNA Licensed Products, we will make a one-time $10.0 million payment per option, each, an Option Payment, to Sirius, in cash, our common shares or a combination thereof. The Option Payment is payable up to two (2) times.

- *Financial Terms*. We will pay Sirius certain specified future development, regulatory and sales milestones of up to an aggregate of $300.0 million for the first siRNA Licensed Product relating to each licensed target, as well as tiered royalty payments in the mid-single digits to low double digits range on future sales of a commercialized siRNA Licensed Product. The royalty payments are subject to reduction under certain specified conditions set forth in the Sirius Agreement. In addition, at our sole election, certain development and regulatory milestones may be paid in cash, our common shares or a combination thereof. We are solely responsible for all research, development, manufacturing and global commercialization activities and associated costs for siRNA Licensed Products, as well as all associated costs related to Sirius activities set forth in any applicable research plan relating thereto.
- *Exclusivity*. Under the Sirius Agreement, Sirius has agreed to certain exclusivity obligations with respect to siRNA-based products targeting reserved targets or licensed targets. Upon expiration of the nomination period, the reserved targets that are not licensed targets by us will no longer be subject to the exclusivity obligations.
- *Rights In-lieu of Termination*. If circumstances arise pursuant to which we would have the right to terminate the Sirius Agreement with respect to siRNA Licensed Products for any reason (except termination by us for convenience), we may elect to keep the Sirius Agreement in effect and all amounts due under the Sirius Agreement with respect to siRNA Licensed Products on or after the date of the applicable material breach would be reduced by a specified percentage.

The foregoing descriptions of our strategic agreements are qualified in their entirety by reference to the full text of such agreements, copies of which are filed as exhibits to this Annual Report on Form 10-K.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, know-how and improvements that we believe are commercially important to our business by seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties, that cover our gene editing technology and existing and planned therapeutic programs. We also rely on trade secret protection and confidentiality agreements to protect our proprietary technologies and know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, as well as continuing technological innovation and seeking in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene editing. We additionally rely on trademark protection, copyright protection and regulatory protection available via orphan drug designations, data exclusivity, market exclusivity, and, if relevant, patent term extensions. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for our technology, our ability to defend and enforce our intellectual property rights and our ability to operate without infringing any valid and enforceable patents and proprietary rights of third parties. We also protect the integrity and confidentiality of our data, know-how and trade secrets by maintaining physical security of our premises and physical and electronic security of our information systems. Our granted patents and any other patents that may ultimately issue from our wholly-owned and in-licensed patent families described below are expected to expire starting in 2033, not including any applicable patent term extensions.

CRISPR-Owned Intellectual Property

We have developed a broad intellectual property estate intended to provide multiple layers of protection around our proprietary gene editing technologies, including CRISPR/Cas9 platform and next-generation editing technologies, and our other technologies, including *in vivo* delivery, as well as our product candidates. These patent families encompass filings covering our development programs (such as composition of matter, method of use, manufacturing processes, dosing and formulations), the use and improvement modifications of CRISPR/Cas9 systems for gene editing and next generation editing systems (such as improvements to component systems including nucleases and single or modified gRNAs, as well as novel Cas9 and polymerase variants and codon-optimized novel constructs), *in vivo* targets, technologies for delivering protein/nucleic acid complexes and RNA into cells (such as improved viral vector or lipid nanoparticle systems), and technology relevant to stem cell-based therapies and cancer therapies.

Overall, our wholly-owned intellectual property estate includes approximately eighty (80) active patent families and over one hundred twenty (120) granted or allowed patents, including in the United States, China, Europe, South Africa, Australia, Canada, China, Japan, Mexico and other selected countries in South America, the Middle East and Asia. In addition, we have patent

applications pending throughout the world, including in the United States, Europe, Australia, China, Canada and Japan.

Our U.S. trademark estate consists of approximately thirteen (13) pending applications, including, for example, for CRISPR-X, SYNTASE, CTX112, CTX213, CTX321, CTX340, CTX460 and CTX611, as well as nine U.S. registrations, including for CRISPR THERAPEUTICS, the CRISPR THERAPEUTICS logo, and CTX310. Our international trademark estate consists of multiple pending applications and registrations in various jurisdictions covering similar subject matter.

In-Licensed Intellectual Property from Dr. Charpentier

In addition to our wholly-owned intellectual property estate, in April 2014, we in-licensed all of Dr. Charpentier's worldwide rights under a patent application filed in March 2013 pursuant to exclusive license agreements with Dr. Charpentier, which we collectively refer to as the Charpentier License Agreement. The Charpentier License Agreement covers certain aspects of our CRISPR/Cas9 technology platform including, for example, compositions of matter (e.g., CRISPR/Cas9 systems) and methods of use, including the use of CRISPR/Cas9 systems for gene editing. The Charpentier License Agreement is limited to therapeutic products, such as pharmaceuticals and biologics and any associated companion diagnostics, for the treatment or prevention of human diseases, disorders, or conditions. For further information about this license, please see "*Business— License Agreements— License Agreements with Dr. Charpentier*."

The intellectual property exclusively licensed to CRISPR under the Charpentier License Agreement has named inventors who assigned their rights either to the Regents of the University of California, or California, or the University of Vienna, or Vienna. California's rights are subject to certain overriding obligations to the sponsors of its research, including the Howard Hughes Medical Institute and the U.S. Government. Caribou Biosciences, or Caribou, has reported that it had an exclusive license to patent rights from California and Vienna, subject to a retained right to allow non-profit entities to use the inventions for research and educational purposes. Intellia Therapeutics, Inc., or Intellia, has reported that it had an exclusive license to such rights from Caribou in certain fields. We refer collectively to Dr. Charpentier, California, and Vienna as the "CVC Group". We are or have been and will likely be in the future subject to quasi-litigation, *inter partes* administrative proceedings in various jurisdictions around the world including the U.S. Patent and Trademark Office, or USPTO, the European Patent Office and patent offices in Australia, Japan, China and India involving the patent portfolio. For further information regarding risks regarding these proceedings, please see generally "*Risk Factors—Risks Related to Intellectual Property*."

In December 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement, or the IMA, with California, Vienna, Dr. Charpentier, Intellia, Caribou, ERS Genomics Ltd., or ERS, and our wholly-owned subsidiary TRACR Hematology Ltd., or TRACR. Under the IMA, California and Vienna retroactively consent to Dr. Charpentier's licensing of her rights to the CRISPR/Cas9 intellectual property to CRISPR and TRACR pursuant to the Charpentier License Agreement and to ERS, in the United States and globally. The IMA also provides retroactive consent of co-owners to sublicenses granted by us, TRACR and other licensees, prospective consent to sublicenses they may grant in future, retroactive approval of prior assignments by certain parties, and provides for, among other things, (i) good faith cooperation among the parties regarding patent maintenance, defense and prosecution, (ii) cost-sharing arrangements, and (iii) notice of and coordination in the event of third-party infringement of the subject patents and with respect to certain adverse claimants of the CRISPR/Cas9 intellectual property. Unless earlier terminated by the parties, the IMA will continue in effect until the later of the last expiration date of the patents underlying the gene editing technology, or the date on which the last underlying patent application is abandoned. For further information regarding the effects of joint ownership in the United States and in other jurisdictions worldwide, please see "*Risk Factors—The Intellectual Property That Protects Our Core Gene Editing Technology Is Jointly Owned, And Our License Is From Only One Of The Joint Owners, Materially Limiting Our Rights In The United States And In Other Jurisdictions*."

License Agreements

License Agreements With Dr. Charpentier

In April 2014, Dr. Charpentier concurrently entered into the following exclusive license agreements:

CRISPR License Agreement: We entered into an exclusive license agreement with Dr. Charpentier pursuant to which we were granted an exclusive worldwide, royalty-bearing license, including the right to sublicense, under Dr. Charpentier's joint ownership interest in the intellectual property subject to such license agreement, to research, develop and commercialize therapeutic products such as pharmaceuticals or biological preparations, and any associated companion diagnostics, for the treatment or prevention of human diseases, disorders, or conditions, other than hemoglobinopathies, which we refer to as the CRISPR Field. Additionally, we were granted an exclusive, worldwide, royalty-free sublicense, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic products relating to the CRISPR Field which incorporate any intellectual property that TRACR develops under its license with Dr. Charpentier. In turn, we granted to Dr. Charpentier an exclusive license with the obligation to sublicense to TRACR any intellectual property we develop under the license with Dr. Charpentier for treatment and prevention of hemoglobinopathies in humans, including, without limitation, sickle cell disease and thalassemia. CRISPR is solely responsible for all clinical, regulatory and development costs.

TRACR License Agreement: TRACR entered into an exclusive license agreement with Dr. Charpentier pursuant to which we were granted an exclusive, worldwide, royalty-bearing license, including the right to sublicense, under Dr. Charpentier's joint ownership interest in the intellectual property subject to such license agreement to research, develop, produce, commercialize and sell therapeutic and diagnostic products for the treatment and prevention of hemoglobinopathies in humans, including sickle cell disease and thalassemia, which we refer to as the TRACR Field. Additionally, TRACR received a non-exclusive, worldwide, royalty-free license, including the right to sublicense, to carry out internal pharmaceutical research for therapeutic products outside of the TRACR Field and an exclusive, worldwide, royalty-free sublicense, including the right to sublicense, to research, develop, produce, commercialize and sell therapeutic products relating to the TRACR Field which incorporate any intellectual property that CRISPR develops under its license with Dr. Charpentier. In turn, TRACR granted to Dr. Charpentier an exclusive license to sublicense to CRISPR any intellectual property that TRACR develops under the license with Dr. Charpentier for use in the CRISPR Field. TRACR is solely responsible for all clinical, regulatory and development costs.

As a general matter, the material terms and conditions of the CRISPR License Agreement and TRACR License Agreement are substantially the same other than the permitted fields of use under each such agreement (as noted above). As such, for ease of reference, we refer to the CRISPR License Agreement and the TRACR License Agreement individually and collectively as the Charpentier License Agreement.

The licenses granted under the Charpentier License Agreement are exclusive, even as to Dr. Charpentier, except that she retains a non-transferable right to use the technology for her own research purposes and in research collaborations with academic and non-profit partners. The exclusive license granted under the Charpentier License Agreement is granted only under Dr. Charpentier's interest in the patent applications and the exclusivity is not granted under any other joint owner's interest.

Under the terms of the Charpentier License Agreement, as consideration for the license, Dr. Charpentier received a technology transfer fee, as well as the right to receive an immaterial annual maintenance fee, immaterial clinical and regulatory milestone payments that are due after the initiation of certain clinical trial and regulatory events a low single digit percentage royalty on net sales of licensed products, and a low single digit percentage royalty on sublicensing revenue. We are obligated to use commercially reasonable efforts to obtain regulatory approval to market of a licensed therapeutic product under each Charpentier License Agreement.

Unless terminated earlier, the term of each Charpentier License Agreement will expire on a country-by-country basis, upon the expiration of the last to expire valid claim of the patents in-licensed to us or TRACR under the applicable Charpentier License Agreement in such country. We and TRACR have the right to terminate the agreement at will upon 60 days' written notice to Dr. Charpentier. Each Charpentier License Agreement may be terminated by either party thereto upon 90 days' notice in the event of a material breach by the other party, which is not cured during the 90-day notice period. Dr. Charpentier may terminate the license agreement immediately if we challenge the enforceability, validity, or scope of any in-licensed patent right under the Charpentier License Agreement.

Manufacturing

The manufacturing processes for cell and genetic therapies are complex and require customized systems, equipment, facilities and expertise for each program and therapy. Due to the critical importance of high-quality manufacturing and control of production timing and know-how, we are establishing internal manufacturing capabilities and have established our own cell therapy manufacturing facility to support our multifaceted strategy to develop treatments and therapies for people suffering from serious diseases through transformative gene-based medicines.

We have an approximately 50,000 square foot manufacturing facility in Framingham, Massachusetts intended for clinical and commercial production of our product candidates and certain components thereof for certain of our programs. The facility was designed with flexibility and scalability in mind in order to accommodate manufacturing and supply for our product pipeline. We believe it has the capacity to support, in whole or in part, the manufacture and supply of product for certain of our current clinical programs with the capability to scale-up to support potential commercial supply. In addition, we believe our facility has the capacity and necessary technology to support additional programs we may advance in the future, including some of our *in vivo* programs and our T1D program, as well as the production of various critical components, such as mRNA, we may utilize in the future. Our operations at this facility are compliant with current Good Manufacturing Practice, or cGMP, and in 2023 we began manufacturing certain of our product candidates, including zugo-cel, at this facility for our clinical trials of such product candidates.

In addition to utilizing our internal manufacturing facility, we expect we will continue to rely on external manufacturing capabilities realized via contract manufacturing organization relationships in the United States and abroad. We have entered into certain manufacturing and supply arrangements with third-party suppliers to support production of our product candidates and their components. We plan to continue to rely on qualified third-party organizations to produce or process bulk compounds, formulated compounds, viral vectors or engineered cells for IND-supporting activities and early-stage clinical trials. We expect that commercial quantities of any compound, vector, or engineered cells that we may seek to develop will be manufactured in facilities and by processes that comply with FDA and other regulations. At the appropriate time in the product development process, we will determine

whether to utilize our own manufacturing facility or continue to rely on third parties to manufacture commercial quantities of any products that we may successfully develop.

We continue to expect to make significant investment in our manufacturing capabilities in Framingham, Massachusetts and in partnerships with third-party organizations for our gene editing programs in order to continue to advance and, in the future, commercialize these programs.

In addition, 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. 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.

Competition

The biotechnology and pharmaceutical industries, including in the gene editing, gene therapy, nucleic acids therapies, 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 currently face, and will continue to face, substantial competition from many different sources, including large pharmaceutical, specialty pharmaceutical and biotechnology companies; academic institutions and governmental agencies; and public and private research institutions, some or all of which may have greater access to capital or resources than we do. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, but we will also have to compete with new therapies that 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 gene editing and gene therapy, nucleic acid therapy, and cell therapy. In addition, we compete with companies working to develop these therapies by utilizing advanced extrahepatic delivery vectors. Companies across each of these vectors serve as competitive threats for CRISPR Therapeutics AG.

Gene editing and gene therapy competition

Our platform and product focus is on the development of therapies using CRISPR/Cas gene editing technology. We are aware of several companies focused on developing therapies in various indications using CRISPR/Cas gene editing technology, including Editas Medicine, Intellia Therapeutics, Metagenomi, and Scribe Therapeutics. In addition, several academic groups have developed new gene editing technologies, such as base editing, reverse transcriptase editing, and gene insertion via recombinases that may have utility in therapeutic development. Companies seeking to develop therapies based on these technologies include Beam Therapeutics, Prime Medicine, Tessera Therapeutics, and Verve Therapeutics (recently acquired by Eli Lilly).

Several companies are also pursuing alternative gene editing approaches using epigenetic editing, TALENs, meganucleases, and RNA editing. These companies include Allogene Therapeutics, Cellectis, Iovance Biotherapeutics, Factor Bioscience, Korro Bio, nChroma Bio, Precision BioSciences, Sangamo Therapeutics, Scribe Therapeutics, Tune Therapeutics, and Wave Life Sciences.

Several companies are pursuing traditional approaches toward gene therapy, primarily utilizing gene supplementation via AAVs or lentiviral vectors. These companies may also serve as competitive threats and include 4D Molecular Therapeutics, AskBio, Passage Bio, Sarepta Therapeutics, UniQure, and Voyager Therapeutics.

Nucleic acid therapies competition

In addition to our gene editing platform, we are engaged in development activities related to transient transcript silencing via siRNA. Several companies are developing nucleic acid therapies related to our siRNA development pipeline, including Alnylam, Arrowhead Therapeutics, Avidity Biosciences, Bayer, Biogen, Dyne Therapeutics, Eli Lilly, Ionis Pharmaceuticals, Novartis, Novo Nordisk, Sarepta Therapeutics, Stoke Therapeutics, and Wave Life Sciences.

Cell therapy competition

We are aware of several companies developing both autologous and allogeneic cell therapies, of which both serve as key competitors. These competitors are developing *ex vivo* CAR T therapies, *in vivo* CAR T therapies, and stem cell-derived cell therapies and include Allogene, Autolus, BlueRock Therapeutics (acquired by Bayer in 2019), Bristol Myers Squibb, Caribou Biosciences, Cellectis, Fate Therapeutics, Iovance Biotherapeutics, Johnson & Johnson, Kite Pharma (acquired by Gilead Sciences in 2017), and Novartis.

Extrahepatic delivery

We are also aware of companies developing targeted lipid nanoparticles, lentiviral vectors, and/or non-viral approaches for the delivery of genetic medicine payloads to extrahepatic tissues. Of these companies, those focused on transduction of hematopoietic stem progenitor cells or their progeny (e.g., T-cells, B-cells, NK cells, dendritic cells) pose the greatest competitive threat, including Azalea Therapeutics, Beam Therapeutics, Capstan (recently acquired by AbbVie), Editas Medicine, Ensoma, Interius Biotherapeutics (recently acquired by Kite Pharma / Gilead Sciences), Tessera Therapeutics, Kelonia, Orbital (recently acquired by Bristol Myers Squibb), Sana Biotechnology, Stylus Medicine, and Umoja Biopharma.

Therapeutic area competition

We are also aware of companies developing therapies in various areas related to our specific research and development programs and therapeutic areas. In hemoglobinopathies, these companies include Azalea Therapeutics, Beam Therapeutics, Capstan (recently acquired by AbbVie), Editas Medicine, Ensoma, Interius Biotherapeutics (recently acquired by Kite Pharma / Gilead Sciences), Kelonia, Merck, Novartis Pharmaceuticals, Orbital (recently acquired by Bristol Myers Squibb), Pfizer, Sana Biotechnology, Stylus Medicine, Tessera Therapeutics and Umoja Biopharma. In immuno-oncology, these companies include Adicet Bio, Allogene Therapeutics, Bristol Myers Squibb, Caribou Biosciences, Cellectis, Century Therapeutics, Fate Therapeutics, Gilead Sciences, Legend Biotech, Novartis Pharmaceuticals and Poseida Therapeutics. In autoimmune disease, these companies include Allogene Therapeutics, AstraZeneca, Bristol Myers Squibb, Cabaletta Bio, Capstan (recently acquired by AbbVie), Caribou Biosciences, Century Therapeutics, Fate Therapeutics, Interius Biotherapeutics (recently acquired by Kite Pharma / Gilead Sciences), Kelonia, Nkarta Inc., Novartis, Orbital (recently acquired by Bristol Myers Squibb), Stylus Medicine, Tessera Therapeutics and Umoja Bio. In regenerative medicine, these companies include BlueRock Therapeutics (acquired by Bayer in 2019), Century Therapeutics, Sana Biotechnology, and Semma Therapeutics (acquired by Vertex in 2019).

In *in vivo* gene editing, the companies include Beam Therapeutics, Capstan (recently acquired by AbbVie), Editas Medicine, Intellia Therapeutics, Interius Biotherapeutics (recently acquired by Kite Pharma / Gilead Sciences), Kelonia, Metagenomi, Orbital (recently acquired by Bristol Myers Squibb), Prime Medicine, Sana Biotechnology, Scribe Therapeutics, Tessera Therapeutics, Umoja Biopharma and Verve Therapeutics (recently acquired by Eli Lilly).

Development of genetic medicines has rapidly increased outside of the United States, with a particular emphasis in China. There are several genetic medicine companies advancing therapies in this region with planned clinical trials outside of China and pose a competitive threat to CRISPR Therapeutics AG, including AccurEdit, HudiaGene, and Yoltech Therapeutics.

Gene editing is a highly active field of research and new technologies, related or unrelated to CRISPR, may be discovered and create new competition. These new technologies could have advantages over CRISPR/Cas9 gene editing in some applications and there can be no certainty that other gene editing technologies will not be considered better or more attractive than our technology for the development of products. For example, Cas9 may be determined to be less attractive than other CRISPR proteins, such as Cas12a or novel Cas enzymes that have yet to be discovered, or other CRISPR-associated nuclease variants that can edit human DNA, such as base editors and reverse transcriptase editors.

In addition to competition from other gene editing therapies or gene or cell therapies, any product we may develop may also face competition from other types of therapies, such as small molecule, antibody or protein therapies. New scientific discoveries may also cause CRISPR/Cas9 technology, or gene editing as a whole, to be considered an inferior form of therapy.

Many of our current or potential competitors, either alone or with their collaboration partners, 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 and cell 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, have broader acceptance and higher rates of reimbursement by third-party payors 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. 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 may develop against competitors. 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 gene editing, gene therapy, and cell therapy products. Competition with

other related products currently under development may include competition for clinical trial sites, patient recruitment, and product sales. In addition, due to the intense research and development taking place in the gene editing field, including by us and our competitors, the intellectual property landscape is in flux and highly competitive. 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. For example, see our discussion of the '048 interference, the '115 interference and European opposition proceedings in "*Risk Factors—Risks Related to Intellectual Property—Third-party Claims Of Intellectual Property Infringement Against Us, Our Licensors Or Our Collaborators May Prevent Or Delay Our Product Discovery and Development Efforts.*"

Moreover, 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 and our patents may not be sufficient to prevent our competitors from commercializing competing 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.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the EU, extensively regulate, among other things, the research, development, testing, manufacture, 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. Some jurisdictions outside of the United States also regulate the pricing of such products. The processes for obtaining marketing approvals in the United States and in other 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 product candidates are regulated as biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug, and Cosmetic Act, or FDCA, and their implementing regulations. The failure to comply with the applicable U.S. requirements at any time during the product development process, including nonclinical testing, clinical testing, the approval process or post-approval process, may subject an applicant to delays in the conduct of a study, regulatory review and approval, and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, untitled or warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or the Department of Justice or other governmental entities.

An applicant 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, or GLP, regulations;
- submission to the FDA of an Investigational New Drug, or IND, application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated, or by a central IRB if appropriate;
- 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 the FDA's Good Clinical Practice, or GCP, regulations;
- preparation and submission to the FDA of a Biologics License Application, or 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 and proposed labeling;
- 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, or CGTP, for the use of human cellular and tissue products;
- satisfactory completion of any FDA audits of the nonclinical study and clinical trial sites to assure compliance with GLPs and GCPs, respectively, and the integrity of clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and

Mitigation Strategy, or REMS, adverse event reporting, and compliance with 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 animals. 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. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA imposes a clinical hold based on concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research subjects would be exposed to unreasonable and significant health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trials can begin.

As a result, submission of the IND may result in the FDA not allowing the trials to commence or not 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 conduct of the IND study, including safety concerns or concerns due to non-compliance, it may impose a partial or complete clinical hold. This order issued by the FDA would either delay a proposed clinical study or cause suspension of an ongoing study, or in the case of a partial clinical hold limit a study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed or recommence but only under terms authorized by the FDA. This could cause significant delays or difficulties in completing planned clinical studies in a timely manner.

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 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. If a non-U.S. clinical trial is not conducted under an IND, the sponsor may submit data from a well-designed and well-conducted clinical trial to the FDA in support of the BLA so long as the clinical trial is conducted in compliance with GCP and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems it necessary.

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, subject informed consent, ethical factors, and the safety of human subjects. An IRB must operate in compliance with FDA regulations. The FDA or the clinical trial sponsor may suspend or terminate 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. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent. 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 or committee. 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 access to certain data from the study.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the United States, certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight of institutional biosafety committees, or IBCs, as set forth in the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, or NIH Guidelines. Under the National Institutes of Health, or NIH, Guidelines, recombinant and synthetic nucleic acids are defined as: (i) molecules that are constructed by joining nucleic acid molecules and that can replicate in a living cell (i.e., recombinant nucleic acids); (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules (i.e., synthetic nucleic acids); or (iii) molecules that result from the replication of those described in (i) or (ii). Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. While the NIH Guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not

otherwise subject to the NIH Guidelines voluntarily follow them.

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 cancer patients.
- ***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 costlier Phase 3 clinical trials.
- ***Phase 3*** clinical trials are undertaken within an expanded patient population to further evaluate dosage and gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling.

Progress reports detailing the results, if known, of the clinical trials must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators within 15 calendar days of receipt by the sponsor or its agents after determining that the information qualifies for such expedited reporting. IND safety reports are required for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk to humans exposed to the drug, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Additionally, a sponsor must notify FDA within 7 calendar days after receiving information concerning any unexpected fatal or life-threatening suspected adverse reaction.

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. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Guidance Governing Gene Therapy Products

The FDA has defined a gene therapy product as one that mediates its effects by transcription and/or translation of transferred genetic material or by specifically altering host (human) genetic sequences. Examples of gene therapy products include nucleic acids (e.g., plasmids, *in vitro* transcribed ribonucleic acid), genetically modified microorganisms (e.g., viruses, bacteria, fungi), engineered site specific nucleases used for human genome editing and *ex vivo* genetically modified human cells. 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, or CBER, regulates gene therapy products. Within the CBER, the review of gene therapy and related products is consolidated in the Office of Therapeutic Products, and the FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols.

Although the FDA has indicated that its guidance documents regarding gene therapies are not legally binding, we believe that our compliance with them is likely necessary to gain approval for any product candidate we may develop. 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. Depending on the product type, long term follow up can be up to 15 years or as little as five years.

Compliance with cGMP and CGTP 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 CGTP. These requirements are found in FDA regulations 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, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the CGTP 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, and those supplying products, ingredients, and components of them, must also register their establishments with the FDA and certain state agencies for products intended for the U.S. market, and with analogous health regulatory agencies for products intended for other markets globally. Both U.S. and non-U.S. manufacturing establishments must register and provide additional information to the FDA and/or other health regulatory agencies upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether U.S. or non-U.S., is deemed misbranded under the FDCA, and could be affected by similar as well as additional compliance issues in other jurisdictions. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA or other governing health regulatory agency may lead to a product being deemed to be adulterated.

Review and Approval 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 a 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.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. 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 Prescription Drug User Fee Act, or the PDUFA, the FDA has ten months in which to complete its initial review of a standard application and respond to the applicant, 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 applicant otherwise provides through the submission of a major amendment additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

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 nonclinical study and clinical trial sites to assure compliance with GLPs and GCPs, respectively, 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, 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 complete response letter 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 an applicant 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. Alternatively, sponsors that receive a complete response letter may either withdraw the application or request a hearing.

The FDA may also 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.

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, or ETASU. ETASU can include, but are not limited to, specific or 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, certain manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Expedited Programs

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review, and regenerative medicine advanced therapy designation.

Specifically, the FDA may 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. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the application is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process, or if the designated drug development program is no longer being pursued.

Second, FDA has a regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or 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. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting adverse reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Finally, the FDA can accelerate review and approval of products designated as regenerative medicine 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 has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative medicine advanced therapy designation include early interactions with 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.

In addition, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, a platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under a BLA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may expedite the development and review of any subsequent original BLA for a drug that uses or incorporates the platform technology. Designated platform technology status does not ensure that a drug will be developed more quickly or receive FDA approval. In addition, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

Further, in June 2025, the FDA announced the creation of a new program, the Commissioner's National Priority Voucher, or

CNPV, program, to expedite the development and approval of drug and biological products with potential to address a major national priority, such as addressing a large unmet medical need, reducing downstream health care utilization, addressing a public health crisis, boosting domestic manufacturing, or increasing medication affordability. The FDA has stated that voucher recipients will receive a decision with respect to a drug or biological product marketing application on an accelerated basis, as well as enhanced communication with review staff throughout the development process prior to final submission of the application and during the review period. The FDA has further indicated that a CNPV can expire, and the voucher process must be commenced within two years following receipt from the FDA.

The FDA expects the CNPV program to accelerate drug or biological product application or efficacy supplement review times from 10 months to 1-2 months by convening a multidisciplinary team of physicians and scientists for a team-based review, interacting frequently with the sponsor to clarify questions, and completing review of the application concurrently. Following completion of these steps, the multidisciplinary team will convene for a one-day "tumor board style" review meeting. The faster timeframe is contingent upon additional requirements from the company, and FDA reserves the right to extend the review as needed.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally could support accelerated approval where a study demonstrates a relatively short-term clinical benefit in a chronic disease setting in which assessing durability of the clinical benefit is essential for traditional approval, but the short-term benefit is considered reasonably likely to predict long-term benefit.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit, and the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

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 has 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 are required to comply with applicable product tracking and tracing 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 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 of a failure to comply with regulatory requirements 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, untitled or 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 marketing, labeling, advertising and promotion of licensed and approved products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Drug Designation

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, or OOPD, at the FDA based on acceptable confidential requests made under the regulatory provisions. The product must then go through the review and approval process for commercial distribution 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.

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.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003 (PREA), as amended, 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 applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, 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 applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, 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. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation; however, they will apply to a BLA for a new active ingredient that is orphan-designated if the biologic is a molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer.

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. 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 existing periods of regulatory exclusivity of each drug product containing the studied active moiety 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 Patient Protection and Affordable Care Act, or ACA, which was signed into law in March 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. The FDA has issued several guidance documents outlining an approach to review and approval of 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.

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, and FDA may approve multiple "first" interchangeable products so long as they are all approved on the same first day of marketing. This exclusivity period, which may be shared amongst multiple first interchangeable products, lasts until the earlier of: (1) one year after the first commercial marketing of the first interchangeable product; (2) 18 months after resolution of a patent infringement suit instituted under 42 U.S.C. § 262(l)(6) against the applicant that submitted the application for the first interchangeable product, based on a final court decision regarding all of the patents in the litigation or dismissal of the litigation with or without prejudice; (3) 42 months after approval of the first interchangeable product, if a patent infringement suit instituted under 42 U.S.C. § 262(l)(6) against the applicant that submitted the application for the first interchangeable product is still ongoing; or (4) 18 months after approval of the first interchangeable product if the applicant that submitted the application for the first interchangeable product has not been sued under 42 U.S.C. § 262(l)(6). At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Patent Term Restoration and Extension

A patent claiming a new biologic product may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments, 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 an IND and the submission date of a marketing application, plus the time between the submission date of the marketing application and the ultimate approval date, less any time the applicant failed to act with due diligence. 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.

Regulation and Procedures Governing Approval of Medicinal Products in Europe

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, an applicant will need to obtain the necessary approvals by the comparable health 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 Europe generally follows the same lines as in the United States, although the approval of a medicinal product in the United States is no guarantee of approval of the same product in Europe, either at all or within the same timescale as approval may be granted in the United States. The process 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 EMA, or the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by the European Commission or these authorities before the product can be marketed and sold in Europe.

Clinical Trial Approval

An applicant for a clinical trial authorization in the EU must obtain approval from the national competent authority, or NCA, of an EU 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 applicant may only start a clinical trial at a specific study site after the applicable ethics committee, or EC, has issued a favorable opinion in relation to the clinical trial.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on 31 January 2022. It overhauled the current system of approvals for clinical trials in the EU. Specifically, the new legislation, which is directly applicable in all EU Member States (meaning that no national implementing legislation in each EU Member State is required), aims at simplifying and streamlining the approval of clinical trials in the EU. For instance, the Clinical Trials Regulation provides for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications.

Marketing Authorization

To obtain a marketing authorization for a product in the EU, an applicant must submit an MAA, either under a centralized procedure administered by the EU or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure, or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EEA (comprising the EU Member States plus Iceland, Norway and Liechtenstein). Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in an EMA-approved pediatric investigation plan, or 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 throughout the EEA. 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 medicinal products, or ATMPs, and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer, HIV or AIDS, diabetes, neurodegenerative disorders, auto-immune and other immune dysfunctions and viral diseases. For those products for which the use of the centralized procedure is not mandatory, applicants may elect to use the centralized procedure where either the product contains a new active substance indicated for the treatment of other diseases, or where the applicant can show that the product constitutes a significant therapeutic, scientific or technical innovation or for which a centralized process is in the interest of patients at an EU level.

Specifically, the grant of a marketing authorization in the EU for advanced therapy medicinal products, including gene therapy medicinal products, somatic cell therapy medicinal products and tissue-engineered products, is governed by Regulation (EC) No 1394/2007 on ATMPs, read in combination with Directive 2001/83/EC of the European Parliament and of the European Council, which is the EU Directive governing medicinal products for human use. Regulation (EC) No 1394/2007 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 the Committee for Advanced Therapies, or CAT, at the EMA, which conducts a scientific assessment of the MAA and provides an opinion regarding the MAA for an ATMP. The European Commission grants or refuses marketing authorization in light of the opinion delivered by the EMA.

The Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for issuing a final opinion on whether an ATMP meets the required quality, safety and efficacy requirements, and whether a product has a positive benefit/risk profile. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days from receipt of a valid MAA, excluding clock stops when additional information or written or oral explanation is to be

provided by the applicant in response to questions of the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion, together with supporting documentation, to the European Commission, which makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated evaluation may be granted by the CHMP in exceptional cases, when a medicinal product is expected to be 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 frame of 210 days for assessment will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

Now that the UK (which comprises Great Britain and Northern Ireland) has left the EU, the UK is no longer covered by centralized marketing authorizations. However, on January 1, 2024, a new international recognition framework was put in place by MHRA under which the MHRA may have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators.

PRIME scheme

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, by, amongst other things, offering early dialogue with, and regulatory support from, the EMA. The scheme is intended to stimulate innovation, optimize development and enable accelerated assessment of PRIority MEdicines, or PRIME, by building upon the scientific advice scheme and accelerated assessment procedure offered by EMA. The scheme is voluntary and eligibility criteria must be met for a medicine to qualify for PRIME.

The PRIME scheme is open to medicines under development and for which the applicant intends to submit an initial marketing authorization application through the centralized procedure. Eligible products must target conditions for which there is an unmet medical need (meaning there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Applicants will typically be at the exploratory clinical trial phase of development, and will have preliminary clinical evidence in patients to demonstrate the promising activity of the medicine and its potential to address, to a significant extent, an unmet medical need. In exceptional cases, applicants from the academic sector or SMEs (small and medium sized enterprises) may submit an eligibility request at an earlier stage of development if compelling non-clinical data in a relevant model provide early evidence of promising activity, and first in human studies indicate adequate exposure for the desired pharmacotherapeutic effects and tolerability.

If a medicine is selected for the PRIME scheme, the EMA:

- appoints a rapporteur from the CHMP or from the CAT to provide continuous support and to build up knowledge of the medicine in advance of the filing of a marketing authorization application;
- issues guidance on the applicant’s overall development plan and regulatory strategy;
- organizes a kick-off meeting with the rapporteur and experts from relevant EMA committees and working groups;
- provides a dedicated EMA contact person; and
- provides scientific advice at key development milestones, involving additional stakeholders, such as health technology assessment bodies and patients, as needed.

Medicines that are selected for the PRIME scheme are also expected to benefit from the EMA’s accelerated assessment procedure at the time of application for marketing authorization. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

Data and Market Exclusivity

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon grant of a 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 applicants for authorizations of generics or biosimilars from referencing the innovator’s preclinical and clinical data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the EU, during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted and the innovator’s data may be referenced, but no generic or biosimilar medicinal product can be marketed in the EU until the expiration of the market exclusivity period. 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, are held to bring a significant clinical benefit in comparison with existing therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so

that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained a 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

In the European Union, 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 EU Member State for a nationally authorized product. 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 marketing authorization that is not followed by the actual placing of the medicinal product on the EU market (in the case of the centralized procedure), or on the market of the authorizing EU Member State, within three years of the grant of the authorization, or where the product is no longer marketed for a continuous period of three years ceases to be valid (the so-called sunset clause).

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 medicinal product by the European Commission, following review by the EMA's Committee for Orphan Medicinal Products, if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five (5) in ten thousand (10,000) persons in the EU when the application is made; or (b) it is unlikely that the product, without benefits derived from orphan status, would generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention, or treatment of such condition authorized for marketing in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

An orphan designation provides a number of benefits, including fee reductions, regulatory assistance, and the ability to apply for a centralized marketing authorization. The grant of a marketing authorization for an orphan medicinal product leads to a ten-year period of market exclusivity for the authorized therapeutic indication. During this market exclusivity period, neither the European Commission, EMA nor the competent authorities of the EU Member States can accept an application or grant a marketing authorization in respect of a "similar medicinal product" for the same therapeutic indication. 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 designation because, for example, the product is sufficiently profitable not to justify market exclusivity. There are a few limited of derogations from the ten-year period of market exclusivity pursuant to which the European Commission may grant a marketing authorization for a similar medicinal product in the same therapeutic indication, which are:

- where the second applicant can establish that although their product is similar to the orphan medicinal product already authorized, the second product is safer, more effective or otherwise clinically superior;
- where the marketing authorization holder for the authorized orphan product consents to the second orphan medicinal product application; or
- where the marketing authorization holder for the authorized orphan product cannot supply enough orphan medicinal product.

Regulatory Requirements after Marketing Authorization has been obtained

If an authorization for a medicinal product in the EU is obtained, 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 EU'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 applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive (EU) 2017/1572, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. 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 EU. The advertising of prescription-only medicines to the general public is not permitted in the EU.

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 EU. The provision of benefits or advantages to induce or

reward improper performance generally is also governed by the national anti-bribery laws of EU Member States, and the Bribery Act 2010 in the UK. Infringement of these laws could result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, further provides that, where medicinal products are being promoted to persons qualified to prescribe or supply them, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such persons unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision has been transposed into the Human Medicines Regulations 2012 and so remains applicable in the UK despite its departure from the EU.

Payments made to physicians in certain EU 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 EU Member States. These requirements are provided in the national laws, industry codes, or professional codes of conduct applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines, or imprisonment.

The aforementioned EU rules are generally applicable in the EEA. For other markets in which we might in the future seek to obtain marketing approval for the commercialization of products, there are other health regulatory regimes for seeking approval, and we would need to ensure ongoing compliance with applicable health regulatory procedures and standards, as well as other governing laws and regulations for each applicable jurisdiction.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). In April 2024, the European Parliament adopted its position on the legislative proposals and, in June 2025, the Council of the European Union adopted its position. A common position on the text has been agreed upon on December 11, 2025 in the context of subsequent inter-institutional trilogue negotiations. The proposed revisions remain to be adopted, and are not expected to become applicable before 2028.

European Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Economic Area or EEA and the UK, including personal health data, is subject to the EU General Data Protection Regulation, or EU GDPR, with respect to the EEA, and the UK General Data Protection Regulation, or UK GDPR, with respect to the UK, and collectively with the EU GDPR referred to as the "GDPR" in this report unless specified otherwise. The GDPR applies to companies established in the EEA/UK, as well as to any company established outside the EEA/UK, if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA/UK or the monitoring of their behavior in the EEA/ Switzerland/UK. 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, having legal bases and/or conditions for processing personal data, providing details to those individuals regarding the processing of their personal data, implementing safeguards to protect the security and confidentiality of personal data, having data processing agreements with third parties who process personal data, responding to individuals' requests to exercise their rights in respect of their personal data, ensuring appropriate technical and organisational measures are in place and reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, ensuring certain accountability measures are in place and record keeping. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, 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 (£17.5 million under the UK GDPR) 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.

Switzerland has adopted a data protection regime similar to the GDPR. Compliance with the GDPR and the Swiss data -protection regime remains 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.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU on January 31, 2020 and the EU and the UK have concluded a trade and cooperation agreement, or TCA, which has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not provide for wholesale mutual recognition of UK and EU pharmaceutical regulations.

At present, the UK has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended). The regulatory regime in the UK therefore aligns in many ways with EU regulations, however it is possible that these regimes will more significantly diverge in future now that the UK's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation. However,

notwithstanding that there is no wholesale recognition of EU pharmaceutical legislation under the TCA, under a new international recognition framework mentioned above which was put in place by the MHRA on January 1, 2024, the MHRA may take into account decisions on the approval of a marketing authorization from the EMA (and certain other regulators) when considering an application for a UK marketing authorization.

On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". The medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changed the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA is now responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has any role in approving medicinal products under the centralized procedure destined for Northern Ireland. A single UK-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK.

The UK regulatory framework in relation to clinical trials is governed by the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, which are derived from the Clinical Trials Directive 2001/20/EC, as implemented into UK national law through secondary legislation. In April 2025, the UK introduced the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025. The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 will take full effect from April 28, 2026, and aim to create a streamlined, risk-proportionate system that accelerates approvals while maintaining robust safety standards. In addition, in October 2023, the MHRA announced a new Notification Scheme for clinical trials which enables a more streamlined and risk-proportionate approach to initial clinical trial applications for Phase 4 and low-risk Phase 3 clinical trial applications.

There is no pre-marketing authorization orphan designation in the UK. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same as in the EU, but have been tailored for the market, i.e., the prevalence of the condition in the UK, rather than the EU, must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in the UK.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products or product candidates for which we have received or 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 products or 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 approved, sales of any product or 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. Factors a payor considers in determining reimbursement are based on whether the 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.

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, products or 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 various federal, state and/or local governments, as well as other payors, within the United States and in other countries globally, and the prices of pharmaceuticals have been a focus in these efforts. Governments and other payors 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 products or 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 EU, 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, or HTAs) in order to obtain reimbursement or pricing approval. For example, the EU 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. EU 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 EU 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 EU have increased the level of discounting required in relation to the pricing of 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 EU. 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 EU Member States, and parallel trade (arbitrage between low-priced and high-priced Member States), can further reduce prices. Special pricing and reimbursement rules may apply to orphan medicinal products. Inclusion of orphan medicinal products in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any drug. Acceptance of any medicinal product for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. In addition, results-based rules of reimbursement may apply. 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, or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind, in exchange for or intended 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 U.S. 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 be made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the U.S. False Claims Act;
- the federal false statements statute 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; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific

intent to violate it in order to have committed a violation;

- the anti-inducement law, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, collectively HIPAA, which imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program (including private payors) or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services;
- HIPAA, which impose obligations with respect to safeguarding the privacy, security, and transmission of individually identifiable information that constitutes protected health information, including mandatory contractual terms and restrictions on the use and/or disclosure of such information without proper authorization;
- the federal transparency requirements known as the federal U.S. Physician Payments Sunshine Act, under the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, or HHS, information related to payments and other transfers of value made by that entity to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician providers such as physician assistants and nurse practitioners, and teaching hospitals, and requires certain manufacturers and applicable group purchasing organizations to report ownership and investment interests held by physicians or their immediate family members;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- The Foreign Corrupt Practices Act 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; and
- analogous laws and regulations in other national jurisdictions and states, 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 and other 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.

Certain state laws also govern the privacy and security of health information in some circumstances, many of which are not preempted by HIPAA and differ from each other in significant ways, thus complicating compliance efforts. For example, in California, the California Consumer Protection Act, or CCPA, established a comprehensive privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of sensitive categories of data, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices. While clinical trial data and information governed by HIPAA are currently exempt from the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope. In addition, the California Privacy Rights Act, or CPRA, amended the CCPA and imposes additional obligations on companies covered by the legislation. The CPRA significantly modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information.

Similar laws have been passed in numerous other states which add additional complexity, variation in requirements, restrictions and potential legal risk. The existence of comprehensive privacy laws in different states in the United States may make our compliance obligations more complex and require additional capital and investment of resources, may impact or limit the availability of previously useful data and could require us to make costly changes to our business practices and policies. Enforcement of such laws is not yet clear and may increase the likelihood that we will be subject to enforcement actions, fines or otherwise incur liability and be required to incur litigation expenses to defend against claims of noncompliance. There are also states that are specifically regulating health information. For example, Washington state's My Health My Data Act, or MHMDA, regulates the collection and sharing of health information, and has a private right of action, which further increases compliance risk. Connecticut and Nevada have also

passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information including biometric data. These laws and regulations, including their interpretation by governmental agencies, are subject to frequent change and may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Regulators and legislators in the U.S. are increasingly scrutinizing and restricting certain personal data transfers and transactions involving foreign countries. For example, the Department of Justice's January 8, 2025, Rule on Preventing Access to U.S. Sensitive Personal Data and Government-Related Data by Countries of Concern or Covered Persons, prohibits transfers of data, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and/or civil sanctions, and may result in exclusion from participation in federal and state programs. and could restrict our ability to use certain vendors, sites, investigators, or service providers in global clinical trials.

Further data privacy and security laws and regulations in foreign jurisdictions that may be more stringent than those in the United States (such as the European Union's GDPR).

All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects. Any failure or perceived failure by us to comply with any applicable federal, state or foreign laws and regulations relating to data privacy and security could result in damage to our reputation, as well as proceedings or litigation by governmental agencies or other third parties, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, sanctions, awards, injunctions, penalties or judgments. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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 2010, the United States Congress enacted the ACA, which, among other things, modified how drug products are covered and paid by government health care programs. Among the provisions of the ACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- increasing the minimum rebate liability owed by manufacturers under the Medicaid Drug Rebate Program for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- establishing a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expanding the types of entities eligible for the 340B drug discount program;
- establishment of the Medicare Part D coverage gap discount program which, although later further modified and replaced by the Inflation Reduction Act, required manufacturers to provide a 70% point-of-sale-discount off the negotiated price of applicable products to eligible beneficiaries during the so-called "donut hole" or coverage gap period as a condition of the manufacturers' outpatient products being covered under Medicare Part D;
- creating a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishing the Center for Medicare and Medicaid Innovation, or CMMI, within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, including prescription product spending.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example:

- The Budget Control Act of 2011 included aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031.
- The Statutory Pay-As-You-Go Act of 2010 and subsequent legislation including the One Big Beautiful Bill Act of 2025, created further reductions to Medicare payments to providers that go into effect starting in 2026 absent further legislation.
- The American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.
- The American Rescue Plan Act of 2021 eliminated the statutory Medicaid drug rebate cap, previously set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs.
- The One Big Beautiful Bill Act of 2025 also imposed significant reductions in Medicaid funding and enrollment requirements, which are expected to reduce Medicaid enrollment and covered services, which may further reduce demand for our products, if approved.

These laws and regulations 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 its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. It is unclear how other healthcare reform measures of the Trump administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business.

At the federal level, FDA released implementing regulations in 2020 for how states can build and submit importation plans for drugs from Canada. Also in 2020, CMS stated drugs imported by states under this rule will not be eligible for federal Medicaid drug rebates and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since imported drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. On January 5, 2024, Florida became the first state in the United States to receive the FDA's approval for its plan to import certain prescription drugs from Canada. Importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates.

Further, on December 2, 2020, HHS published 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 rule also created a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. This deadline was later pushed back to January 1, 2032 by the Inflation Reduction Act of 2022 ("IRA").

There has also been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Individual states in the United States have also become increasingly active in enacting legislation and implementing regulations designed to control pharmaceutical 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.

The IRA was signed into law in August 2022. The IRA included several provisions that will impact our business to varying degrees, including provisions that allow the U.S. government to negotiate and set price caps for Medicare Part B and Part D pricing for certain high-cost, single-source drugs and biologics without generic or biosimilar competition; reduce the out-of-pocket spending cap for Medicare Part D beneficiaries to $2,000 starting in 2025, effectively eliminating the so-called "donut hole" for Medicare Part D; require companies to pay rebates to Medicare for drug prices that increase faster than inflation; and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge, among other areas. The effect of the IRA on our business and the healthcare industry in general is not yet known.

In addition, recent executive and agency actions have advanced various most-favored-nation ("MFN")-type pricing concepts that could materially affect the prices we may obtain for any products, if approved. On May 12, 2025, President Trump signed an executive order directing the Secretary of HHS to set and communicate MFN price targets to manufacturers and propose a rulemaking plan to impose MFN pricing if "significant progress" is not made, and also directing the federal government to support regulatory

paths to allow direct-to-patient sales for companies that meet these targets. The executive order further states that the Administration will take additional action (for example, examining whether marketing approvals should be modified or rescinded or considering individual drug importation waiver authorities) should manufacturers fail to offer American consumers the MFN lowest price. In July 2025, President Trump sent letters to certain pharmaceutical companies demanding that these companies extend MFN pricing to Medicaid and newly launched drugs as well as move to direct-to-consumer models priced at MFN pricing, and soliciting binding commitments by September 29, 2025. Since this time, multiple drug manufacturers have announced plans to, for certain of their drugs, lower prices to reflect similar pricing around the world, and to sell these reduced-price drugs on a direct-to-consumer purchasing platform developed by the federal government; however, it is not known what results will occur to the extent the recipients of these letters do not reduce their U.S. prices.

On December 19, 2025, CMS released two proposed rules that would incorporate MFN pricing principles into federal reimbursement for prescription drugs. The first proposal, the Global Benchmark for Efficient Drug Pricing Model ("GLOBE") for Medicare Part B, would require manufacturers of specified single source drugs and sole source biologics to pay incremental rebates based on international benchmark prices, with participation triggered for products meeting CMS's spending and eligibility criteria. The second proposal, the Guarding U.S. Medicare Against Rising Drug Costs ("GUARD") model for Medicare Part D, would similarly mandate manufacturer rebates for qualifying sole source drugs where the Medicare net price exceeds an MFN benchmark derived from international reference pricing methodologies. As proposed, GLOBE would begin a five year performance period on October 1, 2026 and GUARD would begin its performance period in 2027. These proposals will likely be subject to legal challenges that could delay their implementation or modify their impact on manufacturer pricing and revenue. Additionally, in November 2025, CMS introduced the GENErating cost Reductions fOr U.S. Medicaid ("GENEROUS") Model, a voluntary MFN framework for manufacturers participating in the Medicaid Drug Rebate Program. Although it is voluntary, the GENEROUS Model could also impact the drug pricing landscape for manufacturers.

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 authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other 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.

There have been, and likely will continue to be, legislative and regulatory proposals at the national level in the United States and other jurisdictions globally, as well as at some regional, state and/or local levels within the United States or other jurisdictions, directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Additional Regulation

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

We are dedicated to conducting business with the highest standards of corporate responsibility. Our goal is to build an engaged and passionate workforce striving to positively impact patients, our communities, and broader society. We are committed to recruiting the best people for the job regardless of gender, race, ethnicity, age, disability, sexual orientation, gender identity, cultural background, or religious belief in accordance with all applicable laws. Our human capital resource priorities include skill-based hiring aligned to our business priorities and merit-based recognition across the organization.

The principal purposes of our comprehensive equity and cash compensation and benefits programs are to attract, motivate, retain, and reward new and existing employees. We do this by using a mix of compensation elements that balance achievement of our short-term goals with our long-term performance. In addition, employees are eligible to participate in our standard employee benefit plans, such as our retirement, health and welfare benefits plans, including medical, dental, and life and disability insurance plans. We also offer our employees the opportunity to participate in a tax-qualified retirement plan, or the 401(k) Plan, and have the ability to

make matching contributions under the 401(k) Plan, which is competitive with other companies in our industry.

We consider our human capital resources strategy to be comprehensive and is built around our core way of working: collaborative, undaunted, entrepreneurial, and results-oriented. We foster a strong relationship with and among our employees with ongoing efforts such as training and development programs, including skill development courses, manager training, leadership development opportunities, tuition reimbursement and robust online course training libraries for reference on a myriad of development topics. We also support cross-functional career development pathways, in addition to traditional promotions within functions in the organization. We plan to continue to evolve and add to our suite of human capital resources as we grow.

Information Available on the Internet

Investors and others should note that we announce material information to our investors using our investor relations website (https://crisprtx.gcs-web.com/), U.S. Securities and Exchange Commission, or SEC, filings, press releases, public conference calls and webcasts. We use these channels as well as social media to communicate with the public about our company, our business, our product candidates and other matters. It is possible that the information we post on social media could be deemed to be material information. Therefore, we encourage investors, the media, and others interested in our company to review the information we post on the social media channels listed on our investor relations website. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act are available on our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC at its website (https://www.sec.gov).

Item 1A. Risk Factors.

This report contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this report and in any documents incorporated in this report by reference.

You should carefully consider the following risk factors, together with all other information in this report, including our financial statements and notes thereto, and in our other filings with the U.S. Securities and Exchange Commission, or SEC. If any of the following risks, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common shares could decline, and shareholders may lose all or part of their investment.

Risks Related to Our Financial Position and Need for Additional Capital

We Have Incurred Significant Operating Losses Since Our Inception And Anticipate That We Will Incur Continued Losses For The Foreseeable Future.

We have funded our operations through public and private offerings of our equity securities, private placements of our preferred shares, convertible loans and collaboration agreements with strategic partners. While we were profitable for the year ended December 31, 2021 due to an upfront payment associated with our collaboration with Vertex, we are not currently profitable and we do not expect to be profitable in future years. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our shareholders' deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- continue our clinical trials for our various wholly-owned and partnered programs;
- continue our current research programs and our preclinical and clinical development of product candidates;
- seek to identify additional research programs and additional product candidates;
- conduct preclinical studies to support U.S. Investigational New Drug, or IND, applications and foreign equivalents and initiate clinical trials for our product candidates;
- initiate preclinical studies and clinical trials for any other product candidates we identify and choose to develop;
- expand, maintain, enforce and/or defend our intellectual property estate;
- seek marketing approvals for any of our product candidates that successfully complete clinical trials;
- further develop our gene editing and other proprietary technologies;
- hire additional clinical, quality control and scientific personnel;
- establish, expand or contract for manufacturing capabilities;
- add personnel, including personnel to support our product candidate development;
- acquire or in-license other technologies; and
- establish a sales, marketing, and distribution infrastructure to commercialize any products for which we, or our partners and collaborators, may obtain or have obtained marketing approval.

In addition, we and our partner, Vertex, have received marketing approval for CASGEVY in certain jurisdictions. Under the Amended A&R Vertex JDCA, for the years ended December 31, 2022, 2023 and 2024, we had the option to defer and did defer costs on the CASGEVY program in excess of $110.3 million annually, subject to certain adjustments under certain circumstances. Beginning in 2025, we no longer have the option to defer such costs on the CASGEVY program, and, as a result, we have incurred increased development and commercialization expenses for the CASGEVY program. We expect that such expenses will exceed our share of revenue for the foreseeable future.

As a result of all of the foregoing, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing product candidates, including gene-based product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

We Will Need To Raise Substantial Additional Funding, Which Will Dilute Our Shareholders. If We Are Unable To Raise Capital When Needed, We Would Be Forced To Delay, Reduce Or Eliminate Some Of Our Product Development Programs Or Commercialization Efforts.

The development of product candidates, including gene-based product candidates, is capital intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate preclinical

studies and clinical trials for and seek marketing approval for our product candidates, as well as 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 our collaborators currently or in the future if we obtain marketing approval for any of our product candidates. For example, beginning in 2025, we no longer have the option to defer certain costs on the CASGEVY program under the Amended A&R Vertex JDCA, and, as a result, we have incurred increased development and commercialization expenses for the CASGEVY program. We expect that our share of expenses for the development and commercialization of CASGEVY will increase, and has increased, and that such expenses will exceed, and have exceeded, our share of revenue for the foreseeable future. We may also need to raise additional funds sooner if we choose to pursue additional indications or geographies for our product candidates, investigate new technologies, including delivery modalities, or otherwise expand more rapidly than we presently anticipate. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate certain of our research and development programs or future commercialization efforts.

As of December 31, 2025 and 2024, we had cash, cash equivalents and marketable securities of approximately $1,975.8 million and $1,903.8 million, respectively. With our cash, cash equivalents and marketable securities on hand as of December 31, 2025, we expect cash, cash equivalents and marketable securities to be sufficient to fund our current operating plan through at least the next 24 months.

Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the scope, progress, results and costs of clinical trials, drug discovery, preclinical development and laboratory testing for our wholly-owned and partnered product candidates;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of establishing and maintaining a supply chain for the development and manufacture of our product candidates;
- the success of our collaborations with Vertex and Sirius;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under any additional collaboration or license agreements we obtain;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of various expenses, including clinical trial, development, manufacturing and commercialization costs, under our current or future collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the costs of fulfilling our obligations under the Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement to reimburse other parties for costs incurred in connection with the prosecution and maintenance of associated patent rights;
- the extent to which we acquire or in-license other product candidates, intellectual property and technologies;
- the costs of establishing, expanding or contracting for manufacturing capabilities if we obtain regulatory approvals to manufacture our product candidates;
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates; and
- our ability to establish and maintain healthcare coverage and adequate reimbursement.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our shareholders and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a shareholder. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborators or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or

more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

We Have A Limited Operating History, Which May Make It Difficult To Evaluate Our Technology And Product Development Capabilities And Predict Our Future Performance.

Our overall development efforts are ongoing and the first clinical trial for any of our product candidates was initiated at the end of 2018. In general, our programs require preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions; obtaining manufacturing supply, capacity, and expertise; building a commercial organization; substantial investment and significant marketing efforts before we generate any revenue from product sales. Our product candidates must be approved for marketing by the FDA or certain other regulatory agencies, including the EMA, before we may commercialize any product. Although we and our partner, Vertex, have received marketing approvals for CASGEVY in certain jurisdictions, we cannot guarantee we and Vertex will receive additional marketing approvals for CASGEVY or we will receive marketing approvals for our other product candidates in the future. For additional information, see also "*Risk Factors —Risks Related to Our Relationships with Third Parties—We Have Partnered With Vertex On Our Lead Program CASGEVY; Vertex Has Significant Control Over The CASGEVY Program*" and "*Risk Factors —Risks Related to Our Business, Technology and Industry—If We Are Unable To Advance Our Product Candidates To Clinical Development, Obtain Regulatory Approval And Ultimately Commercialize Our Product Candidates, Or Experience Significant Delays In Doing So, Our Business Will Be Materially Harmed.*"

Our limited operating history, particularly in light of the rapidly evolving gene editing field, may make it difficult to evaluate our technology and industry and predict our future performance. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer. Similarly, we expect that our financial condition and operating results will fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. As a result, our shareholders should not rely upon the results of any quarterly or annual period as an indicator of future operating performance.

In addition, as a development stage company, we have encountered unforeseen expenses, difficulties, complications, delays and other known and unknown circumstances. As we advance our product candidates, we will need to continue to transition from a company with a research focus to a company focused on researching, developing, manufacturing and commercializing product candidates, as applicable. We may not be successful in such a transition.

Our Ability To Use Tax Loss Carryforwards In Switzerland May Be Limited.

Under Swiss law, we are entitled to carry forward losses we incur for a period of seven years and we can offset future profits, if any, against such losses. Tax losses are only finally assessed by the tax authorities when offset with taxable profit (which will not be the case if we are loss making). If not used, these tax losses will expire seven years after the year in which they occurred. Due to our limited income, there is a high risk that the tax loss carry forwards will expire partly or entirely and as a result they would not be applied to reduce future cash tax payments.

Risks Related to Our Business, Technology and Industry

If We Are Unable To Advance Our Product Candidates To Clinical Development, Obtain Regulatory Approval And Ultimately Commercialize Our Product Candidates, Or Experience Significant Delays In Doing So, Our Business Will Be Materially Harmed.

Our development efforts are ongoing and we have primarily focused our research and development efforts to date on gene editing and other technologies, including CRISPR/Cas9 and next-generation platform technologies, as well as delivery technologies, and our initial product candidates. Our future success depends heavily on the successful development of our next-generation product candidates and other future product candidates. We have invested substantially all of our efforts and financial resources in the development of our proprietary technologies and identification and development of our current product candidates. Our ability to generate product revenue will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. For example, while we and our partner, Vertex, have received marketing approvals for CASGEVY in certain jurisdictions, we cannot guarantee we and Vertex will receive additional marketing approvals for CASGEVY or we will receive marketing approvals for our other product candidates in the future, and our research programs, including additional programs subject to current and future collaboration agreements with third parties, may fail to identify potential product candidates for clinical development for a number of reasons or may fail to successfully advance any product candidates through clinical development. Our potential product candidates may be shown to have harmful side effects or may have other characteristics or unforeseeable consequences that may make the product candidates impractical to manufacture, unmarketable, or unlikely to receive marketing approval, or that lead to product-related claims or litigation, including without limitation personal injury or product liability claims, adverse or serious adverse events, regulatory enforcement actions, or product recalls or market withdrawals. Our partner,

Vertex, generates product sales from CASGEVY, of which we receive 40% through our collaboration arrangement with Vertex. This amount is currently insufficient to cover program expenses and as such, we are responsible for 40% of losses, subject to certain limitations. We currently generate no revenue from sales of any wholly-owned product and we may never be able to again research, develop or commercialize a marketable product.

We must file IND applications, clinical trial applications, or CTAs, or their equivalents with regulatory authorities to commence clinical trials. The filing of INDs, CTAs or their equivalents for any product candidate is subject to the identification and selection of one or more guide RNAs with acceptable efficiency, among other activities. In addition, commencing any future clinical trial is also subject to acceptance by the European regulatory authorities, or its equivalent, of our CTAs, or by the FDA of our INDs, and finalizing the trial design based on discussions with the applicable regulatory authorities. In the event that the European regulatory authorities, FDA or their equivalent require us to complete additional preclinical studies or we are required to satisfy other requests, our clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, they could disagree that we have satisfied their requirements to commence a clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. Regulatory authorities have limited experience with the clinical development of CRISPR/Cas9-based therapeutics, including *in vivo* therapeutics, which may require additional significant testing or data compared to more traditional therapies or otherwise delay the development of our product candidates. There is no certainty that the FDA or other similar regulatory agencies will continue to apply to all our gene-editing product candidates, including CRISPR/Cas9 product candidates, the same regulatory pathway and requirements it applied to CASGEVY and is applying to other *ex vivo* engineered therapeutics and *in vivo* therapies.

To become and remain profitable, we must develop and commercialize product candidates with significant market potential, which will require us to be successful in a range of challenging activities. In general, our product candidates require preclinical and clinical development; regulatory and marketing approval in multiple jurisdictions; obtaining manufacturing supply, capacity, and expertise; building a commercial organization; substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product development programs must be approved for marketing by the FDA, EMA or certain other health regulatory agencies before we may commercialize our product candidates. We may never succeed in any or all of these activities and, even if we do, we may never generate revenues that are significant or large enough to achieve profitability. Although we and our partner, Vertex, have received marketing approvals for CASGEVY in certain jurisdictions, we cannot guarantee we and Vertex will receive additional marketing approvals for CASGEVY or we will receive marketing approvals for our other product candidates in the future, or that CASGEVY, or any other future product candidate we develop, will be profitable. For additional information, see also "*Risk Factors—Risks Related to Our Relationships with Third Parties—We Have Partnered With Vertex On Our Lead Program CASGEVY; Vertex Has Significant Control Over The CASGEVY Program*."

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 our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in our value also could cause shareholders to lose all or part of their investment.

The success of our product candidates will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical trials and preclinical studies;
- sufficiency of our financial and other resources to complete the necessary clinical trials and preclinical studies;
- ability to develop safe and effective delivery mechanisms for our *in vivo* therapeutic programs;
- ability to identify optimal RNA sequences to guide genomic editing;
- maintenance of current, and entry into additional, collaborations to further the development of our product candidates;
- approval of INDs, CTAs or their equivalents for our product candidates to commence clinical trials;
- successful data from our clinical programs that support an acceptable risk-benefit profile of our product candidates for the intended patient populations;
- receipt of regulatory and marketing approvals from applicable regulatory authorities;
- establishing and maintaining arrangements with third-party manufacturers for clinical and commercial supply and, where applicable, commercial manufacturing capabilities;
- successful development of our internal manufacturing processes and transfer to larger-scale facilities operated by either a third-party contract manufacturing organization or by us;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;

- effective competition with other therapies and treatment options;
- establishment and maintenance of healthcare coverage and adequate reimbursement;
- enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of our product candidates following approval; and
- achieving desirable medicinal properties for the intended indications.

Additionally, because our technology involves gene editing across multiple cell and tissue types, we are subject to many of the challenges and risks that gene therapies face, including:

- regulatory requirements and guidance governing gene and cell therapy products have changed frequently and may continue to change in the future, including, e.g., the final guidance document titled "Human Gene Therapy Products Incorporating Human Genome Editing" that the FDA issued in January 2024;
- to date, only a limited number of products that involve the genetic modification of patient cells have been approved in the United States, the European Union, or EU, and globally;
- the administration processes or related procedures for certain of our product candidates (e.g., treatment with myeloablative busulfan conditioning prior to receiving CASGEVY or undergoing a lymphodepletion regimen prior to receiving our immunotherapy product candidates);
- improper modulation of a gene sequence, including unintended editing events, insertion of a gene sequence into certain locations in a patient's chromosome or other effects related to the technology underlying our product candidates could lead to lymphoma, leukemia or other cancers, or other aberrantly functioning cells, or other diseases, including death;
- transient expression of the Cas9 protein or other genome editing components of our product candidates could lead to patients having an immunological reaction towards those cells, which could be severe or life-threatening;
- corrective expression of a missing protein in patients' cells could result in the protein being recognized as foreign, and lead to a sustained immunological reaction against the expressed protein or expressing cells, which could be severe or life-threatening; and
- the FDA recommends a follow-up observation period of up to 15 years for all patients who receive treatment using gene therapies, and we may need to adopt and support, and have adopted and are supporting for certain of our trials, such an observation period for our product candidates.

If we do not succeed in one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business. Ultimately, if we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Similarly, relatively few siRNA product candidates have been tested in humans and to date few have received regulatory approval and market authorizations.

In addition, if any product candidates encounter safety or efficacy problems, development delays, regulatory issues or other problems, our development plans and business could be significantly harmed. For the reasons described above, among others, regulatory authorities, particularly the FDA, have requested, and may request in the future, additional preclinical studies for genome editing products, such as additional studies related to toxicology, biodistribution or reproductive health, and/or preclinical studies earlier in clinical development compared to other therapeutic modalities. Although to date the FDA has cleared the INDs that we have submitted for certain of our clinical trials, it is possible that the FDA may impose requirements that result in a delay of any of our programs or their regulatory approval. If we are unable to complete any required studies satisfactorily, the FDA or other regulatory authorities could require that we exclude certain patient populations from clinical studies, place our clinical studies on hold, or require us to cease further clinical studies or deny approval of such product candidates. Further, competitors that are developing *ex vivo* or *in vivo* products with similar technology may experience problems with their product candidates or programs that could in turn cause us to identify problems with our product candidates and programs, or cause the FDA or other regulatory authorities to impose additional requirements, that could cause us to delay or pause development of our product candidates. Any of these occurrences may harm our ability to identify and develop product candidates, and may harm our business, financial condition, results of operations and prospects significantly. We cannot guarantee that the FDA or other regulatory authorities will not change their requirements in the future or approve amendments to our INDs or equivalent regulatory filings on the timelines we expect.

Our CRISPR/Cas9 Gene Editing Product Candidates Are Based On A Relatively New Gene Editing Technology, Which Makes It Difficult To Predict The Time And Cost Of Development And Of Subsequently Obtaining Regulatory Approval, If At All. There Have Only Been A Limited Number Of Clinical Trials Of Product Candidates Based On Gene Editing Technology.

We aim to develop treatments and therapies for people suffering from serious diseases through transformative gene-based medicines, including *ex vivo* engineered cell therapies and *in vivo* therapies. Although there have been significant advances in recent years in the fields of gene therapy and genome editing, including CRISPR/Cas9 gene editing technology, such technologies, including

in vivo CRISPR-based genome editing technologies in particular, are relatively new and only a limited number of clinical trials of product candidates based on such gene editing technologies have been commenced and their therapeutic utility is largely unproven. As such it is difficult to accurately predict the developmental challenges we may incur for our product candidates as they proceed through product discovery or identification, preclinical studies and clinical trials. For example, to date, no genome editing *in vivo* therapy has been approved in the United States, EU or other key jurisdictions. While we and our partner, Vertex, have received marketing approvals for CASGEVY in certain jurisdictions, we cannot guarantee we and Vertex will receive additional marketing approvals for CASGEVY or we will receive marketing approvals for our other product candidates in the future. In addition, because we have only recently commenced clinical trials for certain of our other product candidates, we have not yet been able to fully assess safety in humans. There may be long-term effects from treatment with any product candidates that we develop that we cannot predict at this time. Any product candidates we may develop will act at the level of DNA, and, because animal DNA differs from human DNA, testing of our product candidates in animal models may not be predictive of the results we observe in human clinical trials of our product candidates for either safety or efficacy. Also, animal models may not exist for some of the diseases we choose to pursue in our programs. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our gene editing technology, or any similar or competitive gene editing technologies, will result in the identification, development, and regulatory approval of any products. There can be no assurance that any development problems we experience in the future related to our gene editing technology or any of our research and development programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. 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 may develop on a timely or profitable basis, if at all.

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 product candidate. Although we and our partner, Vertex, have received marketing approvals for CASGEVY in certain jurisdictions, we cannot guarantee we and Vertex will receive additional marketing approvals for CASGEVY or we will receive marketing approvals for our other product candidates in the future, and the regulatory approval process for product candidates such as ours remains uncertain and may be more expensive and take longer than the approval process for product candidates based on other, better known or more extensively studied technologies. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our future product candidates in either the United States or the EU or how long it will take to commercialize our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product candidate to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects may be harmed.

Our Engineered Allogeneic T cell Product Candidates Represent A Novel Approach To Autoimmune and Cancer Treatment That Creates Significant Challenges For Us.

For our autoimmune disease and immuno-oncology programs, we are developing allogeneic T cell product candidates that are engineered from healthy donor T cells to express chimeric antigen receptors, or CARs, and are intended for use in any patient with certain autoimmune diseases or cancers. Unlike for autologous chimeric antigen receptor, or CAR T, therapies, for allogeneic CAR T therapies, we are reliant on receiving healthy donor material to manufacture our product candidates. Healthy donor T cells vary in type and quality, and this variation makes producing standardized allogeneic CAR T product candidates challenging and makes the development and commercialization pathway of those product candidates uncertain.

We have developed screening processes designed to enhance the quality and consistency of T cells used in the manufacture of our CAR T cell product candidates, but our screening processes may fail to identify suitable donor material and we may discover failures with the material after production. We may also have to update our specifications for new risks that may emerge, such as to screen for new viruses.

We have strict specifications for donor material, which include specifications required by regulatory authorities. If we are unable to identify and obtain donor material that satisfy specifications, agree with regulatory authorities on appropriate specifications, or address variability in donor T cells, there may be inconsistencies in the product candidates we produce or we may be unable to initiate or continue ongoing clinical trials on the timelines we expect, which could harm our reputation and adversely impact our business and prospects.

In addition, approved autologous CAR T therapies and those under development have shown frequent rates of cytokine release syndrome, neurotoxicity, serious infections, prolonged cytopenia and hypogammaglobulinemia, and other serious adverse events that have resulted in patient deaths. We expect similar adverse events for our allogeneic CAR T product candidates. Moreover, patients eligible for allogeneic CAR T cell therapies but ineligible for autologous CAR T cell therapies due to aggressive cancer and inability to wait for autologous CAR T cell therapies may be at greater risk for complications and death from therapy or underlying disease. Our allogeneic CAR T cell product candidates may also cause unique adverse events related to the differences between the donor and patients, such as Graft versus Host Disease, or GvHD, or infusion reactions. GvHD results when allogeneic T cells start recognizing the patient’s normal tissue as foreign.

We have aimed to eliminate the T-cell receptor from the healthy donor T cells using our CRISPR/Cas9 gene editing technology to reduce the risk of GvHD from our product candidates, as well as to remove the class I major histocompatibility complex from the cell surface in order to limit the patient's immune system from attacking the allogeneic T cells and to improve the persistence of the CAR T cells. However, the gene editing of our product candidates may not be successful in limiting the risk of GvHD or premature rejection by the patient. In addition, results of our autoimmune disease and immuno-oncology clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

If significant GvHD or other adverse events are observed with the administration of our product candidates, or if any of the product candidates are viewed as less safe or effective than autologous therapies or other allogenic therapies, our ability to develop allogeneic therapies may be adversely affected.

Further, in November 2023, the FDA announced that it would be conducting an investigation into reports of T-cell malignancies following B-cell maturation antigen, or BCMA, directed or CD19-directed autologous CAR T cell immunotherapies following reports of T cell lymphoma in patients receiving these therapies. In January 2024, the FDA determined that new safety information related to T cell malignancies should be included in the labeling with boxed warning language on these malignancies for all BCMA- and CD19-directed genetically modified autologous T cell immunotherapies. FDA's investigation into CAR T therapies and other similar actions could result in increased government regulation, unfavorable public perception and publicity, and, although we are developing allogeneic CAR T candidates, the FDA's investigation could result in potential impacts on enrollment in our clinical trials, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

The FDA, MHRA And The EMA Have Demonstrated Caution In Their Regulation Of Gene Therapy Treatments, And Ethical And Legal Concerns About Gene Therapy And Genetic Testing May Result In Additional Regulations Or Restrictions On The Development And Commercialization Of Our Product Candidates, Which May Be Difficult To Predict.

The FDA, MHRA and the EMA have each expressed interest in further regulating biotechnology, including gene therapy and genetic testing. For example, the EMA advocates for a risk-based approach to the development of a gene therapy product. Agencies at both the federal and state level in the United States, as well as the U.S. congressional committees and other governments or governing agencies, have also expressed interest in further regulating the biotechnology industry. Such action may delay or prevent commercialization of some or all of our product candidates.

Regulatory requirements in the United States and in other jurisdictions governing gene therapy products have changed frequently and may continue to change in the future. The FDA has issued several guidance documents on gene therapy products. The FDA established the Office of Therapeutic Products within its Center for Biologics Evaluation and Research to consolidate the review of gene therapy and related products, and established the Cellular, Tissue and Gene Therapies Advisory Committee to advise this review. In addition to the government regulators, institutional biosafety committees and institutional review boards of each institution at which we conduct clinical trials of our product candidates, or a central institutional review board if appropriate, would need to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other oversight authorities to change the requirements for approval of any of our product candidates. Similarly, the EMA governs the development of gene therapies in the EU and may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. These regulatory review agencies and committees and the new requirements or guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates and seek regulatory approval, we will be required to consult with these regulatory agencies and committees and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our or our collaborators' ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

If Any Of The Product Candidates We May Develop Or Administration Processes And Delivery Modalities 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.

Product candidates we may develop may be associated with undesirable or unacceptable side effects, unexpected characteristics or other serious adverse events, including death or off-target cuts of DNA, or the introduction of cuts in DNA at locations other than the target sequence. These off-target cuts could lead to disruption of a gene or a genetic regulatory sequence at an unintended site in the DNA, or, in those instances where we also provide a segment of DNA to serve as a repair template, it is possible that following off-target cut events, DNA from such repair template could be integrated into the genome at an unintended site, potentially disrupting

another important gene or genomic element.

There also is the potential risk of delayed adverse events following exposure to gene editing therapy due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that could occur with treatment with gene editing products include an immunologic reaction after administration which could substantially limit the effectiveness of the treatment.

Immunotherapy, and its method of action of harnessing the body's immune system, is powerful and could lead to serious side effects that we only discover in clinical trials. Unforeseen side effects could arise either during clinical development or, if such side effects are rare, after our product candidates have been approved by regulatory authorities and the approved product has been marketed, resulting in the exposure of additional patients. If our technology or technology we in-license from third parties, including CRISPR/Cas9 gene editing technology and gene silencing technology, or delivery modalities we utilize demonstrate a similar effect, we may decide or be required to halt or delay preclinical development, clinical development or commercialization of our product candidates. For example, through internal efforts and external collaborations, we are pursuing the development of multiple delivery technologies, including LNPs, to support our current and future *in vivo* product candidates. Possible adverse side effects that could occur with treatment with a product or product candidate utilizing such delivery modalities could include an immunologic reaction early after administration which, while not necessarily adverse to the patient's health, could substantially limit the effectiveness of the treatment. While we have designed our proprietary LNP platform to minimize any LNP vehicle-related toxicities with repeat administration *in vivo* by engineering amino lipids to avoid the immune system and to be rapidly biodegradable relative to prior LNP formulations, we cannot provide assurances that our product candidates utilizing our proprietary LNP platform or similar other delivery modalities will not activate one or more immune responses giving rise to potential immune reaction related adverse events, like liver toxicities or enzyme elevations.

In addition to serious adverse events or side effects caused by any product candidate we may develop, the administration process or related procedures also can cause undesirable side effects. For example, patients who receive CASGEVY or enroll in the ongoing CASGEVY clinical trials have their own CRISPR/Cas9 edited-hematopoietic stem and progenitor cells, CASGEVY, infused back into the patient as part of a stem cell transplant, a process which involves, among other things, a patient being treated with myeloablative busulfan conditioning. Patients undergoing stem cell transplants may also encounter side effects (ranging from mild to severe) that are unrelated to the administration of a product candidate. Patients who enroll in our immunotherapy trials undergo a lymphodepletion regimen, which generally includes fludarabine and cyclophosphamide that may cause serious adverse events. Because these regimens will cause a transient and sometimes prolonged immune suppression, patients will have an increased risk of certain infections that may be unable to be cleared by the patient and could ultimately lead to death.

Any side effects may not be appropriately recognized or managed by the treating medical staff. We or our collaborators expect to have to educate medical personnel using any product or product candidates we may develop to understand the side effect profiles for our clinical trials and upon any commercialization of such product or product candidates. Inadequate recognition or management of the potential side effects of such product or product candidates could result in patient injury or death. If any undesirable or unacceptable side effects, unexpected characteristics or other serious adverse events occur, our clinical trials or commercial distribution of any product candidates or products we develop alone or with collaborators could be suspended or terminated, and our business and reputation could suffer substantial harm.

If in the future we are unable to demonstrate that such adverse events were caused by factors other than our product candidate or approved products, the FDA, EMA or other comparable regulatory authorities could order us to cease further clinical studies of, or deny approval of, any product candidates we are able to develop for any or all targeted indications or cease the sale of approved products. 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, 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.

Additionally, 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, or 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 approved product or product candidate that we develop alone or with our collaborators, several potentially significant negative consequences could result, including:

- regulatory authorities may revoke licenses or suspend, vary or withdraw approvals of such product or product candidate;
- regulatory authorities may require additional warnings on the label;
- we may be required to change the way a product or 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.

Moreover, gene therapy product candidates investigated by other parties have resulted in serious adverse events, including deaths, and it is possible that the FDA or other regulatory authorities could impose a clinical hold on clinical trials of our product candidates after becoming aware of adverse events with products or product candidates in the same class as our products or product candidates.

Any of these events could prevent us from achieving or maintaining market acceptance of our gene editing technology and any products or product candidates we may identify and develop and could have a material adverse effect on 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 product candidates we identify or develop 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. Enrollment may be particularly challenging for any rare genetically defined diseases we may target in the future. In addition, if patients are unwilling to participate in our gene editing trials because of negative publicity from adverse events related to the biotechnology, gene therapy or gene editing fields, competitive clinical trials for similar patient populations, clinical trials with competing products, or for other reasons, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of any product candidates we may 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 may 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 clinical trial participants;
- design of the trial protocol;
- availability of eligible prospective patients that are otherwise eligible patients for competitive clinical trials;
- availability and efficacy of approved medications for the disease under investigation;
- availability of genetic testing for potential patients;
- ability to obtain and maintain clinical trial participant consent;
- risk that enrolled clinical trial participants 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 gene editing and cellular therapies as therapeutic approaches;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Enrollment delays in our clinical trials may result in increased development costs for any product candidates we may develop, which would cause our value 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.

Positive Results From Early Preclinical Studies Or Preliminary Results from Clinical Trials Of Our Product Candidates Are Not Necessarily Predictive Of The Results Of Later Preclinical Or Clinical Studies And Any Future Clinical Trials Of Our Product Candidates. If We Cannot Replicate The Positive Results From Our Earlier Preclinical Or Clinical Studies Of Our Product Candidates In Our Later Preclinical Studies, Clinical Trials And Future Clinical Trials, We May Be Unable To Successfully Develop, Obtain Regulatory Approval For And Commercialize Our Product Candidates.

Any positive results from our preclinical studies or preliminary results from our clinical trials of our product candidates may not necessarily be predictive of the results from required later preclinical studies and clinical trials. For example, for our *in vivo* product

candidates, our proposed delivery modalities combined with or separate from our product candidates, have a limited history of being evaluated in human clinical trials. Any of our product candidates, including our *in vivo* candidates, candidates utilizing siRNA and CAR T candidates, may fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical trials. Preliminary, interim and top-line data from clinical trials may change as more patient data become available. Preliminary, interim or top-line data from clinical trials are not necessarily predictive of final results, including the results submitted in support of approval in a BLA or equivalent submission outside the United States. Interim, top-line and preliminary data remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously announced. As a result, preliminary, interim and top-line data should be viewed with caution until the final data are available. Material adverse changes in the final data compared to the interim data could significantly harm our business prospects. Moreover, preliminary, interim and top-line data are subject to the risk that one or more of the clinical outcomes may materially change as more patient data become available when patients mature on study, patient enrollment continues or as other ongoing or future clinical trials with a product candidate further develop. For example, consistent with the FDA's recommendation, certain of our clinical trials include a 15 year follow-up observation period in which we will continue to collect patient data.

The information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically more extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. Similarly, even if we are able to complete our planned preclinical studies or any future clinical trials of our product candidates according to our current development timeline, the positive results from such preclinical studies and clinical trials of our product candidates may not be replicated in subsequent preclinical studies or clinical trial results.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. Similarly, many companies in the pharmaceutical and biotechnology industries have failed to receive regulatory approval despite completing registrational trials. These setbacks have been caused by, among other things, preclinical and other nonclinical findings made while clinical trials were underway or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical, nonclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA or EMA approval.

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 Product Candidates We May Develop. 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, Product Candidates We May Develop, And Our Ability To Generate Revenue Will Be Materially Impaired.

Any product candidates we may develop 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, by EMA in the EU 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. While CASGEVY has received approval or clearance to be marketed from certain regulatory authorities in certain jurisdictions, it is possible that none of our other product candidates or any product candidates we may seek to develop, alone or in conjunction with collaborators, in the future will ever obtain regulatory approval or clearance or that we and Vertex will receive additional marketing approvals for CASGEVY. For example, while we have multiple product candidates in clinical development and advanced preclinical development for a range of diseases, we have not yet submitted BLAs to the FDA or similar marketing applications to comparable foreign authorities for any of our other product candidates.

We have limited experience in submitting and supporting the applications necessary to gain regulatory and marketing approvals. We expect to rely on third-party contract research organizations, or CROs, and/or regulatory consultants to assist us in this process for our wholly-owned product candidates and, pursuant to our Amended A&R Vertex JDCA, we have relied on Vertex for submitting such applications for our hemoglobinopathies product candidates. Submission of a BLA or other similar marketing applications to comparable foreign authorities and 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, efficacy and potency, also known as safety and effectiveness, for each desired therapeutic indication. A BLA must also include significant information regarding the chemistry, manufacturing and controls for the product candidate. 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.

In general, the FDA requires the successful completion of two pivotal trials to support approval of a BLA, but in certain circumstances, will approve a BLA based on only one pivotal trial; and our ability to submit and obtain approval of a BLA is

ultimately an FDA review decision, which will be dependent upon the data available at such time, and the available data may not be sufficiently robust from a safety and/or efficacy perspective to support the submission or approval of a BLA. For example, there is no assurance that data obtained at the completion of any of our clinical trials, including for our ongoing wholly-owned product candidates, will indicate clinically meaningful benefit or support submission of a BLA, or will be sufficiently robust from a safety and/or efficacy perspective to support either accelerated or conditional approval or full approval. Moreover, there is no assurance that the data obtained to date in the ongoing clinical trials of CASGEVY and being submitted or planned to be submitted is or will be sufficiently robust from a safety and/or efficacy perspective to support either accelerated or conditional approval or full approval of a BLA or a foreign equivalent in all jurisdictions for which regulatory applications are submitted. Depending on the outcome of these ongoing clinical trials and robustness of the data submitted, once submitted, the FDA may require that we conduct additional or larger pivotal trials before we can submit or obtain approval of a BLA. Furthermore, if any undesirable or unacceptable side effects, unexpected characteristics or other serious adverse events occur, and if we are unable to demonstrate such adverse events were caused by factors other than our product candidate, the FDA could suspend our clinical trial until we are able to gather sufficient information or order us to cease further clinical studies of our product candidate. If this were to occur this would likely result in delays in our ability to submit a BLA for regulatory approval. We may face similar challenges with foreign regulatory authorities.

Furthermore, failure of one or more clinical trials can occur at any stage in the clinical trial process. Any product candidates we develop 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. Accordingly, the regulatory pathway for our product candidates is still uncertain, complex, and lengthy, and ultimately, approval may not be obtained. Even if our product candidates demonstrate safety and efficacy in clinical studies, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development.

The process of obtaining marketing approvals, both in the United States and in other foreign jurisdictions, 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 are 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 product not commercially viable.

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

We May Never Obtain FDA Approval For Any Of Our Wholly-Owned Product Candidates In The United States, And Even If We Do, We May Never Obtain Approval For Or Commercialize Any Of Our Wholly-Owned Product Candidates In Any Other Jurisdiction, Which Would Limit Our Ability To Realize Their Full Market Potential.

In order to eventually market any of our product candidates in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a jurisdiction-by-jurisdiction basis regarding safety and efficacy. Approval by the FDA in the United States, if obtained, does not ensure approval by regulatory authorities in other countries or jurisdictions. Similarly, approval by foreign regulatory authorities does not ensure approval by the FDA. In addition, data from clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking regulatory approval in multiple jurisdictions could result in difficulties and costs for us and require additional preclinical studies or clinical trials which could be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in certain countries. Regulatory approval processes outside the United States involve all of the risks associated with FDA approval. We do not have any wholly-owned product candidates approved for sale in any jurisdiction, including international markets, and, as a company, do not have experience in being solely responsible for obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

Breakthrough Therapy Designation, Fast Track Designation, Regenerative Medicine Advanced Therapy Designation or Priority Review by the FDA, or PRIME Scheme by the EMA, Even If Granted for Any of Our Product Candidates, May Not Lead to a Faster Development, Regulatory Review or Approval Process, and It May Not Increase the Likelihood That Any of Our Product Candidates Will Receive Marketing Approval.

We may seek a Breakthrough Therapy Designation for some of our product candidates. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to therapies 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 qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

We have obtained and may seek Fast Track Designation for some of our product candidates. For instance, CASGEVY was granted Fast Track Designation by the FDA for the treatment of TDT and SCD. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. 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 marketing application before the application is complete. However, the FDA's time period goal for reviewing an application does not begin until the last section of the application is submitted. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track Designation alone does not guarantee qualification for the FDA's priority review procedures.

We have obtained and may seek RMAT designation for some of our product candidates. For instance, CASGEVY was granted RMAT designation by the FDA for the treatment of TDT and SCD, as well as zugo-cel for the treatment of relapsed or refractory follicular lymphoma and marginal zone lymphoma. There is no assurance that we will be able to obtain RMAT designation for other of our product candidates. RMAT designation does not change the FDA's standards for product approval, and there is no assurance that such designation will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the designation. Additionally, RMAT designation can be revoked if the criteria for eligibility cease to be met as clinical data emerges.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, 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. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

Finally, we have obtained and may seek to qualify our product candidates under the PRIME scheme from the EMA. For instance, CASGEVY was granted PRIME designation for the treatment of TDT and SCD. There is no assurance that we will be able to obtain PRIME qualification for other of our product candidates. PRIME does not change the standards for product approval, and there is no assurance that such qualification will result in expedited review or approval. Moreover, where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

For additional information regarding Breakthrough Therapy Designation, Fast Track Designation, RMAT Designation and priority review by the FDA, see the section entitled, “Business—Government Regulation—Licensure and Regulation of Biologics in the United States – Expedited Programs.” For additional information regarding the PRIME scheme from the EMA, see the section entitled “Business—Government Regulation—Regulation and Procedures Governing Approval of Medicinal Products in Europe – PRIME scheme.”

We May Seek Designation For Our Platform Technology As A Designated Platform Technology, But We Might Not Receive Such Designation, And Even If We Do, Such Designation May Not Lead To A Faster Regulatory Review Or Approval Process.

We may seek designation for our platform technology as a designated platform technology. Under FDORA, a platform technology incorporated within or utilized by a drug or biological product is eligible for designation as a designated platform technology if (1) the platform technology is incorporated in, or utilized by, a drug approved under a BLA; (2) preliminary evidence submitted by the sponsor of the approved or licensed drug, or a sponsor that has been granted a right of reference to data submitted in the application for such drug, demonstrates that the platform technology has the potential to be incorporated in, or utilized by, more than one drug without an adverse effect on quality, manufacturing, or safety; and (3) data or information submitted by the applicable person indicates that incorporation or utilization of the platform technology has a reasonable likelihood to bring significant efficiencies to the drug development or manufacturing process and to the review process. A sponsor may request the FDA to designate a platform technology as a designated platform technology concurrently with, or at any time after, submission of an IND application for a drug that incorporates or utilizes the platform technology that is the subject of the request. If so designated, the FDA may

expedite the development and review of any subsequent original BLA for a drug that uses or incorporates the platform technology. Even if we believe our platform technology meets the criteria for such designation, the FDA may disagree and instead determine not to grant such designation. In addition, the receipt of such designation for a platform technology does not ensure that a drug will be developed more quickly or receive FDA approval. Moreover, the FDA may revoke a designation if the FDA determines that a designated platform technology no longer meets the criteria for such designation.

We May Be Unable To Obtain Orphan Drug Designation Or Exclusivity. If Our Competitors Are Able To Obtain Orphan Drug Exclusivity For Products That Constitute The Same Drug And Treat The Same Indications As Our Product Candidates, We May Not Be Able To Have Competing Products Approved By The Applicable Regulatory Authority For A Significant Period Of Time.

We have received orphan drug designation in the United States from the FDA for certain of our programs and the European Commission for certain of our programs or partnered programs, including for CASGEVY for the treatment of TDT and SCD. We may in the future seek orphan drug designation for certain of our other product candidates, but we may be unable to maintain orphan drug designation or obtain any benefits associated with orphan drug designation, including market exclusivity.

Certain of our current product candidates and our future product candidates may target patient populations that are smaller than the numbers required for orphan drug designation. If we request orphan drug designation for our product candidates, there can be no assurances that FDA or the European Commission will grant any of our product candidates such designation. Additionally, the designation of any of our product candidates as an orphan product does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation 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 authorization application for a product that constitutes the same drug (or, in the EU, a "similar medicinal product") treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the European Union. The exclusivity period in the United States can be extended by six months if the sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The exclusivity period in the European Union can be extended by two years for medicines that have complied with an agreed pediatric investigation plan prior to authorization of the product. The exclusivity period in the European Union can also 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 designation, because, for example, the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be withdrawn if the relevant regulatory authority 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 patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug, including if it is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication as an authorized orphan product if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

There is no assurance that we will be able to obtain orphan drug designation for other of our other product candidates. Orphan drug designation does not change the standards for product approval, and there is no assurance that such designation will result in expedited review or approval.

For additional information regarding orphan drug designation in the United States, see the section entitled, "*Business — Government Regulation — Licensure and Regulation of Biologics in the United States – Orphan Drug Designation."* For additional information regarding orphan drug designation in the European Union, see the section entitled "*Business — Government Regulation — Regulation and Procedures Governing Approval of Medicinal Products in Europe – Orphan Drug Designation and Exclusivity."*

We Expect The Product Candidates We Develop Will Be Regulated Biologics And Therefore They May Be Subject To

Competition Sooner Than Anticipated.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Affordable Care Act 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, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. 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. While it is uncertain when processes intended to implement BPCIA may be fully adopted by the FDA, any of these processes 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 that is approved in the United States 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 generic 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 is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In addition, the approval of a biologic product biosimilar to one of our products could have a material adverse impact on our business as it may be significantly less costly to bring to market and may be priced significantly lower than our products.

While We May Seek Accelerated Approval For Some Of Our Product Candidates, We May Not Be Able To Obtain It As The Sufficiency Of Our Clinical Trial Results For Accelerated Approval Are Subject To The FDA's Discretion.

We plan to seek approval for some of our product candidates under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. For more information, see the section of this report entitled "Business—Government Regulation—Licensure and Regulation of Biologics in the United States—Accelerated Approval Pathway.

There can be no assurance that the FDA would allow any of the product candidates we may develop to proceed on an accelerated approval pathway, and even if the FDA did allow such pathway, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. Moreover, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. The FDA may further withdraw approval of a drug or biologic granted accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit. Accordingly, even if we received accelerated approval, any post-approval studies required to confirm and verify clinical benefit may not show such benefit, which could lead to withdrawal of any approvals we have obtained. Receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

Adverse Public Perception Of Gene Editing And Cellular Therapy Products May Negatively Impact Demand For, Or Regulatory Approval Of, Our Product Candidates.

Our product candidates involve editing the human genome. The clinical and commercial success of our product candidates will depend in part on public acceptance of the use of gene editing therapies for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene editing is unsafe, unethical, or immoral, and, consequently, our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements of gene editing products, including any of our product candidates, and could cause a decrease in the demand for any products we may develop. 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 may 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 particular, gene editing technology is subject to public debate and heightened regulatory scrutiny due to ethical concerns relating to the application of gene editing technology to human embryos or the human germline. Public attitudes may be influenced by claims that gene editing is unsafe, unethical, or immoral, and, consequently, our product candidates 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 may 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.

Although we do not use our technologies to edit human embryos or the human germline, such public debate about the use of gene 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. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing gene editing technologies, even if not ultimately attributable to product candidates we may identify and develop, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of potential product candidates we may identify and develop, stricter labeling requirements for those product candidates that are approved, and a decrease in demand for any such product candidates.

If We Are Unable To Establish Sales And Marketing Capabilities Or Enter Into Agreements With Third Parties To Sell And Market Products Based On Our Technologies, We May Not Be Successful In Commercializing Our Products If And When Any Products Candidates Are Approved And We May Not Be Able To Generate Any Revenue.

We do not currently have a sales or marketing infrastructure and, as a company, have no experience in the sale, marketing or distribution of therapeutic products. To achieve commercial success for any approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates, if any are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force 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 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 sales and marketing personnel.

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

- our inability to recruit, train 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 product that we may develop;
- the lack of complementary treatments 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 sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability to us from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. For example, pursuant to our Amended A&R Vertex JDCA, Vertex has the right to conduct all commercialization activities relating to CASGEVY throughout the world and net profits and net losses, as applicable, incurred under the agreement with respect to CASGEVY are allocated 40% to CRISPR and 60% to Vertex. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will 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 product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing our product candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

Even If We, Or Any Collaborators We May Have, Obtain Marketing Approvals For Any Product Candidates We Develop, 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, or any collaborators we may have, obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such product, 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, current Good Manufacturing Practice, or cGMP, requirements relating to quality control, quality assurance and corresponding maintenance of records and documents and requirements regarding 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 product 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 product. The FDA also may place other conditions on approvals including the requirement for a REMS to assure the safe use of the product. If the FDA concludes a REMS is

needed, the sponsor of the BLA, must submit a proposed REMS before it can obtain approval. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Accordingly, assuming we, or any collaborators we may have, receive marketing approval for one or more product candidates we develop, we, and such collaborators, and our and their third-party contract manufacturers will continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, and quality control. In addition, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

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.

Any Product Candidate For Which We, Or Any Collaborators We May Have, Obtain Marketing Approval Could Be Subject To Restrictions Or Withdrawal From The Market, And We Or They May Be Subject To Substantial Penalties If We Or They Fail To Comply With Regulatory Requirements Or If We Or They Experience Unanticipated Problems With Our Products, When And If Any Of Them Are Approved.

The FDA and other regulatory agencies closely regulate the post-approval marketing and promotion of biologics 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, or any collaborators we may have, do not market our products for their approved indications, we or they may be subject to enforcement action for off-label marketing by the FDA and other federal and state enforcement agencies, including the United States Department of Justice. Violation of the Federal Food, Drug, 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 a product candidate, including adverse events of unanticipated severity or frequency, or with our or other collaborators' manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on such products, manufacturers, or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on the distribution or use of a product;
- requirements to conduct post-marketing clinical trials;
- receipt of warning or untitled letters;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory biologic recalls;
- refusal to approve pending applications or supplements to approved applications that we or our collaborators submit;
- fines, restitution, or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals or revocation of biologics licenses;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our products;
- product seizure or detention; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, we or our collaborators may lose any marketing approval that we or our collaborators may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Any government investigation of alleged violations of law, including investigations of any of our vendors, 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 also inhibit our or our collaborators' ability to commercialize any product candidates we may develop and adversely affect our business, financial condition, results of operations, and prospects.

The Commercial Success Of Any Of Our Products or Product Candidates Will Depend Upon Its Degree Of Market Acceptance By Healthcare Providers, Patients, Third-party Payors And Others In The Medical Community.

Ethical, social and legal concerns about gene therapy could result in additional regulations restricting or prohibiting our products. Even with the requisite approvals from FDA in the United States, the European Commission in the EU and other regulatory authorities internationally, the commercial success of our products or product candidates will depend, in significant part, on the acceptance of healthcare providers, patients and health care payors of gene therapy products in general, and our products or product candidates in particular, as medically necessary, cost-effective and safe. Any product that we commercialize may not gain acceptance by healthcare providers, patients, health care payors and others in the medical community. The degree of market acceptance of gene therapy products and, in particular, our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in any future clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by FDA, the European Commission or other regulatory authorities;
- patient awareness of, and willingness to seek, genotyping;
- the willingness of healthcare providers to prescribe new therapies and the target patient population to try new therapies;
- our and our partners efforts to educate healthcare providers and patients about our products;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of 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 strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- adverse publicity concerning our products or competing products and treatments, including social and ethical controversies in the field of gene editing;
- establishment of authorized treatment centers;
- sufficient third-party payor coverage and reimbursement; and
- approval of new products or technologies that are more favorably received than our products, are more cost effective or render our products obsolete.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and future clinical trials, market acceptance of the product will not be fully known until after it is launched. If our product candidates do not achieve an adequate level of acceptance following regulatory approval, if ever, we may not generate significant product revenue and may not become profitable.

We Face Significant Competition In The Biotechnology And Pharmaceutical Industries.

The biotechnology and pharmaceutical industries, including in the gene editing, gene therapy 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 currently face, and will continue to face, substantial competition from many different sources, including large pharmaceutical, specialty pharmaceutical and biotechnology companies; academic institutions and governmental agencies; and public and private research institutions, some or all of which may have greater access to capital or resources than we do. For any products that we may ultimately commercialize, not only will we compete with any existing therapies and those therapies currently in development, but we will also have to compete with new therapies that 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 gene editing and gene therapy, nucleic acid therapies, and cell therapy. In addition, we compete with companies working to develop therapies in areas related to our specific research and development programs. Our platform and product focus is on the development of therapies using gene-based technology, including CRISPR/Cas9, as well as other technologies, including next-generation editing technologies for targeted gene correction and gene insertion with non-viral delivery approaches. For a detailed discussion of the competition that we face with respect to our business,

including our platform, product indications, other technologies (e.g. small molecule, antibody, or protein therapies), gene editing technology, gene or cell therapies, intellectual property, new technologies, personnel, clinical trial locations, reimbursement opportunities and collaborators, please see the section entitled "*Business—Competition*". If we are unable to compete successfully in this highly competitive biopharmaceutical industry, our business, financial condition and results of operations could be materially adversely affected.

Even 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 biologic products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some non-U.S. 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 product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Third-party payors, such as private health insurers, health maintenance organizations, and governmental programs such as Medicare and Medicaid, 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. Governmental and private third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. 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 product 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 products, and reimbursement coverage may be more limited than the purposes for which the product is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any product 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 products, 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 product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products 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 products 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 products we may develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition. For additional information, see the sections entitled "Business—Coverage, Pricing and Reimbursement" and "Business—Healthcare Reform." See also, "*Risk Factors—Risks Related to Our Relationships with Third Parties—We Have Partnered With Vertex On Our Lead Program CASGEVY; Vertex Has Significant Control Over The CASGEVY Program.*"

Risks Related to Our Relationships with Third Parties

We Have Partnered With Vertex On Our Lead Program CASGEVY; Vertex Has Significant Control Over The CASGEVY Program.

Subject to the terms and conditions of the Amended A&R Vertex JDCA, Vertex has the right to conduct all research, development, manufacturing and commercialization activities relating to specified product candidates and products (including CASGEVY) throughout the world subject to our reserved rights to participate in certain aspects of such activities in an observer capacity and conduct certain other activities. Therefore, Vertex controls the development and commercialization of CASGEVY and certain future hemoglobinopathies product candidates that are subject to the Amended A&R Vertex JDCA, including, for example, clinical development, manufacturing, regulatory submission and commercialization activities for CASGEVY and any other future hemoglobinopathies product candidate. As a result, we do not control the timing of and completion of IND and BLA filings or other applicable regulatory or required pricing approvals, including foreign equivalents, for the product candidates, including CASGEVY,

under the Amended A&R Vertex JDCA. This could cause delays or difficulties in the development and commercialization of certain product candidates, including CASGEVY, and have a material adverse effect on our business, financial condition, results of operations, and prospects.

We must rely on Vertex to manufacture and commercialize CASGEVY. For example, the manufacture of cell and genetic therapies requires significant expertise, and even with the relevant experience and expertise, manufacturers of cell and genetic therapy products often encounter difficulties in production, including difficulties with production costs and yields, quality control, and compliance with federal, state and foreign regulations. We cannot make any assurances that Vertex will not encounter any of these problems or that it will be able to resolve or address problems that occur in a timely manner, or at all. In addition, to increase production to commercial levels, Vertex is making significant investments to coordinate manufacturing, testing, and logistics activities at a larger scale across multiple facilities to serve the geographies in which CASGEVY is approved. We cannot make any assurances that Vertex will be able to increase production to commercial levels in a timely manner, or at all. In addition, we must rely on Vertex to obtain pricing approvals in certain jurisdictions, establish and maintain relationships with authorized treatment centers that will be treating the patients who receive CASGEVY, and manage manufacturing capabilities and supply chain operations in the coordination and delivery of CASGEVY to patients at such authorized treatment centers. We have no involvement in these and other commercialization efforts for CASGEVY from which we may receive revenue and cannot control the extent or effectiveness of such commercialization efforts. Our revenues from CASGEVY may fall below our expectations and the expectations of our shareholders, which could have a material adverse effect on our results of operations and the market price of our common shares.

Subject to the terms set forth in the A&R Vertex JDCA, we are obligated to share equally the net profits and net losses, as applicable, incurred under the Amended A&R Vertex JDCA with respect to all product candidates and products specified in the A&R Vertex JDCA other than for CASGEVY. With respect to CASGEVY only, beginning in July 2021, the net profits and net losses are allocated 40% to CRISPR and 60% to Vertex. Vertex has had and may again have additional expenditures related to the CASGEVY program or other programs under the Amended A&R Vertex JDCA that we cannot predict and that we will be required to pay our portion of or agree to pay a portion of in the future pursuant to the terms of the agreement. For example, under certain circumstances, either party can propose to in-license intellectual property that it believes is necessary or commercially reasonable to obtain to develop and commercialize CASGEVY or future hemoglobinopathies product candidates that are subject to the Amended A&R Vertex JDCA, and any costs associated with acquiring such intellectual property rights would be shared by the parties in accordance with the terms of the Amended A&R Vertex JDCA. Moreover, under the Amended A&R Vertex JDCA, for the years ended December 31, 2022, 2023 and 2024, we had the option to defer and did defer costs on the CASGEVY program in excess of $110.3 million annually, subject to certain adjustments under certain circumstances. Beginning in 2025, we no longer have the option to defer such costs on the CASGEVY program. As a result, our expenses in 2025 related to the CASGEVY program are significantly greater than in 2022, 2023 and 2024 as a result of Vertex's commercialization efforts for CASGEVY and may be significantly greater than in 2022, 2023 and 2024 in the future.

Disagreements between us and Vertex regarding the development, manufacture and commercialization of CASGEVY or future hemoglobinopathies product candidates that are subject to the Amended A&R Vertex JDCA could lead to delays and, in some cases, result in litigation or arbitration, which would be time-consuming and expensive. If we materially breach the Amended A&R Vertex JDCA, we are forced to opt-out or such agreement is otherwise terminated, we would be prevented from receiving any milestone, royalty payments and other benefits under such agreement, which could have a materially adverse effect on our results of operations and the market price of our common shares.

CASGEVY For SCD Has Received A Commissioner's National Priority Voucher. The Benefits Of Such A Voucher, Including A Potentially Accelerated Timeline For Review Of Any [sBLA] Submission For CASGEVY For SCD By The FDA, May Not Be Able To Be Fully Realized.

In June 2025, the FDA announced the creation of a new program, the Commissioner's National Priority Voucher, or CNPV, program, to expedite the development and approval of drug and biological products with potential to address a major national priority, such as addressing a large unmet medical need, reducing downstream health care utilization, addressing a public health crisis, boosting domestic manufacturing, or increasing medication affordability. The FDA has stated that voucher recipients will receive a decision with respect to a drug or biological product marketing application on an accelerated basis, as well as enhanced communication with review staff throughout the development process prior to final submission of the application and during the review period. For additional information regarding the CNPV program, see the section entitled "Business-Government Regulation-Licensure and Regulation of Biologics in the United States-Expedited Programs."

On November 6, 2025, the FDA announced that CASGEVY for SCD was awarded a CNPV. As a result, the [sBLA] for CASGEVY for SCD is eligible for the benefits of this program. However, receipt of the CNPV does not guarantee that any [sBLA] will be approved on an expedited basis or at all. The FDA has stated that the review time for an application of a CNPV recipient may be extended, including because the application is incomplete, if the results of pivotal trial(s) are ambiguous, or, if the review is particularly complex. The CNPV program is in pilot stage, so its implementation, operation, and ultimate impact or benefits are subject to uncertainty.

Our Collaborators And Strategic Partners May Control Aspects Of Our Clinical Trials and Commercialization Efforts, Which Could Result In Delays And Other Obstacles In The Commercialization Of Our Proposed Products And Materially Harm Our Results Of Operations.

We have entered into strategic collaborations and license agreements and may enter into additional collaborations and license agreements with third parties in the future. For example, we have entered into a series of agreements with Vertex that contemplate certain research, development, manufacturing and commercialization activities involving various targets. Pursuant to these agreements, Vertex has sole authority to conduct certain activities. For instance, under our 2015 Collaboration Agreement with Vertex, Vertex had sole authority to select genetic targets to pursue and we do not have control over the development of any product candidates for the selected genetic targets. Some of these collaborations and license agreements provide us with important technologies in order to more fully develop our product candidates and we may enter into collaborations and license agreements with third parties in the future to provide us with important technologies or funding for our programs. The success of these arrangements will depend heavily on the efforts and activities of our collaborators and licensing partners.

Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations and collaborators may not perform their obligations as expected. For some programs, we also depend on, or may in the future depend on, third-party collaborators and strategic partners to design and conduct our clinical trials, and for any approved products, the commercialization of such products. In some situations, we may not be able to influence our collaboration partners' decisions regarding the development and commercialization of our partnered product candidates, and as a result, our collaboration partners may not pursue or prioritize the development and commercialization of those partnered product candidates in a manner that is in our best interest or may not be fiscally disciplined in their execution. For example, certain of our agreements allow for the parties under certain circumstances to in-license intellectual property that such believes is necessary or commercially reasonable to obtain to develop and commercialize applicable product candidates, and any costs associated with acquiring such intellectual property rights would be shared by the parties in accordance with the terms of the applicable collaboration or license agreement. Disagreements between parties to a collaboration arrangement regarding clinical development, manufacturing and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement or result in litigation or arbitration, which would be time-consuming and expensive. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception and reputation in the business and financial communities could be adversely affected.

Our lack of control over the clinical development, manufacturing, regulatory submission and commercialization activities in certain of our agreements, including our agreements with Vertex, could cause delays or other difficulties in the development and commercialization of product candidates, including CASGEVY, which may prevent among other things, completion of intended IND filings in a timely fashion, if at all, or the completion of or cause a delay in BLA filings or other applicable regulatory or required pricing approvals. Collaborators may also fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product. As a result of the foregoing, we may not be able to conduct any of our partnered programs in the manner, within budget or on the time schedule we currently contemplate, which may negatively impact our business operations. In addition, if any of these collaborators or strategic partners withdraw support for our programs or proposed products or otherwise impair their development or commercialization, our business could be negatively affected. While we include contractual provisions in certain of our collaboration and license agreements to protect our product candidates, we cannot provide any assurances that our collaborators will not independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if such collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.

Licensors generally have sole discretion in determining the efforts and resources that they will apply to the licensed products. In addition, if any of these licensors withdraw support for licensed programs or proposed products or otherwise impair their development or commercialization, our business could be negatively affected. Additionally, if one of our licensors terminates its agreement with us, we may find it more difficult to attract new license partners and our perception in the business and financial communities could be adversely affected.

If Conflicts Arise Between Us And Our Collaborators Or Strategic Partners, These Parties May Act In A Manner Adverse To Us And Could Limit Our Ability To Implement Our Strategies.

If conflicts arise between our corporate or academic licensors, collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates.

In addition, current or future collaborators or strategic partners could also become our competitors in the future. Our

collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts.

Our Collaborators Or Strategic Partners May Decide To Adopt Alternative Technologies Or May Be Unable To Develop Commercially Viable Products With Our Technology, Which Would Negatively Impact Our Financial Results And Our Strategy To Develop These Products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of our gene-editing technology, including CRISPR/Cas9, or other technologies. Additionally, because our current collaborators or strategic partners are and we anticipate that any future collaborators or strategic partners will be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our technology, including CRISPR/Cas9 gene editing technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. For example, ViaCyte (a wholly-owned subsidiary of Vertex) elected to opt-out of our diabetes collaboration in 2023. As a result, following such opt-out, we are solely responsible for the costs associated with our diabetes program and we will owe ViaCyte certain opt-out royalties pursuant to the ViaCyte JDCA, which will increase our expenses. Furthermore, the failure to develop and commercialize a product candidate pursuant to our agreements with our current or future collaborators would prevent us from receiving future milestone and royalty payments which would negatively impact our financial results.

We May Seek To Establish Additional Collaborations And, If We Are Not Able To Establish Them On Commercially Reasonable Terms, We May Have To Alter Our Development And Commercialization Plans.

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

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any additional collaborations 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 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 drugs, 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 for our product candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, we have granted exclusive rights to Vertex for certain genetic targets, and during the term of the collaboration agreements, we will be restricted from granting rights to other parties to use our gene editing technology to pursue therapies that address these genetic targets. The non-competition provisions in such agreements could limit our ability to enter into strategic collaborations with future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. Collaborations are 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. If we are unable to negotiate and enter into new collaborations, 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 our product candidates or bring them to market and generate product revenue or engage in workforce reductions to save capital.

We Rely On and Expect To Rely On Third Parties To Conduct Our Clinical Trials And Certain Aspects Of Our Preclinical Studies For Our Product Candidates. If These Third Parties Do Not Successfully Carry Out Their Contractual Duties, Comply With Regulatory Requirements Or Meet Expected Deadlines, We May Not Be Able To Obtain Regulatory Approval For Or Commercialize

Our Product Candidates And Our Business Could Be Substantially Harmed.

We expect to rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct future clinical trials and we currently rely on third parties to conduct certain aspects of our preclinical studies and clinical trials for our product candidates. Nevertheless, we are responsible for ensuring that each of our preclinical studies, clinical trials and any future preclinical studies and clinical trials we sponsor are conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on CROs or other third parties will not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each such study or clinical trial is conducted in accordance with the general investigational plan and protocols for such study or trial. Moreover, the FDA requires us to comply with regulations, commonly referred to as Good Clinical Practices, or GCPs, 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. For any violations of laws and regulations during the conduct of our preclinical studies and clinical trials, we could be subject to warning letters or enforcement action that may include civil penalties up to and including criminal prosecution. We also rely on and expect to continue to rely on third-party contract manufacturing organizations to produce certain of our clinical trial materials. See, for example, "*Risk Factors--Risks Related to Manufacturing--We Expect To Rely On Third Parties To Manufacture Our Clinical Product Supplies, And We Intend To Rely On Third Parties For At Least A Portion Of The Manufacturing Process Of Our Product Candidates. Our Business Could Be Harmed If The Third Parties Experience Supply Chain Shortages, Fail To Provide Us With Sufficient Quantities Of Product Inputs Or Fail To Do So At Acceptable Quality Levels Or Prices"* for additional information.

We and our CROs are and will continue to be required to comply with regulations, including GCPs, for conducting, monitoring, recording and reporting the results of preclinical studies and clinical trials to ensure that the data and results are scientifically credible and accurate and that the trial patients are adequately informed, among other things, of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable regulatory authorities for any drugs in clinical development. The FDA enforces GCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and FDA or comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCPs. In addition, our future clinical trials must be conducted with product candidates produced in accordance with the requirements in cGMP regulations. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action and require significantly greater expenditures.

Although we generally design the clinical trials for our product candidates and intend to design the clinical trials for our future product candidates, CROs conduct and will continue to conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future preclinical studies and clinical trials will also result in less direct control over the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our preclinical studies and clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform preclinical studies and future clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, regulatory approval and commercialization of our product candidates may be delayed, we may not be able to obtain regulatory approval and commercialize our product candidates, or our development programs may be materially and irreversibly harmed. If we are unable to rely on preclinical and clinical data collected by our CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct and this could significantly delay commercialization and require significantly greater expenditures.

Our Relationships With Healthcare Providers, Physicians, And Third-party Payors Are Subject To Applicable Anti-kickback, Fraud And Abuse And Other Healthcare Laws And Regulations, Which Could Expose Us To Criminal Sanctions, Civil Penalties, Exclusion From Government Healthcare Programs, Contractual Damages, Reputational Harm And Diminished Profits And Future

Earnings.

To the extent that we commercialize product candidates or provide support and assistance to collaborators who commercialize medical products, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the U.S. federal government and states as well as other national, regional or local governments in other jurisdictions in which we conduct our business.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any products or product candidates that we may develop for which we obtain marketing approval. Our current and 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 product candidates for which we obtain marketing approval. See the section entitled "*Business—Healthcare Law and Regulation*."

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. 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, including activities that may be conducted by sales and marketing team we establish, 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 is 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.

Risks Related to Manufacturing and Supply

Gene Editing and Gene Silencing Products Are Novel And May Be Complex And Difficult To Manufacture. We Could Experience Manufacturing Problems Or Regulatory Requirements That Result In Delays In The Development, Approval Or Commercialization Of Our Product Candidates Or Otherwise Harm Our Business.

The manufacturing process used to produce *ex vivo* engineered cell therapies and *in vivo* genome editing products based on gene-editing technology, including CRISPR/Cas9, as well as siRNA product candidates are novel, may be complex, and there is limited industry experience implementing and executing such processes to meet clinical and commercial production demand. Several factors could cause production interruptions, including inability to develop novel manufacturing processes, equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, including pandemics, disruption in utility services, human error or disruptions in the operations of our suppliers, including acquisition of a supplier by a third party or declaration of bankruptcy. The expertise required to manufacture these product candidates may be unique to a particular third-party contract manufacturing organization, and as a result, it would be difficult and time consuming to find an alternative third-party contract manufacturing organization. Failure or process defects in any of the interrelated systems at either our manufacturing facility or those of our third-party manufacturers, could adversely impact our ability to manufacture and supply cell therapy product candidates and certain components thereof intended for research, clinical and, if approved, commercial production. In addition, we may rely on third-party contract manufacturers outside the United States for certain components of our product candidates, and may be subject to importation regulations that may affect our ability to manufacture or increase the cost of our product candidates.

Our product candidates require and will continue to require processing steps that are more complex than those required for most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of biologics generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product or product candidate will perform in the intended manner. Accordingly, we will employ multiple steps to control the manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. 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, or other supply disruptions. If microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities in which our product candidates are made, production at such manufacturing facilities may be interrupted for an extended period of time to investigate and remedy the contamination. We may encounter problems achieving adequate quantities and quality of clinical grade materials that meet FDA, the EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA, the EMA and other health 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 relevant 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 could cause us to delay product launches or clinical trials and we may need to conduct product recalls, all of which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products or supply our clinical trials.

We also may encounter problems hiring and retaining directly or through third-party contract manufacturing organizations the experienced scientific, quality assurance, quality control and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements. Any problems in our supply chain, manufacturing process or facilities could result in delays in planned clinical trials and increased costs, and 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 our manufacturing process could restrict our ability to meet potential future market demand for products.

Our partner, Vertex, is the manufacturer and exclusive license holder of CASGEVY. For additional information regarding the manufacture of CASGEVY, please see "*Risk Factors—Risks Related to Our Relationships with Third Parties—We Have Partnered With Vertex On Our Lead Program CASGEVY; Vertex Has Significant Control Over The CASGEVY Program*."

The Manufacturing Facilities For Our Product Candidates Are Subject To Rigorous Regulations And Failure To Obtain Or Maintain Regulatory Approvals Or Operate In Line With Established cGMPs And International Best Practices Could Delay Or Impair Our Ability To Commercialize Our Product Candidates.

We and the third-party manufacturers of our product candidates are subject to applicable regulatory requirements, known as current Good Manufacturing Practice, or cGMPs, prescribed by the FDA and other rules and regulations prescribed by the EMA and other regulatory authorities. To obtain FDA and European Commission approval for our product candidates in the United States, Europe and other regions around the world, we need to undergo strict pre-approval inspections of our or our third-party manufacturing facilities. When inspecting our or our contractors' manufacturing facilities, the FDA, competent authorities of the EU Member States or other regulatory authorities might cite cGMP deficiencies, both minor and significant, which we may not be required to disclose. Remediating deficiencies can be laborious and costly and consume significant periods of time. Moreover, if the FDA, competent authorities of the EU Member States or another regulatory authority notes deficiencies as a result of its inspection, it will generally reinspect the facility to determine if the deficiency has been remediated to its satisfaction. The FDA, competent authorities of the EU Member States or other regulatory authorities may note further deficiencies as a result of its reinspection, either related to the previously identified deficiency or otherwise. If we or the manufacturers of our product candidates cannot satisfy the FDA, competent authorities of the EU Member States and other regulatory authorities as to compliance with cGMP on a timely basis, marketing approval for our product candidates could be seriously delayed, which in turn would delay commercialization of our product candidates.

We Are Subject To Regulatory And Operational Risks Associated With Our Internal Manufacturing Facility.

We have an approximately 50,000 square foot cell therapy manufacturing facility in Framingham, Massachusetts intended for clinical and commercial production of our product candidates and certain components thereof for certain of our programs. We are following cGMP processes necessary to release product for certain of our clinical trials and meet all requirements from regulatory agencies, including the FDA, to allow us to support research, clinical and commercial production of our wholly-owned cell therapy product candidates and certain components thereof for certain of our programs. We can provide no assurances that we will be able to support or operate our facility to support our intended internal manufacturing capabilities and/or needs or comply with regulatory agency requirements. While the design of our facility is based on current standards for biotechnology facilities, the facility has not yet been inspected by any regulatory agency such as the FDA. In constructing our facility in Framingham, Massachusetts, we have incurred substantial expenditures, and expect to incur significant additional expenditures operating our facility in the future.

We Expect To Rely On Third Parties To Manufacture Our Clinical Product Supplies, And We Intend To Rely On Third Parties For At Least A Portion Of The Manufacturing Process Of Our Product Candidates. Our Business Could Be Harmed If The Third Parties Experience Supply Chain Shortages, Fail To Provide Us With Sufficient Quantities Of Product Inputs Or Fail To Do So At Acceptable Quality Levels Or Prices. Our Third-Party Contract Manufacturing Partners Are Subject To Regulatory And Operational Risks.

Although we have established internal manufacturing capabilities and have established our own cell therapy manufacturing facility, we still rely on outside vendors to manufacture supplies, critical components and process our product candidates in connection with clinical trials we undertake of such product candidates. We have not yet caused any product candidates to be manufactured or processed on a commercial scale and may not be able to do so for any of our product candidates. We will make changes as we work to optimize the manufacturing process, and we cannot be sure that even minor changes in the process will result in therapies that are safe and effective.

The facilities used to manufacture our product candidates must be evaluated by the FDA, or other regulatory agencies in other jurisdictions, pursuant to inspections that will be conducted after we submit an application to the FDA or other regulatory agencies. We may not control the manufacturing process of, and will be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements for manufacture of our product candidates, as well as critical components for such product candidates. If our third-party contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities or regulatory authorities may cite them for deficiencies, and we may not be able to obtain or may be delayed in obtaining regulatory approval from the FDA or other regulatory authorities for our product candidates. In addition, we have no direct control over the ability of our third-party contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable regulatory authority does not approve these facilities or cites these facilities for deficiencies for the manufacture of our product candidates or if it withdraws any such approval or cites deficiencies in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. In addition, if our third-party contract manufacturers are unable to timely perform or become distracted as a result of actions taken by the FDA or a comparable regulatory authority, we may experience manufacturing delays or may need to find alternative manufacturing facilities, which in each case, would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

In addition, our reliance on a limited number of third-party manufacturers exposes us to a number of risks, including the following:

- we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited;
- a new manufacturer would have to be educated in, or develop substantially equivalent processes for, the production of our product candidates;
- a change in manufacturers or certain changes in manufacturing processes and procedures will require that we conduct a manufacturing comparability study to verify that any new manufacturer or manufacturing processes and procedures will produce our product candidate according to the specifications previously submitted to the FDA or other regulatory authority, and such study may be unsuccessful;
- our third-party contract manufacturers might be unable to timely manufacture our product candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any;
- our third-party contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our third-party contract manufacturers may not perform as agreed, may prioritize other customers, may not devote sufficient resources to our product candidates or may not remain in the contract manufacturing business for the time required to supply our clinical trials or commercial needs;
- manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies or other regulatory authorities to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards and we have no control over third-party manufacturers' compliance with these regulations and standards;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates;
- our third-party contract manufacturers could breach or terminate their agreements with us;
- raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects;
- our third-party contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man-made disasters;
- our third-party contract manufacturers may have unacceptable or inconsistent product quality success rates and yields, and we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel; and
- our third-party contract manufacturers may manufacture defective or otherwise dangerous products that could result in injury to consumers during clinical trials or once commercialized for sale to the public, if not discovered by us.

Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our product candidates by the FDA or other regulatory authorities, result in higher costs or adversely impact commercialization of our product candidates, if approved. In addition, we will rely on third parties to perform certain specification tests on our product candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm and the FDA or other regulatory authority could place significant restrictions on our company until deficiencies are remedied.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Our Business

Our Future Success Depends On Our Ability To Retain Key Executives And To Attract, Retain And Motivate Qualified Personnel.

We are highly dependent on the research and development, clinical, commercial and business development expertise of Dr. Samarth Kulkarni, our Chief Executive Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. 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. The loss of the services of our executive officers or other key employees or consultants could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. If we are unable to retain high quality personnel, our ability to pursue our growth strategy will be limited.

We will also need to recruit and retain qualified scientific, clinical and commercial personnel as we advance the development of our product candidates and product pipeline. We may be unable to hire, train, retain or motivate these key 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, clinical and commercial personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

Swiss Corporate Governance With Respect To Executive Compensation May Affect Our Business.

Swiss corporate law, among other things, (a) requires an annual binding shareholder "say on pay" vote with respect to the compensation of members of our executive management team and board of directors, (b) generally prohibits the making of severance, advance, transaction premiums and similar payments to members of our executive management and board of directors and (c) requires companies to specify various compensation-related matters in their articles of association, thus requiring them to be approved by a shareholders' vote. At our annual general meetings, our shareholders are required to approve the maximum aggregate compensation of our board of directors and our executive management team. Swiss law further provides for criminal penalties against directors and members of executive management in case of non-compliance with certain of the requirements regarding compensation. Such provisions may negatively affect our ability to attract and retain executive management and members of our board of directors.

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, consultants, commercial partners, and principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to the FDA, the EMA, and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and in other jurisdictions, 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. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

If We Fail To Comply With Environmental, Health And Safety Laws And Regulations, We Could Become Subject To Fines Or Penalties Or Incur Costs That Could Harm Our Business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of

hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We Are At Risk of Product Liability And Other Product-Related Claims And Lawsuits, Which Could Cause Us To Incur Substantial Liabilities And Could Limit Commercialization Of Any Product Candidates That We May Develop.

We will face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk of claims and litigation relating to our products if and when we commercially sell any product candidates that we may develop. For example, we may be sued, or claims may be made against us, if our informed consents for subjects or patients in any clinical trials are or are alleged to be inadequate or inaccurate in any way or fail to fully inform subjects or patients of any potential risks involved with their participation or other material or required information. We may also be sued, or claims may be made against us, if our product candidates cause or are perceived or alleged to cause injury, or even death, or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or after sale and use by consumers or when used in conjunction with other medications, even if recommended for such use. Any such product liability claims may include, without limitation, allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, fraud/misrepresentation, inadequate labeling, marketing, or promotional claims or a breach of warranties, among other claims. Claims could also be asserted under state consumer protection laws, common law, or other statutes or regulations.

If we cannot successfully defend ourselves against product liability claims or other claims relating to our products, including without limitation that our products caused injuries or death, we could incur substantial liabilities or be required to limit commercialization of our product candidates, as well as risk corresponding regulatory enforcement action. Even successful defense would require significant financial and management resources. Even if our agreements with any past or future corporate collaborators entitle us to indemnification in whole or in part against losses, such indemnification may not be available or adequate should any claim arise. Regardless of merit or eventual outcome, liability claims may result in, among other things:

- decreased demand or a decline in price for any product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants and inability to enroll future participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- initiation of investigations by regulatory authorities or other regulatory actions or proceedings;
- loss of revenue;
- product recalls, withdrawals or labeling, packaging, marketing or promotional modifications or restrictions;
- diversion of management's time and our resources; and
- the inability to commercialize any product candidates that we may develop.

Although we have obtained product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. Further, we anticipate that we will need to increase our insurance coverage if we successfully commercialize any product candidate. 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. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, or under any indemnification agreements with collaborators, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

If We Fail To Establish And Maintain Proper And Effective Internal Control Over Financial Reporting, Our Operating Results And Our Ability To Operate Our Business Could Be Harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. We are required to comply with the requirements of The Sarbanes-Oxley Act of 2002, or SOX, which requires that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation, document our controls and perform testing of our key control over financial reporting to allow management and our independent public accounting firm to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of SOX. Our testing, or the subsequent testing by our independent public accounting firm, may reveal deficiencies in our

internal control over financial reporting that are deemed to be material weaknesses. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock would likely decline and we could be subject to lawsuits, sanctions or investigations by regulatory authorities, which would require additional financial and management resources.

We continue to invest in more robust technology and in more resources in order to manage those reporting requirements. Implementing the appropriate changes to our internal controls may distract our officers and employees, result in substantial costs if we implement new processes or modify our existing processes and require significant time to complete. Any difficulties or delays in implementing these controls could impact our ability to timely report our financial results. In addition, we currently rely on a manual process in some areas which increases our exposure to human error or intervention in reporting our financial results. For these reasons, we may encounter difficulties in the timely and accurate reporting of our financial results, which would impact our ability to provide our investors with information in a timely manner. As a result, our investors could lose confidence in our reported financial information, and our stock price could decline.

In addition, any such changes do not guarantee that we will be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy could prevent us from accurately reporting our financial results. Also, please see, "*Risk Factors--Risks Related to Information Security and Data Privacy--Our Internal Computer Systems, Or Those Of Our Collaborators Or Other Contractors Or Consultants, May Fail Or Suffer Security Breaches, Which Could Result In A Material Disruption Of Our Product Development Programs."*

Our Business Operations Have a Substantial International Footprint and We May Further Expand In The Future, Which Presents Challenges In Managing Our Business Operations.

We are headquartered in Zug, Switzerland and have offices in the United States. In addition, we may expand our international operations into other countries in the future. While we have acquired significant management and other personnel with substantial experience, conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including, among other things:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
- country-specific tax, labor and employment laws and regulations;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations;
- liabilities for activities of, or related to, our international operations or product candidates;
- changes in currency rates; and
- regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

We continue to expand our operations, and our corporate structure and tax structure is complex. In connection with our current and future potential partnerships, we are actively engaged in developing and applying technologies and intellectual property with a view toward commercialization of products globally, often with commercialization partners. In connection with those activities, we already have and will likely continue to engage in complex cross-border and global transactions involving our technology, intellectual property and other assets, between us and other entities such as partners and licensees, and between us and our subsidiaries. Such cross-border and global arrangements are both difficult to manage and can potentially give rise to complexities in areas such as tax treatment, particularly since we are subject to multiple tax regimes and different tax authorities can also take different views from each other, even as regards the same cross-border transaction or arrangement. There can be no assurance that we will effectively manage this increased complexity without experiencing operating inefficiencies, control deficiencies or tax liabilities. Significant management time and effort is required to effectively manage the increased complexity of our company, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Risks Related to Intellectual Property

If We Are Unable To Obtain, Maintain Or Protect Intellectual Property Rights Related to Our Proprietary Gene Editing Technology And Product Candidates, We May Not Be Able To Compete Effectively In Our Markets.

Our success depends in large part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other commercially relevant jurisdictions with respect to our various gene editing technologies, including CRISPR/Cas9 and SyNTase platform technologies, as well as other technologies, including delivery technologies, and any proprietary product candidates we develop. We seek to develop, maintain and protect our proprietary position and intellectual property that is important to our business by relying upon a combination of know-how, technological innovation and intellectual property rights,

including patent rights and trade secret protection, as well as entering into confidentiality agreements and in-licensing arrangements.

Like other companies in the biotech and pharmaceutical sector, obtaining or maintaining adequate patent protection for our proprietary technologies and product candidates is key to our success. Presently we have rights to certain intellectual property, through licenses from third parties and under patent rights that we own, to develop our gene editing and other technologies and product candidates. For example, we have filed numerous patent applications covering key aspects of our CRISPR/Cas9 platform technology and gene editing and other technologies and product candidates, which cover various aspects of our development programs, including, but not limited to, compositions of matter, as well as methods of making and using. Additionally, through our 2014 exclusive licenses with Dr. Charpentier, we exclusively license certain rights to a worldwide patent portfolio, including granted or allowed patents, as well as pending patent applications, which covers various aspects of our gene editing platform technology, including, for example, compositions of matter (e.g., CRISPR/Cas9 systems), and methods of use, including the use of a CRISPR/Cas9 system for gene editing.

The strength of patents in the biotechnology and pharmaceutical field generally, and the gene-editing field in particular, involves complex legal and scientific questions and can be uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our intellectual property, obtain, maintain, defend 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 in-licensed patents. We cannot offer any assurances about which, if any, patent rights that we own or in-license will issue, the breadth of any such patent rights, 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, or if any such patents will be found invalid, unenforceable or not infringed if challenged by our competitors. See, for example, generally *"Risk Factors —Risks Related to Intellectual Property—The Intellectual Property Landscape Around Gene Editing Technology, Including CRISPR/Cas9, Is Highly Dynamic, And Third Parties May Initiate And Prevail In Legal Proceedings Alleging That The Patents That We In-License Or Own Are Invalid Or 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 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. Given the amount of time required for the development, testing and regulatory review of new product candidates, or if we encounter delays in our clinical trials, patents protecting our product candidates might expire before or shortly after such candidates are commercialized. 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, contract research organizations, 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. See, for example, *"Risk Factors —Risks Related to Intellectual Property—If We Are Unable To Protect The Confidentiality Of Our Trade Secrets And Other Proprietary Information, Our Business And Competitive Position Would Be Harmed."*

Our pending and future patent applications or the patent applications that we obtain rights to through in-licensing arrangements may not result in patents being issued which protect our technology or future product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Moreover, the ultimate outcome of any pending or allowed patent application or granted patent is uncertain and 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 currently in the future 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. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. See, for example, *"Risk Factors —Risks Related to Intellectual Property—We May Not Be Able To Protect Our Intellectual Property And Proprietary Rights Throughout The World."* As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we or our licensors are unable to obtain or maintain patent protection with respect to our proprietary gene editing platform technology and any proprietary products and technology we develop, our business, financial condition, results of operations and prospects could be materially harmed.

The growth of our business, including use of our gene editing technology and continued development of our product candidates, could depend in part on our ability to acquire, in-license, or use proprietary rights held by third parties. We may be unable to maintain such intellectual property rights from third parties or acquire or in-license such intellectual property rights from third parties that we identify in the future. See, for example, *"Risk Factors — Risks Related to Intellectual Property— 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."* Companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. We also rely on trade secret protection and confidentiality agreements to maintain our competitive position and to protect our technology, unpatented proprietary know-how, including processes for which patents are difficult to enforce, as well as other

proprietary and confidential information. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business. See, for example, *"Risk Factors —Risks Related to Intellectual Property— If We Are Unable To Protect The Confidentiality Of Our Trade Secrets And Other Proprietary Information, Our Business And Competitive Position Would Be Harmed."*

Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

Issued Patents Covering Our Technology And Product Candidates Could Be Found Invalid Or Unenforceable If Challenged In Court or Before The USPTO Or Comparable Foreign Authority.

Additionally, the issuance of a patent is not conclusive as to its inventorship or ownership, scope, validity or enforceability and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and in other jurisdictions by third parties, including competitors. There is a substantial amount of litigation as well as administrative proceedings for challenging patents and other intellectual property rights in the biotechnology and pharmaceutical industries, including the gene-editing space and in particular with respect to CRISPR/Cas9. See, for example, *"Risk Factors —Risks Related to Intellectual Property—The Intellectual Property Landscape Around Gene Editing Technology, Including CRISPR/Cas9, Is Highly Dynamic, And Third Parties May Initiate And Prevail In Legal Proceedings Alleging That The Patents That We In-License Or Own Are Invalid Or 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."* Consequently, we do not know whether any of our technology advances or novel discoveries, including with respect to our gene editing platform, and product candidates will be protectable or remain protected by valid and enforceable patents. If the breadth or strength of protection provided by the patents or patent applications we hold is threatened, this could dissuade companies from collaborating with us to develop, and could threaten our ability to commercialize, product candidates or provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Competitors may claim that they invented the inventions claimed in such issued patents or patent applications prior to our inventors, or may have filed patent applications before our inventors did. Competitors may also claim that our products and technology infringe its patents and that we therefore cannot practice our technology as claimed under our patent applications, if issued.

Competitors may also contest our patents, if issued, by showing that the invention was not patent-eligible, was not novel, was obvious or that the patent claims failed any other requirement for patentability. An adverse determination in any such submission, proceeding, claim or litigation could reduce the scope of or invalidate our patent rights or allow third parties to commercialize our technology or products and compete directly with us, without payment to us.

For example, we cannot be certain that all of the potentially relevant prior art relating to our wholly-owned and in-licensed patents and patent applications has been found. Third parties can raise challenges to the patentability or validity of our owned or in-licensed patents and patent applications, such as third-party observations and oppositions before administrative bodies in the United States or in other jurisdictions, even outside the context of litigation.

The outcome following legal assertions of invalidity and unenforceability is unpredictable, and such challenges, after exhausting available appeals, may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, revoked, withdrawn, invalidated or held unenforceable, in whole or in part, which could limit our ability to practice the invention or stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products.

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 may develop. Such a loss of patent protection could have a material adverse impact on our business, financial condition, results of operations, and prospects.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering a product candidate we may develop or have developed or our technology, including CRISPR/Cas9 platform technology, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or other jurisdictions, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings and equivalent proceedings in foreign jurisdictions, such as oppositions or derivation proceedings.

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 in the United States or other countries that challenge priority of invention or other features of patentability of our owned or in-licensed patents or patent applications. See, for example, *"Risk Factors —Risks Related to Intellectual Property— Third-party Claims Of Overlapping Intellectual Property Rights May Prevent Or Delay Our*

Product Discovery and Development Efforts." Such challenges may result in loss of patent rights, loss of exclusivity or freedom to operate, or in patent claims being narrowed, revoked, withdrawn, invalidated or held unenforceable, in whole or in part, 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.

Even if they are unchallenged, our owned and in-licensed patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. The loss of exclusivity or the narrowing of our patent claims could limit our ability to stop others from using or commercializing similar or identical technology and products. 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 are using the CRISPR technology in conjunction with a protein other than Cas9, and our owned and in-licensed patents may not cover such technology. 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. Any of the foregoing could result in a material adverse effect on our business, financial condition, results of operations, or prospects, including if our competitors commercialize the CRISPR technology in conjunction with a protein other than Cas9.

The Intellectual Property Landscape Around Gene Editing Technology, Including CRISPR/Cas9, Is Highly Dynamic, And Third Parties May Initiate And Prevail In Legal Proceedings Alleging That The Patents That We In-License Or Own Are Invalid Or 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.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market, and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating, or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. The field of gene editing, especially in the area of gene editing technology, is still evolving. 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.

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 may develop, including re-examinations, interference proceedings, post-grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in other jurisdictions such as oppositions before the European Patent Office. See, for example, *"Risk Factors —Risks Related to Intellectual Property—Third-party Claims Of Overlapping Intellectual Property Rights May Prevent Or Delay Our Product Discovery and Development Efforts."*

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. For example, in the fourth quarter of 2025, ToolGen, Inc., or ToolGen, initiated a lawsuit against us and other third parties alleging patent infringement by CASGEVY of a ToolGen patent relating to CRISPR/Cas9 gene editing technology. If we are found to infringe such third-party patents, we and our partners may be required to pay damages, cease commercialization of the infringing technology or obtain a license from such third parties, which may not be available on commercially reasonable terms or at all. See, for example, *"Risk Factors —Risks Related to Intellectual Property—Third-party Claims Of Intellectual Property Infringement Against Us, Our Licensors Or Our Collaborators May Prevent Or Delay Our Product Discovery and Development Efforts."*

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, ownership, or priority. A court 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 may develop and any other product candidates or technologies covered by the asserted third-party patents.

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.

Defense of these claims, regardless of their merit, would involve substantial litigation expense, would be a substantial diversion of management and other employee resources from our business and may impact our reputation. See for example *"Risk Factors —Risks Related to Intellectual Property—Intellectual Property Litigation Could Cause Us To Spend Substantial Resources And Distract Our Personnel From Their Normal Responsibilities."*

Third-party Claims Of Intellectual Property Infringement Against Us, Our Licensors Or Our Collaborators May Prevent Or Delay Our Product Discovery and Development Efforts.

Third parties may own intellectual property, including patents, that cover all or aspects of our technologies and potential products and product candidates, and such intellectual property may be necessary for us to develop or commercialize viable products. Our commercial success depends in part on our avoiding infringement of the valid patents and proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing our gene editing and other technologies and product candidates, including in areas potentially related to components and methods we use or may use in our research and development efforts. As industry, government, academia and other biotechnology and pharmaceutical research expands and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. We cannot guarantee that our technology, processes, future product candidates or the use of such product candidates do not infringe third-party patents now or in the future. Because patent rights are granted jurisdiction-by-jurisdiction, our freedom to practice certain technologies, including our ability to research, develop and commercialize our product candidates, may differ by country.

Third parties, including competitors, may assert that they invented the inventions claimed in our issued patents or patent applications prior to our inventors, or may have filed patent applications before our inventors did, and that we infringe their patents or that we are otherwise employing their proprietary technology without authorization, and may sue us. See, for example, "*Risk Factors —Risks Related to Intellectual Property—Third-party Claims Of Overlapping Intellectual Property Rights May Prevent Or Delay Our Product Discovery and Development Efforts."* In addition, third parties may obtain patents and claim that use of our technologies or the manufacture, use or sale of our product candidates infringes upon these patents. It is possible that we have failed to identify relevant third-party patents or applications, including those with claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover product candidates we discover and develop. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with any degree of certainty whether the inventors of our patents and patent applications or our licensed patents and patent applications were the first to make the inventions claimed in our owned or in-licensed patents or pending patent applications; that we (or our licensors) were the first to file for patent protection of such inventions, or that our product candidates are not later found to infringe certain issued patents. Moreover, there is no assurance that all of the potentially relevant prior art relating to our owned and in-licensed patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application.

If we or a third party that we are obliged to defend and indemnify 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 and our partners may be required to pay substantial damages, including treble damages and attorneys' fees for willful infringement, cease commercialization of the infringing technology or the applicable product candidate, or we could be required to obtain one or more licenses under the applicable patents from third parties to continue developing, manufacturing, and marketing any product candidates we may develop and our gene-editing and other technologies until such patents expire or are finally determined to be held invalid or unenforceable. These third parties would be under no obligation to grant to us any such licenses and such licenses may not be available on commercially reasonable terms or at all, or may 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. If we are unable to obtain or maintain a necessary license to a third-party patent on commercially reasonable terms, our ability to commercialize our technologies and product candidates may be impaired or delayed, or we may be required to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

Any of these outcomes could materially harm our business and could prevent us from further developing and commercializing such products or future product candidates, thereby causing us significant harm. In addition, third parties asserting their patent rights against us may seek and obtain injunctive or other equitable relief, which could effectively limit or block our ability to further develop and commercialize our product candidates.

In order to successfully challenge the validity of any such third party U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent and such court could hold that any such third-party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third-party patents.

Third-party Claims Of Overlapping Intellectual Property Rights May Prevent Or Delay Our Product Discovery and Development Efforts.

Third parties may seek to claim intellectual property rights that encompass or overlap with intellectual property that we own or in-license. Legal proceedings may be initiated to determine the scope and ownership of these rights, and could result in our loss of rights, including injunctions or other equitable relief that could effectively block our ability to further develop and commercialize our product candidates. Interference or derivation proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to, or the correct inventorship of, our patents or patent applications or those of our

licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation, interference or derivation proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees.

For example, third parties could assert that we do not have rights to certain technologies, including CRISPR/Cas9 technologies, or could assert and have asserted in the past, that the CVC Group does not have rights to certain CRISPR/Cas9 technologies, including inventorship and ownership rights to some of the CVC Group's patents included in the worldwide patent portfolio we have in-licensed from Dr. Charpentier, or that such rights are limited. Specifically, the Broad Institute and Massachusetts Institute of Technology and, in some instances, the President and Fellows of Harvard College, or Harvard University, which we refer to individually and collectively as the "Broad", owns a patent family that includes issued patents in the United States and Europe that claim certain aspects of CRISPR/Cas9 systems to edit DNA in eukaryotic cells, including human cells. In addition to the Broad, other third parties, such as Vilnius University, ToolGen, MilliporeSigma (a subsidiary of Merck KGaA and formerly known as "Sigma-Aldrich") and Harvard University, filed patent applications claiming CRISPR/Cas9-related inventions around or within a year after the CVC Group application was filed and allege (or may allege) that they were first to invent one or more of the inventions claimed by the CVC Group and/or claimed by Broad, i.e. before the CVC Group, before Broad, and before the other parties.

To date, the CVC Group has been involved in a series of interferences declared by the USPTO involving fourteen (14) pending U.S. patent applications co-owned by the CVC Group, on the one hand and on the other hand, thirteen (13) patents and a patent application co-owned by the Broad; a ToolGen patent application; and a patent application and two patents owned by MilliporeSigma. Because the CVC Group and these other third parties all allege owning intellectual property claiming overlapping aspects of CRISPR/Cas9 systems and methods to edit DNA in eukaryotic cells, including human cells, our ability to market and sell CRISPR/Cas9-based human therapeutics may be adversely impacted depending on the scope and actual ownership over the inventions claimed in the competing patent portfolios. An adverse decision in any interference can be appealed to the Federal Circuit and through to the Supreme Court, and in the past has been and currently is working through this appeal process. Moreover, as a general matter, interferences can be, and currently have been, stayed pending the outcome of other interferences. For example, the CVC Group's interferences against ToolGen and MilliporeSigma have been temporarily paused pending resolution of its interference with the Broad.

Going forward, the USPTO could declare new interferences involving the CVC Group related to the same patents and patent applications referenced above, or any of the CVC Group's existing or new patents and patent applications. Additionally, the USPTO could declare new interferences with us individually related to our existing wholly-owned patent portfolio or new patents and patent applications we file in the future.

If any third party were to succeed in its interference and prevail in their claims of being first-to-invent, or obtain patent claims that cover our product candidates or related activities through these various legal proceedings, such party could seek to assert its issued patents against us based on our business activities, including commercialization of any CRISPR/Cas9-based product or product candidate. Moreover, in such event, we may be required to obtain licenses from such third parties, which may not be available on commercially reasonable terms or at all. See, for example, "*Risk Factors —Risks Related to Intellectual Property—The Intellectual Property Landscape Around Gene Editing Technology, Including CRISPR/Cas9, Is Highly Dynamic, And Third Parties May Initiate And Prevail In Legal Proceedings Alleging That The Patents That We In-License Or Own Are Invalid Or 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."* and "*We May Not Be Successful In Obtaining Or Maintaining Necessary Rights To Any Product Candidates or Other Technologies We May Develop Through Acquisitions And In-Licenses."*

We cannot be certain which of these results, if any, will actually occur. In any case, it may be years before there is a final determination on priority in the United States with respect to CVC Group's patents included in the worldwide patent portfolio we have in-licensed from Dr. Charpentier.

Further, third parties routinely file international counterparts of their U.S. applications, some of which have been granted or could in the future be granted in Europe and/or other non-U.S. jurisdictions. We, as well as other parties have initiated opposition proceedings against some of these grants, and we may in the future oppose other grants to these or other applicants. Similarly, various aspects of our intellectual property estate (both in-licensed and wholly-owned) has been, is and may in the future become involved in opposition proceedings in Europe or other jurisdictions, such as, for example, in Australia, Japan, China, and India. Opposition proceedings can lead to the revocation of a patent in its entirety; the maintenance of the patent as granted, or the maintenance of a patent in amended form, including claims being narrowed in a way that could impair or preclude our ability to enforce the patents against competitors in Europe. Opposition proceedings typically take years to resolve, including the time taken by appeals that can be filed by any of the parties. For example, several parties have filed oppositions in the European Patent Office to the grant of certain related European patents in-licensed from Dr. Charpentier that expire in 2033. As a result of certain opposition activities, certain patents were revoked, either due to revocation after opposition proceedings or voluntary withdrawal for procedural reasons, while other opposition proceedings remain ongoing. Furthermore, for example, EP 3597749 was revoked in November 2025; the CVC

Group may appeal the decision in 2026.

We cannot guarantee the outcome of the oppositions to our in-licensed patents in Europe or other jurisdictions outside the United States included in the worldwide patent portfolio we have in-licensed from Dr. Charpentier, and an adverse result could preclude us from enforcing our rights against third parties in Europe or such other jurisdictions. The effects that any such proceedings and results may have on us and our intellectual property position are currently unknown.

We are unable to predict the outcome of any of these matters and are unable to make a meaningful estimate of the amount or range of loss, if any, that could result from an unfavorable outcome in any current or future proceeding related to our intellectual property position. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects, and limit our ability to research, develop and obtain approval of product candidates, or to commercialize products.

In the future, we may also become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

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 reliant upon licenses to certain intellectual property from third parties that are important or necessary to the development of our gene editing and other 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 or cover 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.

Moreover, under our current and future in-license agreements, including our 2014 exclusive license agreement with Dr. Charpentier, and other technology agreements, we are or may be required to pay milestones and royalties based on our revenues from sales of our products utilizing the technologies acquired, licensed or sublicensed from third parties and these milestones and royalty payments could adversely affect our ability to research, develop and obtain approval of product candidates, as well as the overall profitability for us of any products that we may seek to commercialize. Further, our licensors may dispute the terms, including amounts, that we are required to pay under the respective agreements. If these claims were to result in a material increase in the amounts that we are required to pay to our licensors our ability to research, develop and obtain approval of product candidates, or to commercialize products, could be significantly impaired.

In addition, in order to maintain our intellectual property rights under these agreements, we will need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates, including certain diligence requirements, and we may not be successful in meeting all such requirements in the future on a timely basis or at all. Our failure to meet our obligations under any license agreements and other technology agreements may give the licensor the right to terminate our license rights. We will need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our license agreements and other technology agreements. Delay or failure by these third parties could adversely affect our ability to meet our diligence obligations and the continuation of our license agreements with third-party licensors.

In spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and other technology agreements and might therefore terminate such agreements, thereby removing our ability to develop and commercialize products and technology covered by these agreements. If any such licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties (potentially including our competitors) to receive licenses to a portion of the intellectual property that is subject to our existing licenses. Any of these events could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects, and limit our ability to research, develop and obtain approval of product candidates, or to commercialize products.

The Intellectual Property That Protects Our Core Gene Editing Technology Is Jointly Owned, And Our License Is From Only One Of The Joint Owners, Materially Limiting Our Rights In The United States And In Other Jurisdictions.

The worldwide patent portfolio we have in-licensed from Dr. Charpentier is currently co-owned by Dr. Charpentier, California, and Vienna. Because other parties share rights in this patent portfolio, we do not have the exclusive right to license and exploit the technology that is the subject of this patent portfolio. Further, we need the consent of the other co-owners, and in some instances, other licensees to enforce the patent portfolio, which could leave us unable to prevent third parties from competing with us and could make it more difficult to sublicense parts of our platform technology, either of which could have a material adverse effect on our business.

We May Experience Disputes With The Third Parties That We In-license Intellectual Property Rights From Or Those We

License Intellectual Property To. Any Disputes With These Parties Could Adversely Affect Our Business And We Could Lose License Rights That Are Important To Our Business.

We license the intellectual property that covers certain parts of our platform gene editing technology from a third party, and we expect to continue to in-license additional third-party intellectual property rights as we expand our gene editing and other technology. Disputes may arise with the third parties from whom we license our intellectual property rights from for a variety of reasons, 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, or derive from, intellectual property of the licensor that is not subject to a licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships and obligations associated with sublicensing;
- our diligence obligations under our license and collaboration agreements 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 in-license intellectual property or technology from third parties, or maintain consents under the IMA, are complex, and certain provisions in such agreements may be susceptible to multiple interpretations, or may conflict in such a way that puts us in breach of one or more agreements, which would make us susceptible to lengthy and expensive disputes with one or more of our licensing partners or the parties to such agreements. 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, either of which 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.

Similarly, as we continue to enter into license agreements, collaboration agreements and partnerships with third parties to expand our development programs, we have, and expect to continue to, out-license some of our intellectual property to these third parties. Disputes may arise with these third parties to whom we out-license our intellectual property rights for a variety of reasons, including, the scope of rights granted under any such agreement and other interpretation-related issues. Any disputes with our current or future collaboration partners or licensees regarding the scope of intellectual property rights granted to such partner or licensee by us could result in the delay of development programs and would make us susceptible to lengthy and expensive disputes with our partners or licensees.

We May Not Be Successful In Obtaining Or Maintaining Necessary Rights To Any Product Candidates or Other Technologies We May Develop Through Acquisitions And In-Licenses.

We currently have rights to intellectual property, through in-licenses from third parties, to identify and develop product candidates, as well as use other technologies, including delivery methods for our product candidates. Many pharmaceutical companies, biotechnology companies, and academic institutions are competing with us in the field of gene editing, including delivery technology, and filing patent applications potentially relevant to our business. For example, we are aware of several third-party patent applications that, if issued, may be construed to cover our gene editing technology and product candidates. In order to avoid infringing these third-party patents, 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 modified or improved components of gene editing technology, such as modified nucleic acids or proteins, as well as non-CRISPR/Cas9 technologies such as delivery methods that we are evaluating for use with product candidates we may develop. In addition, with respect to any patents we co-own with third parties, we may require licenses to such co-owners' interest to 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 product candidates we may develop and gene editing and other technologies. The licensing or acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established, or have greater resources than we do may be pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. More established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates or technology

that we may seek to acquire. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program, technology, or product candidate, or discontinue the practice of our core CRISPR/Cas9 gene editing technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Intellectual Property Litigation Could Cause Us To Spend Substantial Resources And Distract Our Personnel From Their Normal Responsibilities.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. There may be significant intellectual property related litigation and proceedings relating to our owned and in-licensed intellectual property and proprietary rights, as well as other third party intellectual property rights, in the future. See, for example, "*Third-party Claims Of Overlapping Intellectual Property Rights May Prevent Or Delay Our Product Discovery and Development Efforts."*

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical personnel and management from their normal responsibilities and generally harm our business. For example, pursuant to the terms of our license agreements with Dr. Charpentier, we are responsible for covering or reimbursing Dr. Charpentier's patent prosecution, defense and related costs associated with our in-licensed technology and the worldwide patent portfolio we have in-licensed from her. For example, in the fourth quarter of 2025, ToolGen initiated a lawsuit against us and other third parties alleging patent infringement by CASGEVY of a ToolGen patent relating to CRISPR/Cas9 gene editing technology.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation in certain countries, including the United States, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Some Intellectual Property Which We Have In-licensed May Have Been Discovered Through Government Funded Programs And Thus May Be Subject To Federal Regulations Such As "march-in" Rights, Certain Reporting Requirements And A Preference For U.S.-based Manufacturers. Compliance With Such Regulations May Limit Our Exclusive Rights, And Limit Our Ability To Contract With Non-U.S. Manufacturers.

Some of our in-licensed intellectual property rights, including patents we have in-licensed under Dr. Charpentier's joint interest, are subject to certain federal regulations. The U.S. government has certain rights pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act, to patents covering government rights in certain inventions developed under a government-funded program. These rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to achieve practical application of the invention in the field of use; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." The U.S. government also has the right to take title to these inventions if we, or the applicable contractor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable contractor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future patents covering inventions is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

We May Not Be Able To Protect Our Intellectual Property And Proprietary Rights Throughout The World.

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in intellectual property laws in various jurisdictions worldwide. Additionally, the patent laws of some countries do not afford intellectual property protection to the same extent as the laws of the United States. For example, unlike patent law in the United States, the patent law in Europe and many other jurisdictions precludes the patentability of methods of treatment of the human body and imposes substantial restrictions on the scope of claims it will grant if broader than specifically disclosed embodiments.

Many companies have encountered significant problems in protecting and defending intellectual property rights in various jurisdictions globally. 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 pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in various jurisdictions globally 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 third parties, including 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. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Changes To The Patent Law In The United States And Other Jurisdictions Could Diminish The Value Of Patents In General, Thereby Impairing Our Ability To Protect Our Product Candidates.

Our success, like other companies in the biotech and pharmaceutical sectors, relies heavily on intellectual property, especially patents. Patent acquisition and enforcement in our industry are complex, expensive, and uncertain due to technical and legal intricacies.

Changes in patent laws or their interpretation can exacerbate these uncertainties and increase costs, particularly with the shift in the United States from a “first to invent” to a “first-to-file” patent system since March 2013. This change means that the first applicant, not necessarily the first inventor, can secure a patent. As patent applications are confidential initially, it is uncertain whether we were the first to file or invent our technology.

The Leahy-Smith America Invents Act introduced significant changes, including a lower burden of proving patent invalidity in USPTO proceedings compared to federal courts, which could make it easier for third parties to challenge our patents. Recent decisions from the U.S. Supreme Court and U.S. Court of Appeals for the Federal Circuit have also narrowed patent protections and weakened patent owners' rights, creating uncertainty about patent validity and enforceability. These changes, along with potential future legal developments, could weaken our ability to secure new patents or enforce existing ones.

Geopolitical events can also affect patent processes. For instance, U.S. and foreign government actions regarding Russia’s invasion of Ukraine might impede patent filing and maintenance in Russia. A 2022 Russian decree allows exploitation of patents from certain foreign entities without consent, potentially affecting our competitive position and business.

Furthermore, the recently-formed European Unified Patent Court, or UPC, allows for centralized patent revocation proceedings in the EU. Certain of our European patents are subject to this court’s jurisdiction. The UPC’s evolving laws may affect our ability to defend or enforce those European patents. In some instances, we have opted out of the UPC’s jurisdiction for certain of our European patents.

Overall, the evolving patent laws present ongoing challenges and may affect our business and intellectual property strategy.

Obtaining And Maintaining Our Patent Protection Depends On Compliance with Various Procedural, Document Submission, Fee Payment and Other Requirements Imposed by Governmental Patent Agencies, And Our Patent Protection Could be Reduced or Eliminated For Non-Compliance With These Requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Although an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In any such event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

If We Do Not Obtain Patent Term Extension And Data Exclusivity For Any Product Candidates We May Develop, Our Business May Be Materially Harmed.

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 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 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 our business, financial condition, results of operations, and prospects could be materially harmed.

Intellectual Property Rights Do Not Necessarily Address All Potential Threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapy products that are similar to any product candidates we may develop or utilize similar gene therapy technology but that are not covered by the claims of the patents that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material 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 Confidential Information Of Their Current Or Former Employers Or Other Third Parties 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. 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 confidential information or intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer or other third party. 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 our management and employees.

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 of intellectual property rights may not be self-executing, or 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 And Other Proprietary Information, Our Business And Competitive Position Would Be Harmed.

We seek to protect our proprietary technology and processes, including these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors, and other third parties. We cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. See, for example, *"Risk Factors—Risks Related to Information Security and Privacy—Our Internal Information Technology Systems, Or Those Of Our Collaborators Or Other Contractors Or Consultants, May Fail Or Suffer Security Breaches, Which Could Result In A Material Disruption Of Our Product Development Programs."* In addition, our trade secrets may otherwise become known or be independently discovered by competitors. 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. Moreover, while it is our policy to require our employees, consultants 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 of intellectual property rights may not be self-executing, or 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. 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.

If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. 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 proprietary information. Moreover, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. In addition, in the EU, the EMA proactively publishes clinical data submitted by companies to support a marketing authorization application for a medicinal product under the centralized procedure, with limited exceptions for the redaction of commercially confidential information or protection of personal data. If any of our trade secrets or proprietary information were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them, or those to whom

they communicate it, 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 Our Trademarks Are Not Adequately Protected, Then We May Not Be Able To Build Name Recognition In Our Markets Of Interest And Our Business May Be Adversely Affected.

If our trademarks are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our unregistered trademarks may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks. Over the long term, if we are unable to successfully register our trademarks and establish name recognition based on our trademarks, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to The Ownership of Our Common Shares

We Have Broad Discretion In The Use Of Our Cash Reserves And May Not Use Such Cash Reserves 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 shares. 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 shares to decline, and delay the development or commercialization 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.

Sales Of A Substantial Number Of Our Common Shares In The Public Market Could Cause Our Share Price To Fall.

Sales of a substantial number of our common shares in the public market or the perception that these sales might occur could depress the market price of our common shares, could make it more difficult for you to sell your common shares at a time and price that you deem appropriate and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common shares. For example, we actively maintain a sales agreement with Jefferies under which we are able to offer and sell, from time to time at our sole discretion through Jefferies, as our sales agent, our common shares, par value of CHF 0.03 per share. As of December 31, 2025, we have issued and sold an aggregate of 8.7 million common shares under our sales agreement with Jefferies at an average price of $73.64 per share for aggregate proceeds of $634.5 million, which were net of equity issuance costs of $8.3 million, excluding stamp taxes of $6.3 million. As of December 31, 2025, common shares having aggregate gross proceeds up to $557.2 million remain available under our sales agreement.

We Do Not Expect To Pay Dividends In The Foreseeable Future.

We have not paid any dividends since our incorporation. Even if future operations lead to significant levels of distributable profits, we currently intend that any earnings will be reinvested in our business and that no dividends will be paid prior to the time we have an established revenue stream to support continuing dividends. The proposal to pay future dividends to shareholders will in addition effectively be at the discretion of our board of directors and shareholders after taking into account various factors including our business prospects, cash requirements, financial performance and new product development. In addition, payment of future dividends is subject to certain limitations pursuant to Swiss law or by our articles of association. Accordingly, investors cannot rely on dividend income from our common shares and any returns on an investment in our common shares will likely depend entirely upon any future appreciation in the price of our common shares. Dividends, if any, paid on our common shares are subject to Swiss federal withholding tax, except if paid out of reserves from capital contributions, or *Kapitaleinlagen*. For additional information, please see "*Risk Factors—Risks Related to The Ownership of Our Common Shares—Our Status As A Swiss Corporation May Limit Our Flexibility With Respect To Certain Aspects Of Capital Management And May Cause Us To Be Unable To Make Distributions Without Subjecting Our Shareholders To Swiss Withholding Tax"*.

We Are A Swiss Corporation. The Rights Of Our Shareholders May Be Different From The Rights Of Shareholders In Companies Governed By The Laws Of U.S. Jurisdictions.

We are a Swiss corporation. Our corporate affairs are governed by our articles of association and by Swiss law. The rights of our shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and directors of companies governed by the laws of U.S. jurisdictions. In the performance of its duties, our board of

directors is required by Swiss law to consider the interests of our Company, our shareholders and our employees with due observation of the principles of reasonableness and fairness. It is possible that the board of directors will consider interests that are different from, or in addition to, your interests as a shareholder. Swiss corporate law limits the ability of our shareholders to challenge resolutions made or other actions taken by our board of directors in court. Our shareholders generally are not permitted to file a suit to reverse a decision or an action taken by our board of directors but are instead only permitted to seek damages for breaches of the duty of care and loyalty. As a matter of Swiss law, shareholder claims against a member of our board of directors for breach of the duty of care and loyalty would have to be brought in Zug, Switzerland, or where the relevant member of our board of directors is domiciled. In addition, under Swiss law, any claims by our shareholders against us must be brought exclusively in Zug, Switzerland.

As A Swiss Corporation, We Are Subject To Swiss Legal Provisions That May Limit Our Flexibility To Swiftly Implement Certain Initiatives Or Strategies.

We are required, from time to time, to evaluate the carrying amount of our investments in affiliates, as presented on our Swiss standalone balance sheet. If we determine that the carrying amount of any such investment exceeds its fair value, we may conclude that such investment is impaired. The recognized loss associated with such a non-cash impairment could result in our net assets no longer covering our statutory share capital and statutory capital reserves. Under Swiss law, if our net assets cover less than 50 percent of our statutory share capital, statutory capital reserves and statutory earnings reserves that are not repayable to shareholders, the board of directors must take appropriate measure to overcome the situation and, if necessary, convene a general meeting of shareholders and propose measures to remedy such a capital loss. The appropriate measures depend on the relevant circumstances and the magnitude of the recognized loss and may include seeking shareholder approval for offsetting the aggregate loss, or a portion thereof, with our statutory capital reserves including qualifying additional paid-in capital otherwise available for distributions to shareholders or raising new equity. Depending on the circumstances, we may also need to use qualifying additional paid-in capital available for distributions in order to reduce our accumulated net loss and such use might reduce our ability to make distributions without subjecting our shareholders to Swiss withholding tax. These Swiss law requirements could limit our flexibility to swiftly implement certain initiatives or strategies.

Anti-takeover Provisions In Our Articles Of Association Could Make An Acquisition Of Our Company, Which May Be Beneficial To Our Shareholders, More Difficult And May Prevent Attempts By Our Shareholders To Replace Or Remove Our Current Management.

Provisions in our articles of association may discourage, delay or prevent an acquisition of our Company or changes in the composition of our board of directors. Among other things, these provisions require the approval of at least two thirds of represented shares present or voting at a shareholder meeting for the removal of a member of our board of directors and to increase the maximum number of members of our board of directors; limit the accumulated voting rights of any person or entity to 15% of our registered share capital; limit the voting rights of an acquirer of more than 5% of our registered share capital in a transaction or series of transactions in which our board of directors did not provide for an exemption, which could prevent or delay a change in control of our Company; provide that the board of directors is authorized to conduct one or more increases of the Company's share capital, at any time until June 8, 2028, or the expiry of the capital band, if earlier (see "*Risk Factors—Risks Related to The Ownership of Our Common Shares—Our Status As A Swiss Corporation May Limit Our Flexibility With Respect To Certain Aspects Of Capital Management And May Cause Us To Be Unable To Make Distributions Without Subjecting Our Shareholders To Swiss Withholding Tax"*), to issue a specified number of shares within the limit of the capital band, which under our current capital band is approximately eight percent of the issued share capital, and to limit or withdraw the preemptive rights of existing shareholders in various circumstances; provide for a conditional share capital that authorizes the issuance of additional shares up to a maximum amount of approximately twenty-nine percent of the issued share capital, without obtaining additional shareholder approval, (i) through the exercise of conversion and/or option rights granted in connection with bonds or similar instruments, including convertible debt instruments, and (ii) in connection with the exercise of options granted to employees or other service providers of the Company or any of its subsidiaries; and provide that a merger or demerger transaction requires the affirmative vote of at least two thirds of the shares represented at a shareholders' meeting.

Although we believe these provisions collectively provide for an opportunity to obtain greater value for shareholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some shareholders. In addition, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Our Common Shares Are Issued Under The Laws Of Switzerland, Which May Not Protect Investors In A Similar Fashion Afforded By Incorporation In A U.S. State.

We are organized under the laws of Switzerland. However, there can be no assurance that Swiss law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the United States, which could adversely affect the rights of investors.

Our Status As A Swiss Corporation May Limit Our Flexibility With Respect To Certain Aspects Of Capital Management And May Cause Us To Be Unable To Make Distributions Without Subjecting Our Shareholders To Swiss Withholding Tax.

Our articles of association as in force allow our shareholders to introduce a capital band authorizing the board of directors to increase the share capital without additional shareholder approval. The capital band currently approved by our shareholders will expire on June 8, 2028 and is limited to approximately eight percent of our issued share capital. Subject to specified exceptions, Swiss law grants preemptive rights to existing shareholders to subscribe to any new issuance of shares. Swiss law also does not provide as much flexibility in the various terms that can attach to different classes of shares as the laws of some other jurisdictions. Swiss law also reserves for approval by shareholders certain corporate actions over which a board of directors would have authority in some other jurisdictions. For example, the payment of dividends and the cancellation of treasury shares must be approved by shareholders. These Swiss law requirements relating to our capital management may limit our flexibility, and situations may arise where greater flexibility would have provided substantial benefits to our shareholders.

Under Swiss law, a Swiss corporation may pay dividends only if the corporation has sufficient distributable profits, or if the corporation has distributable reserves, each as evidenced by its audited standalone statutory balance sheet, and after allocations to reserves required by Swiss law and our articles of association have been deducted. Freely distributable reserves are generally booked either as "statutory capital reserves" (*gesetzliche Kapitalreserven,* contributions received from shareholders) or in the statutory or voluntary "retained earnings". Distributions may be made out of registered share capital—the aggregate par value of a company's registered shares—only by way of a capital reduction. We will not be able to pay dividends or make other distributions to shareholders on a Swiss withholding tax-free basis in excess of our aggregate qualifying contributions and registered share capital unless we increase our share capital or our reserves from capital contributions. We would also be able to pay dividends out of distributable profits or freely distributable reserves, but such dividends would be subject to Swiss withholding taxes. There can be no assurance that we will have sufficient distributable profits, capital reserves, retained earnings or registered share capital to pay a dividend or effect a capital reduction, that our shareholders will approve dividends or capital reductions proposed by us or that we will be able to meet the other legal requirements for dividend payments or distributions as a result of capital reductions.

Dividends and similar cash or in-kind distributions made by the Company to a shareholder (including liquidation proceeds and stock dividends) are subject to Swiss withholding tax (*Verrechnungssteuer*), currently at a rate of 35% (applicable to the gross amount of the taxable distribution). The Company is obliged to deduct the Swiss withholding tax from the gross amount of any taxable distribution and to pay the tax to the Swiss Federal Tax Administration within 30 calendar days of the due date of such distribution. However, the repayment of the nominal value of the shares and any repayment of qualifying additional paid-in capital (capital contribution reserves (*Reserven aus Kapitaleinlagen*)) are not subject to Swiss withholding tax. The Swiss withholding tax will also apply to payments (exceeding the respective share capital and used capital contribution reserves) upon a repurchase of shares by the Company, (i) if the Company's share capital is reduced upon such repurchase (redemption of shares), (ii) if the total of repurchased shares exceeds 10% of the Company's share capital or (iii) if the repurchased shares are not resold within six years after the repurchase. This six-year deadline to resell the repurchased shares is suspended for so long as the shares are reserved to cover obligations under convertible bonds, option bonds or employee stock option plans (in the case of employee stock option plans, the maximum suspension is six years). In the event of a taxable share repurchase, Swiss withholding tax is imposed on the difference between the repurchase price and the sum of the nominal value of the repurchased shares and capita contribution reserves paid back upon the repurchase.

Swiss resident individuals who hold their shares as private assets, or Resident Private Shareholders, are in principle eligible for a full refund or credit against income tax of the Swiss withholding tax if they duly report the underlying income in their income tax return. In addition, (i) corporate and individual shareholders who are resident in Switzerland for tax purposes, (ii) corporate and individual shareholders who are not resident in Switzerland, and who, in each case, hold their shares as part of a trade or business carried on in Switzerland through a permanent establishment with fixed place of business situated in Switzerland for tax purposes and (iii) Swiss resident private individuals who, for income tax purposes, are classified as "professional securities dealers" for reasons of, inter alia, frequent dealing, or leveraged investments, in shares and other securities (collectively, "Domestic Commercial Shareholders") are in principle eligible for a full refund or credit against income tax of the Swiss withholding tax if they duly report the underlying income in their income statements or income tax return, as the case may be.

Shareholders who are not resident in Switzerland for tax purposes, and who, during the respective taxation year, have not engaged in a trade or business carried on through a permanent establishment with fixed place of business situated in Switzerland for tax purposes, and who are not subject to corporate or individual income taxation in Switzerland for any other reason (collectively, "Non-Resident Shareholders") may be entitled to a total or partial refund of the Swiss withholding tax if the country in which such recipient resides for tax purposes maintains a bilateral treaty, or Tax Treaty, for the avoidance of double taxation with Switzerland and further conditions of such Tax Treaty are met.

A U.S. shareholder that qualifies for benefits under the U.S.-Swiss Tax Treaty, may apply for a refund of the tax withheld in excess of the 15% treaty rate (or in excess of the 5% reduced treaty rate for qualifying corporate shareholders with at least 10% voting rights, or for a full refund in the case of qualified pension funds). Non-Resident Shareholders should be aware that the procedures for claiming treaty benefits (and the time required for obtaining a refund) may differ from country to country. Non-Resident Shareholders

should consult their own legal, financial or tax advisors regarding receipt, ownership, purchases, sale or other dispositions of shares and the procedures for claiming a refund of the Swiss withholding tax.

Certain U.S. Shareholders May Be Subject To Adverse U.S. Federal Income Tax Consequences If We Are A Controlled Foreign Corporation.

Each "Ten Percent Shareholder" (as defined below) in a non-U.S. corporation that is classified as a "controlled foreign corporation," or a CFC, for United States federal income tax purposes generally is required to include in income for U.S. federal tax purposes such Ten Percent Shareholder's pro rata share of the CFC's "Subpart F income" and investment of earnings in U.S. property, even if the CFC has made no distributions to its shareholders. Subpart F income generally includes dividends, interest, rents and royalties, gains from the sale of securities and income from certain transactions with related parties. Each Ten Percent Shareholder of a CFC is also required to include in income such Ten Percent Shareholder's share of "global intangible low-taxed income" (for tax years beginning after December 31, 2017 and prior to January 1, 2026) and "net CFC tested income" (for tax years beginning after December 31, 2025) with respect to such CFC. In addition, a Ten Percent Shareholder that realizes gain from the sale or exchange of shares in a CFC may be required to classify a portion of such gain as dividend income rather than capital gain. A non-U.S. corporation generally will be classified as a CFC for United States federal income tax purposes if Ten Percent Shareholders own, directly or indirectly, more than 50% of either the total combined voting power of all classes of stock of such corporation entitled to vote or of the total value of the stock of such corporation. A "Ten Percent Shareholder" is a United States person (as defined by the U.S. Internal Revenue Code of 1986, as amended, or the Code, who owns or is considered to own 10% or more of (1) the total combined voting power of all classes of stock entitled to vote or (2) the value of all classes of stock of such corporation. The determination of CFC status is complex and includes attribution rules, the application of which is not entirely certain.

During our 2025 taxable year we believe that we had certain shareholders that were Ten Percent Shareholders for U.S. federal income tax purposes. However, our CFC status for the taxable year ending on December 31, 2025 and our current taxable year is unknown and we may be a CFC for the taxable year ending on December 31, 2025, our current taxable year or a following year. In addition, recent changes to the attribution rules relating to the determination of CFC status may make it difficult to determine our CFC status for any taxable year. Furthermore, it is possible that our non-United States subsidiaries will be CFCs for the current taxable year or a future taxable year even if we are not a CFC for such taxable year(s). U.S. holders should consult their own tax advisors with respect to the potential adverse U.S. tax consequences of becoming a Ten Percent Shareholder in a CFC. If we are classified as both a CFC and a passive foreign investment company, or PFIC, we generally will not be treated as a PFIC with respect to those U.S. holders that meet the definition of a Ten Percent Shareholder during the period in which we are a CFC.

U.S. Holders Of Our Common Shares May Suffer Adverse Tax Consequences If We Are Characterized As A Passive Foreign Investment Company For Any Taxable Year.

Generally, if, for any taxable year, at least 75% of our gross income is passive income, or at least 50% of the value of our assets is attributable to assets that produce passive income or are held for the production of passive income, including cash, we would be characterized as a passive foreign investment company, or "PFIC," for U.S. federal income tax purposes. Passive income for this purpose generally includes dividends, interest, royalties, rents, gains from commodities and securities transactions, the excess of gains over losses from the disposition of assets which produce passive income, and includes amounts derived by reason of the temporary investment of cash, including the funds raised in offerings of our common shares. If we are characterized as a PFIC, U.S. holders (as defined below) of our common shares may suffer adverse tax consequences, including having gains realized on the sale of common shares treated as ordinary income, rather than capital gain, the loss of the preferential rate applicable to dividends received on our common shares by individuals who are U.S. holders, and having interest charges apply to distributions by us and the proceeds of sales of our common shares.

It is possible we were a PFIC with respect to the 2024 taxable year and it is possible we may be a PFIC for the 2025 taxable year or a future taxable year as well, in which case U.S. holders (as defined below) would be subject to a special, generally adverse tax regime. We have not made a determination as to whether we will be a PFIC for any taxable year, and we cannot provide any assurances regarding our PFIC status for past, current or future taxable years. Our status as a PFIC is a fact intensive determination made on an annual basis. Whether we are a PFIC for any taxable year will depend on the composition of our income and assets, and the estimated fair market values of our assets, in each year. The market value of our assets may be determined in large part by reference to the market price of our common shares, which is likely to fluctuate. Our status as a PFIC also depends on the interpretation of the rules governing the PFIC income and asset tests, which are subject to uncertainty (including with respect to the characterization of income from government grants, for which direct legal authority does not exist).

A "U.S. holder" is a beneficial owner of common shares that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity that is treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;

- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if (a) a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial decisions of such trust, or (b) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a United States person.

U.S. Shareholders May Not Be Able To Obtain Judgments Or Enforce Civil Liabilities Against Us Or Our Executive Officers Or Members Of Our Board Of Directors.

We are organized under the laws of Switzerland and our registered office and domicile is located in Zug, Switzerland. Moreover, previously certain of our directors and executive officers were not residents, and again in the future could not be residents, of the United States, and all or a substantial portion of the assets of such persons were located, or could be in the future, located, outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the United States. We have been advised by our Swiss counsel that there is doubt as to the enforceability in Switzerland of original actions, or in actions for enforcement of judgments of U.S. courts, of civil liabilities to the extent solely predicated upon the federal and state securities laws of the United States. Original actions against persons in Switzerland based solely upon the U.S. federal or state securities laws are governed, among other things, by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides that the application of provisions of non-Swiss law by the courts in Switzerland shall be precluded if the result is incompatible with Swiss public policy. Also, mandatory provisions of Swiss law may be applicable regardless of any other law that would otherwise apply.

Switzerland and the United States do not have a treaty providing for reciprocal recognition and enforcement of judgments in civil and commercial matters. The recognition and enforcement of a judgment of the courts of the United States in Switzerland is governed by the principles set forth in the Swiss Federal Act on Private International Law. This statute provides in principle that a judgment rendered by a non-Swiss court may be enforced in Switzerland only if:

- the non-Swiss court had jurisdiction pursuant to the Swiss Federal Act on Private International Law;
- the judgment of such non-Swiss court has become final and non-appealable;
- the judgment does not contravene Swiss public policy;
- the court procedures and the service of documents leading to the judgment were in accordance with the due process of law; and
- no proceeding involving the same position and the same subject matter was first brought in Switzerland, or adjudicated in Switzerland, or was earlier adjudicated in a third state and this decision is recognizable in Switzerland.

Risks Related to Information Security and Privacy

We May Fail To Comply With Evolving European And Other Privacy Laws.

Numerous state, federal, and international laws and regulations govern the collection, dissemination, use, privacy, confidentiality, security, availability, integrity, and other processing of personal data or personal information. In the United States, numerous states have passed comprehensive consumer privacy laws, and several other states have proposed similar legislation. The existence of comprehensive privacy laws in different states in the country make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

We are subject to European privacy laws, such as the GDPR, where we collect and use personal data related to Europe, including in connection with conducting our clinical trials in the EEA and the Swiss data protection regime. The GDPR imposes a broad range of strict requirements on companies subject to the GDPR, including requirements relating to processing special categories of personal data (such as health data), where required obtaining consent of the individuals to whom the personal data relates, having legal bases and/or conditions for processing personal data, including to the United States, providing details to those individuals regarding the processing of their personal data, implementing safeguards to protect the security and confidentiality of personal data, having data processing agreements with third parties who process personal data, responding to individuals' requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments for high risk processing activities, ensuring certain accountability measures and record-keeping.

Failure to comply with the GDPR and any supplemental EEA Member State or UK national data protection laws which may apply by virtue of the location of the individuals whose personal data we collect, may result in substantial penalties, including potential fines of up to the greater of €20 million (£17.5 million under the UK GDPR) or 4% of our total worldwide annual turnover. 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 remains 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 particular, EEA Member States have implemented national laws which may partially deviate from the EU GDPR and impose different and more restrictive obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EEA. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows EU Member State nations to enact laws that impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty.

The UK's data protection regime is independent from but aligned to the EU's data protection regime. Although the UK is regarded as a third country under the EU's GDPR, the European Commission has now issued an adequacy decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. In December 2025, the European Commission adopted a decision to extend the validity of the UK adequacy decision for six years until December 2031, determining that the UK continues to offer a level of data protection that is "essentially equivalent" to the EU standards. This follows the UK's adoption of the Data (Use and Access) Act 2025 (the "DUAA") on 19 June 2025. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK Government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. This lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, complexity and cost to our handling of personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the EEA.

The GDPR also imposes strict rules on the transfer of personal data outside of the EEA and UK to countries that do not ensure an adequate level of protection, like the United States. We must, therefore, ensure that we maintain adequate safeguards to enable the transfer of personal data outside of the EEA or the UK, in compliance with European data protection laws. In some cases, we rely upon the European Commission approved standard contractual clauses to legitimize transfers of personal data out of the EEA from controllers or processors established outside the EEA (and not subject to the GDPR). The UK is not subject to the European Commission's standard contractual clauses but has published its own transfer mechanism, the International Data Transfer Agreement, which enables transfers from the UK. Changes with respect to any of these matters may lead to additional costs and increase our overall risk exposure. The EU and United States have adopted its adequacy decision for the EU-U.S. Data Privacy Framework, or Framework, which entered into force on July 11, 2023. This Framework provides that the protection of personal data transferred between the EU and the U.S. is comparable to that offered in the EU. This provides a further avenue to ensuring transfers to the United States are carried out in line with GDPR. There has been an extension to the Framework to cover UK transfers to the United States. The Framework could be challenged like its predecessor frameworks.

Switzerland has adopted a revised data protection regime which came into effect in September 2023. As a general matter, Switzerland's national data protection regime is aligned to the EU's data protection regime. Switzerland's data protection regime has similar restrictions on data transfers from Switzerland to recipients outside the EEA and UK. There has been an extension to the Framework to cover Swiss transfers to the United States.

We expect that we will continue to face uncertainty as to whether our efforts to comply with any obligations under European privacy laws will be sufficient. A failure to comply with European data protection laws, could result in data protection authority enforcement action, which could result in fines and other penalties, private litigation or adverse publicity and could negatively affect our operating results and business. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business and on our ability to attract and retain new clients or pharmaceutical partners. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could harm our business.

Artificial Intelligence Presents Risks And Challenges That Can Impact Our Business Including By Posing Cybersecurity and Other Risks To Our Confidential Information, Proprietary Information And Personal Data.

We may use, and our vendors may incorporate, artificial intelligence, or AI, both in our own development and implementation of AI and through the adoption of commercially available tools. The use of AI presents risks and challenges that could adversely affect our business and reputation, including cybersecurity, data privacy, IT, confidentiality, regulatory, legal, operational, competitive, reputational, intellectual property and other risks. Specifically, risks related to accuracy, bias, AI hallucinations, discrimination, harmful content, misinformation, fraud, scams, targeted attacks (including model poisoning or data poisoning), surveillance, data leakage, bias and inequality, environmental and other harms may flow from our development or use of AI technologies. For example, use of certain AI tools may lead to false or misleading information being used, relied upon or referenced by us or our vendors. Furthermore, use of certain AI tools may increase the risk of unauthorized disclosure of confidential information, compromise of proprietary intellectual property, or inadvertent inclusion of third-party intellectual property or other protected material, which could result in disputes or claims of infringement.

Additionally, government and supranational regulation related to AI is evolving as new laws and regulations are implemented globally and could increase the burden and operational cost of compliance, including through requirements related to transparency,

accountability, risk management, human oversight, and data governance. We expect to see increasing regulation related to AI governance, use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area. The EU's Artificial Intelligence Act, or the AI Act, started entered into force on August 1, 2024, with important sections scheduled to come into effect in August 2026. As currently enacted, the AI Act imposes significant obligations on providers and deployers of high-risk AI systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles when developing and using AI technology. The scope of requirements depends on legal and risk determinations that rely on legal provisions that have not yet been fully interpreted by courts or regulators, and non-compliance can lead to significant fines.

In the U.S., the regulatory environment is complex and uncertain. Over the past year, states have advanced, and in some cases passed, dozens of laws focusing on AI governance and regulation, including on deployment of AI in healthcare settings. At the federal level, the current administration has endorsed a federal moratorium on the enforcement of state AI laws, including through a December 11, 2025, executive order on "Ensuring a National Policy Framework for Artificial Intelligence." So far, these efforts have not been successful at curtailing state action on AI regulation, contributing to a complicated legislative patchwork, which may be litigated in state and federal courts. In addition, there is continued uncertainty regarding the application of existing federal and state legal frameworks to uses and development of AI, and legal norms and market standards regarding AI continue to evolve. For example, various federal and state regulators have issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The U.S. Food and Drug Administration, for example, issued guidance on the use of artificial intelligence in medical devices, requiring detailed risk management and review processes to obtain approvals. If we develop or use AI systems that are governed by the these laws or regulations, we will need to meet higher standards of data quality, transparency, and human oversight, and we would need to adhere to specific, potentially burdensome and costly ethical, accountability, and administrative requirements. We may also be subject to significant enforcement or litigation in the event of any perceived non-compliance.

The rapid evolution of AI will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that AI is implemented in accordance with applicable law and regulation and to minimize any real or perceived unintended harmful impacts. The use of certain AI technologies can also give rise to intellectual property risks, including by disclosing or otherwise compromising confidential or proprietary intellectual property, or by undermining our ability to assert or defend ownership rights in intellectual property created with the assistance of AI tools.

Our vendors may in turn incorporate AI tools into their offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy, data security and data integrity. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. In addition, the use of generative AI models in our internal or third-party systems may create new attack surfaces or methods for adversaries, which could impact us and our vendors. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

We are committed to implementing governance and control measures to mitigate these risks, but there can be no assurance that such measures will adequately prevent or mitigate the adverse effects that the integration and use of AI may have on our business, financial conditions and results of operations.

Our Internal Information Technology Systems, Or Those Of Our Collaborators Or Other Contractors Or Consultants, May Fail Or Suffer Security Breaches, Which Could Result In A Material Disruption Of Our Product Development Programs.

Our internal information technology systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, ransomware, social engineering (including phishing), unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification of data, records or other information, encryption through ransomware, or intentional or accidental release or loss of information maintained in the information systems and networks of our company and our vendors, including personal information of our employees and study subjects, and company and vendor confidential data. These attacks and activity are also being facilitated or enhanced by evolving technologies, including AI. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or the personnel of our vendors to disclose sensitive information in order to gain access to our data and/or systems. Like other companies in the industry, we, and our third-party vendors, have experienced threats and cybersecurity incidents relating to our information technology infrastructure, data and systems, and may experience threats and cybersecurity incidents in the future. The number and

complexity of these threats continue to increase over time. If a material cybersecurity incident or breach of our information technology systems or those of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engage in more electronic transactions with payors and patients, and rely more on cloud-based information systems, the related security risks will increase and we will need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal information technology systems or those of our third-party contractors, or our consultants will be sufficient to protect us against breakdowns, service disruption, data deterioration, loss, theft or corruption of data in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security or data breach, industrial espionage attacks or insider threat attacks which could result in financial, legal, business or reputational harm.

General Risks

We Incur Significant 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 incur significant legal, accounting and other expenses. SOX, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time towards maintaining compliance with these requirements. Moreover, these requirements increase our legal and financial compliance costs and make some activities more time-consuming and costly.

Pursuant to SOX Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. In this regard, we incur substantial accounting expenses and expend significant management efforts. Our testing may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or significant deficiencies. If we identify one or more material weaknesses, or significant deficiencies that we cannot remediate in a timely manner, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

The Market Price Of Our Common Shares Has Been Volatile and Fluctuate Substantially, Which Could Result In Substantial Losses For Shareholders.

Our share price has been, and in the future may be, subject to substantial volatility. In addition, the stock market in general, and Nasdaq listed biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. For example, our shares have traded within a range of a high price of $220.20 and a low price of $11.63 per share for the period beginning on October 19, 2016, our first day of trading on the Nasdaq Global Market, through December 31, 2025. As a result of this volatility, our shareholders could incur substantial losses. In addition, the market price for our common shares may be influenced by many factors, including:

- the success of existing or new competitive products or technologies;
- the timing and results of any product candidates that we may 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 products, including those that involve gene 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

may develop;

- the results of our efforts to discover, develop, acquire or in-license 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 shares by us, our insiders, or other shareholders;
- expiration of market stand-off or lock-up agreements;
- 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 common shares;
- 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.

These and other market and industry factors may cause the market price and demand for our common shares to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their common shares and may otherwise negatively affect the liquidity of our common shares. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our shareholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

Unfavorable Global Economic Conditions and Uncertain Geopolitical Environment Could Adversely Affect Our Business, Financial Condition Or Results Of Operations.

We are a multinational company and we conduct our clinical trials domestically and internationally. Our business, financial condition and results of operations could be adversely affected by general conditions in the global economy, disruption of global financial markets and a recession or market correction, including, for example, as a result of uncertain trade policy, political unrest, including as a result of geopolitical tension such as a deterioration in the relationship between the United States and China, escalation of tensions between China and Taiwan, the ongoing military conflict between Russia and Ukraine and related sanctions imposed against Russia, or the Israel-Hamas war, and other global macroeconomic factors such as inflation, interest rate and currency rate fluctuations, tariffs, changes in or disruptions of certain U.S. governmental agencies, such as the FDA, whether due to a potential or actual U.S. federal government shutdown or otherwise, new laws and regulations or amendments to existing laws and regulations in the U.S. and foreign countries. Such conditions could reduce our ability to access capital and cause more frequent or acute fluctuations in our share price or that of our sector, which could in the future negatively affect our liquidity and could materially affect our business and the value of our common stock.

In addition, domestic and international political uncertainty, including implementation of aggressive trade policies, could impact our ability to conduct our clinical trials. For example, in early 2025, the United States imposed tariffs on imports on its trading partners, including Canada, Mexico, the EU and China. Historically, tariffs have led to increased trade and political tensions, between not only the U.S. and China, but also between the U.S. and other countries in the international community. In response to tariffs, other countries have implemented retaliatory tariffs on U.S. goods. Adverse reactions resulting from trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. Additionally, in September 2025, the current administration also announced a 100% tariff on brand-name or patented drugs unless pharmaceutical companies expand their manufacturing operations in the U.S., and may impose more restrictions on goods. Although the pharmaceutical tariff is currently on hold, this could have a material adverse effect on our supply chain and business prospects as well as the larger biopharmaceutical industry. While certain tariffs have subsequently been suspended, modified or temporarily reduced, we cannot predict the results of trade negotiations or the outcome of ongoing legal challenges to tariff policies. Tariffs levied by the United States and other countries may lead to uncertainty in our ability to run clinical trials in preferred jurisdictions, impact our ability to import drug product, as well as raw materials to manufacture drug product domestically, and lead to uncertainty in our ability to supply drug product for our clinical trials, and otherwise increase the costs for us to run our business.

Additionally, severe or prolonged economic downturn or additional global financial crises could result in a variety of risks to our business, including weakened demand for any product candidates we develop or our ability to raise additional capital when needed on acceptable terms, if at all. Weak economic conditions or significant uncertainty regarding the stability of financial markets related to stock market volatility, inflation, recession, government shutdowns, changes in tariffs or other trade policies, trade agreements, trade wars or governmental fiscal, monetary and tax policies, among others, could adversely impact our business, financial condition

and operating results.

Conditions In The Banking System And Financial Markets, Including The Failure Of Banks And Financial Institutions, Could Have An Adverse Effect On Our Operations And Financial Results.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. If, for example, certain banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, our ability to access our existing cash, cash equivalents and investments may be threatened. While it is not possible at this time to predict the extent of the impact that high market volatility and instability of the banking sector could have on economic activity and our business in particular, the failure of other banks and financial institutions and the measures taken by governments, businesses and other organizations in response to these events could adversely impact our business, financial condition and results of operations.

If Securities Analysts Do Not Publish Research Or Reports About Our Business Or If They Publish Negative Evaluations Of Our Common Shares, The Price Of Our Common Shares Could Decline.

The trading market for our common shares will rely 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 common shares, the price of our common shares could decline. If one or more of these analysts cease to cover our common shares, we could lose visibility in the market for our common shares, which in turn could cause our common share price to decline.

Our Business Is Subject To Economic, Political, Regulatory And Other Risks Associated With International Operations.

Our business is subject to risks associated with conducting business internationally. We and a number of our suppliers and collaborative and clinical study relationships are located outside the United States. Accordingly, our future results could be harmed by a variety of factors, including:

- economic weakness, including inflation, or political instability in particular non-U.S. economies and markets;
- differing regulatory requirements for drug approvals in non-U.S. countries;
- potentially reduced protection for intellectual property rights;
- difficulties in compliance with non-U.S. laws and regulations;
- changes in non-U.S. regulations and customs, tariffs and trade barriers;
- changes in non-U.S. currency exchange rates and currency controls;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling outside the United States;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities outside the United States; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including floods and fires.

Disruptions At The FDA, The SEC and Other U.S. Government Agencies Or Comparable Foreign Regulatory Authorities 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, Which Could Negatively Impact Our Business And Our Timelines.

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, shifting policy priorities as a result of changes in the Presidential administration and political appointees tasked to oversee the agency, the availability of personnel and other resources, and statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine transactions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of

the SEC, and other U.S. government agencies or comparable foreign regulatory authorities on which our operations may rely is subject to the impacts of political events, including executive and congressional priorities, which are inherently fluid and unpredictable.

Disruptions and personnel turnover, as a result of leadership changes, staff reductions or otherwise, at the FDA and other agencies may slow the time necessary for product applications to be reviewed and/or approved by necessary government agencies, which could adversely affect our business. Changes and cuts in FDA staffing have been reported by some in the pharmaceutical industry as creating instances of delays in the FDA's responsiveness or in its ability to review investigational new drug applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. 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. Specifically, in 2025, the U.S. government issued executive orders and implemented reductions in force that have adversely impacted FDA staffing and resources. If a prolonged government shutdown occurs or if staffing changes prevent the FDA, the SEC or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, including formal and informal interactions with product developers, it could significantly impact the ability of the FDA and the SEC to timely review and process our submissions, which could have a material adverse effect on our business and our timelines. Further, future government shutdown or other substantial disruption at other government agencies, such as the SEC, may also impact our business by delaying review of our public filings, which in turn could delay or frustrate our ability to access the public capital markets. Similar developments at regulators in other countries (including the EMA) could have similar impacts on our applications for marketing approval and on our business.

In addition, changes in the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our products, including applicable pricing and reimbursement frameworks under federal healthcare programs, could affect the commercial viability of our products, create revenue uncertainty, and impact our ability to achieve profitability. Regulatory challenges may introduce new challenges in obtaining FDA approval or navigating commercialization, and any delay in securing applicable regulatory approvals would adversely affect our business and prospects.

The Increasing Use of Social Media Platforms Presents Risks And Challenges.

Social media practices in the biopharmaceutical industry and the FDA's regulation of social media continues to evolve. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us. For example, our employees or agents may use social media channels to inadvertently provide inaccurate or misleading information about our products and commercialization efforts. If regulators become aware of such disclosures, they may take administrative or enforcement action against us. There is also a risk that third parties will use social media to disseminate inaccurate or misleading information about us or our products. If this occurs, we may not be able to adequately defend our business or the public's perception of us or our products. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions, or incur other harm to our business.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Cybersecurity Risk Management

In the ordinary course of our business, we use, store and process data including data of our employees, partners, collaborators, and vendors. We also process anonymized information about participants in clinical trials involving certain of our product candidates. We have implemented a cybersecurity risk management program that is designed to identify, assess, and mitigate risks from cybersecurity threats to this data and our systems.

Our cybersecurity risk management program includes a number of components, including information security program assessments and continuous monitoring of critical risks from cybersecurity threats using automated tools. We periodically engage third parties to conduct risk assessments on our systems, including penetration testing and other vulnerability analyses. Our finance department, with the assistance of outside technical advisors, periodically conducts an internal assessment of different systems to assess our risk management processes, including cybersecurity risk management. We have taken additional steps to further mature our cybersecurity monitoring and response, vulnerability management, and incident response capabilities through new vendor partnerships to centralize and develop additional detection and response capabilities. And updated comprehensive cybersecurity strategy has also been developed to guide cybersecurity risk management activities, align corporate security standards, and guide requirements for all technology across the organization with regards to cybersecurity. Additionally, we have implemented an employee education program that is designed to raise awareness of cybersecurity threats, including risks posed by phishing attempts. This training is included during the employee onboarding process and periodically thereafter. As part of our cybersecurity risk management program, we maintain processes to assess and review the cybersecurity practices of third-party vendors and suppliers. Prior to engaging third-party

vendors and key suppliers, we conduct a security assessment and, as appropriate, include security requirements in contracts. We, like other companies in our industry, face a number of cybersecurity risks in connection with our business. Although our business strategy, results of operations, and financial condition have not, to date, been materially affected by risks from cybersecurity threats, including as a result of previously identified cybersecurity incidents, we have, from time to time, experienced threats to and security incidents related to our data and systems, including phishing attacks. For more information on our cybersecurity related risks, see "*Risk Factors—Risks Related to Information Security and Privacy—Our Internal Information Technology Systems, Or Those Of Our Collaborators Or Other Contractors Or Consultants, May Fail Or Suffer Security Breaches, Which Could Result In A Material Disruption Of Our Product Development Programs*."

Governance

Under the ultimate direction of our chief executive officer, or CEO, and our executive management team (including our General Counsel who serves as our Chief Compliance Officer), with oversight from our audit committee of the board of directors, or Audit Committee, our Head of Information Technology, or Head of IT, has primary responsibility for assessing, operating and managing our cybersecurity threat management program. Our Head of IT meets periodically with our Chief Compliance Officer to discuss current developments in the cybersecurity landscape and our cybersecurity risk management program, including providing updates regarding the sources and nature of critical risks we face and how the IT department assesses those risks, including the likelihood of such risks, the severity of impact, and progress on vulnerability remediation.

Our Chief Compliance Officer and Head of IT consult with other members of our information technology department, and with third parties with expertise in cybersecurity, to develop strategies to assess, address and align cybersecurity efforts with our business objectives and operational requirements. The Head of IT role is currently held by an individual with 17 years of experience leading information security, corporate systems, technology risk, and compliance management, bringing deep expertise in cybersecurity and digital infrastructure operations across diverse industries and regulatory environments.

As part of our board of directors' enterprise risk management program, our board of directors has responsibility for oversight of cybersecurity risk management. Our board of directors has delegated to our Audit Committee oversight of our cybersecurity risk management program, including oversight of information security and cybersecurity threats and related compliance and disclosure requirements. On an annual basis, our Head of IT provides an update to our Audit Committee regarding our cybersecurity risk management program, including as it relates to critical cybersecurity risks, ongoing cybersecurity initiatives and strategies, and applicable regulatory requirements and industry standards. The Audit Committee periodically reports on cybersecurity risk management to the full board of directors.

Item 2. Properties.

Our principal executive offices are located in Zug, Switzerland pursuant to a real estate lease agreement with a term that renews every three months. Our U.S. headquarters for research and development is located at 105 West First Street, Boston, Massachusetts where we lease approximately 263,500 square feet of laboratory and office space. The facility is leased through October 2034 with an option to extend the term of the lease for two additional five-year periods.

In May 2020, we entered into a lease agreement for a 50,249 square foot building in Framingham, Massachusetts, which we are using as a cell therapy manufacturing facility for clinical production, and plan to use for commercial production, of our investigational cell therapy product candidates. This facility is leased through March 2036 with an option to extend the term of the lease for two additional seven-year periods.

We also lease laboratory and office space, for example, in San Francisco, California. We believe that our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

Item 3. Legal Proceedings.

In the ordinary course of business, we are or have been from time to time involved in lawsuits, investigations, proceedings and threats of litigation related to, among other things, our intellectual property estate (including the worldwide patent portfolio we have exclusively licensed from Dr. Charpentier), commercial arrangements and other matters. Such proceedings may include quasi-litigation, *inter partes* administrative proceedings in the U.S. Patent and Trademark Office and the European Patent Office or patent offices in other countries, involving our intellectual property estate including the worldwide patent portfolio we have exclusively licensed from Dr. Charpentier. For example, in the fourth quarter of 2025, ToolGen, Inc., or ToolGen, initiated a lawsuit against us and other third parties alleging patent infringement by CASGEVY of a ToolGen patent relating to CRISPR/Cas9 gene editing technology. The outcome of any of the foregoing, is inherently uncertain. In addition, litigation and related matters are costly and may divert the attention of our management and other resources that would otherwise be engaged in other activities. If we were unable to prevail in any such proceedings, our business, results of operations, liquidity and financial condition could be adversely affected.

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

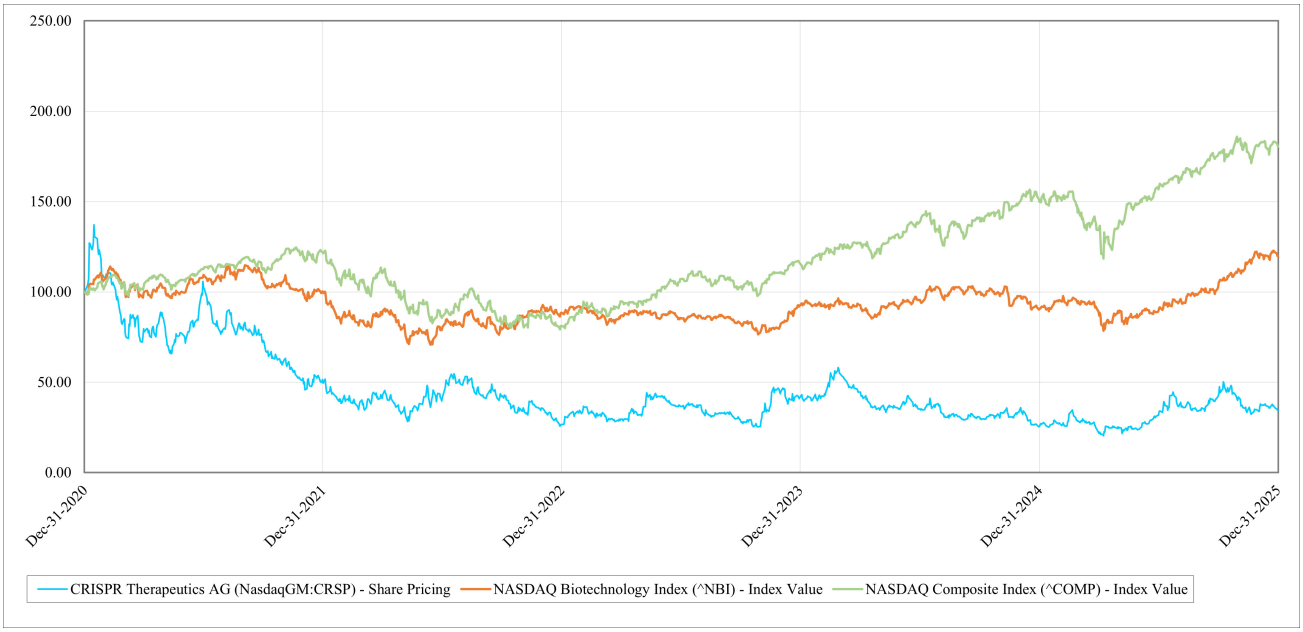
Our common shares are traded on The Nasdaq Global Market under the symbol "CRSP."

Stock Performance Graph

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

The graph set forth below compares the cumulative total stockholder return on our shares between December 31, 2020 and December 31, 2025, with the cumulative total return of (a) the Nasdaq Biotechnology Index and (b) the Nasdaq Composite Index, over the same period. This graph assumes the investment of $100 on December 31, 2020 in our common shares, the Nasdaq Biotechnology Index and the Nasdaq Composite Index and assumes the reinvestment of dividends, if any. The comparisons shown in the graph below are based upon historical data. The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Comparison of Total Return Among CRISPR Therapeutics AG, the Nasdaq Composite Index and the Nasdaq Biotechnology Index



Swiss Tax Considerations

Swiss Withholding Tax

Under present Swiss tax law, dividends due and similar cash or in-kind distributions made by us to a shareholder (including liquidation proceeds and stock dividends) are subject to Swiss federal withholding tax (*Verrechnungssteuer*) ("Withholding Tax"), currently at a rate of 35% (applicable to the gross amount of the taxable distribution). We are obliged to deduct the Withholding Tax from the gross amount of any taxable distribution and to pay the tax to the Swiss Federal Tax Administration within 30 calendar days of the due date of such distribution. However, the repayment of the nominal value of shares and any repayment of qualifying additional paid-in capital (capital contribution reserves (*Reserven aus Kapitaleinlagen*)) are not subject to the Withholding Tax. The

Withholding Tax will also apply to payments (exceeding the respective share capital and used capital contribution reserves) upon a repurchase of shares by us, (i) if our share capital is reduced upon such repurchase (redemption of shares), (ii) if the total of repurchased shares exceeds 10% of our share capital or (iii) if the repurchased shares are not resold within six years after the repurchase. This six year deadline to resell the repurchased shares is suspended for so long as the shares are reserved to cover obligations under convertible bonds, option bonds or employee stock option plans (in the case of employee stock option plans, the maximum suspension is six years). In the event of a taxable share repurchase, Withholding Tax is imposed on the difference between the repurchase price and the sum of the nominal value of the repurchased shares and qualifying additional paid-in capital paid back upon the repurchase.

Swiss resident individuals who hold their shares as private assets ("Resident Private Shareholders") are in principle eligible for a full refund or credit against income tax of the Withholding Tax if they duly report the underlying income in their income tax return. In addition, (i) corporate and individual shareholders who are resident in Switzerland for tax purposes, (ii) corporate and individual shareholders who are not resident in Switzerland, and who, in each case, hold their shares as part of a trade or business carried on in Switzerland through a permanent establishment with fixed place of business situated in Switzerland for tax purposes and (iii) Swiss resident private individuals who, for income tax purposes, are classified as "professional securities dealers" for reasons of, inter alia, frequent dealing, or leveraged investments, in shares and other securities (collectively, "Domestic Commercial Shareholders") are in principle eligible for a full refund or credit against income tax of the Withholding Tax if they duly report the underlying income in their income statements or income tax return, as the case may be.

Shareholders who are not resident in Switzerland for tax purposes, and who, during the respective taxation year, have not engaged in a trade or business carried on through a permanent establishment with fixed place of business situated in Switzerland for tax purposes, and who are not subject to corporate or individual income taxation in Switzerland for any other reason (collectively, "Non-Resident Shareholders") may be entitled to a total or partial refund of the Withholding Tax if the country in which such recipient resides for tax purposes maintains a bilateral treaty for the avoidance of double taxation with Switzerland ("Tax Treaty") and further conditions of such Tax Treaty are met. Non-Resident Shareholders should be aware that the procedures for claiming treaty benefits (and the time required for obtaining a refund) may differ from country to country. Non-Resident Shareholders should consult their own legal, financial or tax advisors regarding receipt, ownership, purchases, sale or other dispositions of shares and the procedures for claiming a refund of the Withholding Tax.

Automatic Exchange of Information

The Automatic Exchange of Information in Tax Matters (the "AEI") is a global initiative led by the Organization for Economic Co-operation and Development. It aims to establish a universal standard for automatic exchange of tax information and to increase tax transparency.

Jurisdictions that are committed to implement or have implemented the AEI (such as Switzerland, the EU member countries and many other jurisdictions worldwide) require their Reporting Financial Institutions in accordance with the respective local implementing law to determine the tax residence(s) of their account holders and controlling persons (as applicable) and, in case of reportable accounts, report certain identification information, account information and financial information (including the account balance and related payments such as interest, dividends, other income and gross proceeds) to the local tax authority which will then exchange the information received with the tax authorities in the relevant reportable jurisdictions.

A list of the AEI agreements of Switzerland in effect or signed and becoming effective can be found on the website of the State Secretariat for International Financial Matters.

Swiss Federal Stamp Taxes

The issuance of the shares and the sale pursuant to and in the course of an offering is subject to Swiss federal securities issuance stamp tax (*Emissionsabgabe*) of 1% and would be borne by us.

The subsequent purchase or sale of our shares, whether by Resident Private Shareholders, Domestic Commercial Shareholders or Non-Resident Shareholders (secondary market transactions), may be subject to the Swiss federal securities transfer stamp tax (*Umsatzabgabe*) at a current rate of up to 0.15%, calculated on the purchase price or the sale proceeds, respectively, if (i) such transfer occurs through or with a Swiss or Liechtenstein bank or by or with involvement of another Swiss securities dealer as defined in the Swiss federal stamp tax duty act and (ii) no exemption applies.

Swiss Federal, Cantonal and Communal Individual Income Tax and Corporate Income Tax

*Non-Resident Shareholder*s

Non-Resident Shareholders are not subject to any Swiss federal, cantonal or communal income tax on dividend payments and similar distributions because of the mere holding of our shares. The same applies for capital gains on the sale of shares. For Withholding Tax consequences, see above.

Resident Private Shareholders and Domestic Commercial Shareholders

Resident Private Shareholders who receive dividends and similar cash or in-kind distributions (including liquidation proceeds as well as stock dividends or taxable repurchases of shares as described above), which are not repayments of the nominal value of the shares or qualifying additional paid-in capital, are required to report such receipts in their individual income tax returns and are subject to Swiss federal, cantonal and communal income tax on any net taxable income for the relevant tax period. Furthermore, for Swiss federal individual income tax purposes, dividends and similar distributions as described above are only taxed at 70% on federal level (*Teilbesteuerung*), if the investment amounts to at least 10% of our share capital. On cantonal and communal level similar provisions were introduced but the regulations may vary, depending on the canton of residency.

A gain or a loss by Resident Private Shareholders realized upon the sale or other disposition of shares to a third party will generally be a tax-free private capital gain or a not tax-deductible capital loss, as the case may be.

Domestic Commercial Shareholders who receive dividends and similar cash or in-kind distributions (including liquidation proceeds as well as bonus shares) are required to recognize such payments in their income statements for the relevant tax period and are subject to Swiss federal, cantonal and communal individual or corporate income tax, as the case may be, on any net taxable earnings accumulated (including the dividends) for such period. Domestic Commercial Shareholders who are corporate taxpayers may qualify for participation relief on dividend distributions (*Beteiligungsabzug*), if shares held have a market value of at least CHF 1 million or represent at least 10% of our share capital or give entitlement to at least 10% of our profit and reserves, respectively.

Domestic Commercial Shareholders are required to recognize a gain or loss realized upon the disposal of shares in their income statement for the respective taxation period and are subject to Swiss federal, cantonal and communal individual or corporate income tax, as the case may be, on any net taxable earnings (including the gain or loss realized on the sale or other disposition of shares) for such taxation period. For Domestic Commercial Shareholders who are individual taxpayers, a gain realized upon the disposal of shares is taxed at 70% on federal level (*Teilbesteuerung*), if (i) the investment is held in connection with the conduct of a trade or business or qualifies as an opted business asset (*gewillkürtes Geschäftsvermögen*) according to Swiss tax law, (ii) the sold shares reflect an interest in the share capital of a company of at least 10% and (iii) were held for at least one year. On cantonal and communal level similar provisions were introduced, but the regulations may vary depending on the canton of residency. Domestic Commercial Shareholders who are corporate taxpayers may be entitled to participation relief (*Beteiligungsabzug*), if shares sold during the tax period (i) reflect an interest in the share capital of a company of at least 10% or if such shares sold allow for at least 10% of the profit and reserves and (ii) were held for at least one year. The participation relief applies to the difference between the sale proceeds and the initial costs of the participation (*Gestehungskosten*), resulting in the taxation of a recapture of previous write-downs of the participation.

Swiss Wealth Tax and Capital Tax

Non-Resident Shareholders

Non-Resident Shareholders holding our shares are not subject to cantonal and communal wealth or annual capital tax because of the mere holding of such shares.

Resident Private Shareholders and Domestic Commercial Shareholders

Resident Private Shareholders are required to report their shares as part of their private wealth and are subject to cantonal and communal wealth tax. Domestic Commercial Shareholders are required to report their shares as part of their business wealth or taxable capital, as defined, and are subject to cantonal and communal wealth or annual capital tax.

Swiss Facilitation of the Implementation of the U.S. Foreign Account Tax Compliance Act

Switzerland has concluded an intergovernmental agreement with the United States to facilitate the implementation of the Foreign Account Tax Compliance Act. The agreement ensures that the accounts held by U.S. persons with Swiss financial institutions are disclosed to the U.S. tax authorities either with the consent of the account holder or by means of group requests within the scope of administrative assistance. Information will not be transferred automatically in the absence of consent, and instead will be exchanged only within the scope of administrative assistance on the basis of the double taxation agreement between the United States and Switzerland. On October 8, 2014, the Swiss Federal Council approved a mandate for negotiations with the United States on changing the current direct notification-based regime to a regime where the relevant information is sent to the Swiss Federal Tax Administration, which in turn provides the information to the U.S. tax authorities.

THE DISCUSSION ABOVE IS A SUMMARY OF MATERIAL SWISS TAX CONSIDERATIONS. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PARTICULAR SHAREHOLDER. EACH SHAREHOLDER IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT IN LIGHT OF THE SHAREHOLDER'S OWN CIRCUMSTANCES.

Holders

As of February 10, 2026, we had approximately 17 holders of record of our common shares. This number does not include beneficial owners whose shares were held in street name.

Dividends

We have not paid any cash dividends on our common shares since inception and do not anticipate paying cash dividends in the foreseeable future.

Securities authorized for issuance under equity compensation plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Item 6. Reserved

Not applicable.

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

You should read the following discussion and analysis of our financial condition and results of operations 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, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

Our mission is to create transformative gene-based medicines for serious human diseases. We are a leading biopharmaceutical company focused on the development of CRISPR-based therapeutics, including by using CRISPR/Cas9 technology. We have established a portfolio of therapeutic programs spanning four core franchises: hemoglobinopathies, *in vivo* approaches, CAR T, and regenerative medicine. Depending on the program, we take either an *ex vivo* approach, in which we edit cells outside of the human body before administering them to the patient, or an *in vivo* editing approach, where we deliver the CRISPR-based therapeutic directly to target cells within the human body.

CRISPR/Cas9 is a revolutionary technology for gene editing, the process of precisely altering specific sequences of genomic DNA. We have advanced this technology from discovery to an approved medicine with unparalleled speed, culminating in the landmark first approval of a CRISPR-based therapy, CASGEVY (exagamglogene autotemcel [exa-cel]), in 2023 with our collaborators at Vertex Pharmaceuticals Incorporated, or Vertex.

We continue to innovate on our platform to develop next-generation technologies that can enable new therapies. We are developing other technologies, including delivery technologies and other gene editing technologies, like SyNTase. Through our efforts, we aim to unlock the full potential of gene-based therapeutics to create medicines that can transform people's lives. We believe that our innovative research, translational expertise, and clinical development experience, position us as a leader in the development of CRISPR-based therapeutics and may enable us to create an entirely new class of highly effective and potentially curative therapies for patients with both common and rare diseases for whom current biopharmaceutical approaches have had limited success.

Hemoglobinopathies

CASGEVY

CASGEVY is a non-viral, *ex vivo* CRISPR/Cas9 gene-edited cell therapy, in which a patient's own hematopoietic stem and progenitor cells are edited at the erythroid specific enhancer region of the BCL11A gene through a precise double-strand break. This edit results in the production of high levels of fetal hemoglobin in red blood cells, which can compensate for the defective adult hemoglobin in patients with SCD and TDT. CASGEVY is the first therapy to emerge from our strategic partnership with Vertex and is being advanced under a joint development and commercialization agreement between us and Vertex and certain of its affiliates.

In 2023, CASGEVY became the first-ever approved CRISPR-based gene-editing therapy in the world. To date, CASGEVY has been approved in the United States, European Union, Great Britain, Canada, Switzerland and certain countries in the Middle East for the treatment of eligible patients 12 years and older with SCD or TDT. We and Vertex continue to investigate CASGEVY, including in clinical trials designed to assess the safety and efficacy of a single dose of CASGEVY in patients 12 to 35 years of age with severe SCD and TDT, respectively, two pivotal trials in patients 5 to 11 years of age, one in severe SCD and a second in TDT, and long-term follow-up clinical trials designed to follow participants for up to 15 years after CASGEVY infusion. Overall, CASGEVY safety data presented to date is generally consistent with an autologous stem cell transplant and myeloablative conditioning. Efficacy data presented to date support the profile of this therapy as a potential one-time functional cure for people with severe SCD and TDT.

Additional Candidates

We continue to advance our internally developed targeted conditioning program, as well as *in vivo* hematopoietic stem cell editing approaches utilizing lipid nanoparticle-mediated delivery through preclinical studies. Both initiatives could significantly expand the addressable patient populations for SCD and TDT.

***In Vivo* Liver Editing**

We have established a leading platform for *in vivo* gene editing and are rapidly advancing a pipeline of *in vivo* gene editing candidates that target the liver, taking advantage of validated lipid nanoparticle, or LNP, delivery technologies, and aim to treat diseases where we can produce a strong therapeutic effect by safely disrupting a gene with well-understood genetic association. We have established a proprietary LNP delivery platform to enable gene-editing in the liver using both CRISPR/Cas9 and our novel, proprietary SyNTase editing technologies.

Our *in vivo* portfolio includes cardiovascular programs, such as CTX310, directed towards angiopoietin-related protein 3 or ANGPTL3, which is currently in an ongoing Phase 1b clinical trial in patients with heterozygous familial hypercholesterolemia, homozygous familial hypercholesterolemia, mixed dyslipidemias, or severe hypertriglyceridemia.

Additional candidates

In addition, we have a number of earlier stage investigational *in vivo* programs leveraging gene disruption in the liver for both common and rare diseases, including CTX340, directed towards angiotensinogen for the treatment of refractory hypertension; our next-generation *LPA* program, CTX321 directed towards *LPA*, the gene encoding apolipoprotein(a), a major component of lipoprotein(a), or Lp(a), and CTX460, directed towards SERPINA1 using our proprietary SyNTase editing platform, for the treatment of alpha-1 antitrypsin deficiency. CTX340 and CTX321 are currently in IND-enabling studies in patients with refractory hypertension and in patients with elevated Lp(a), which has been shown to have an independent association with major adverse cardiovascular events, respectively. We are progressing CTX460 through preclinical studies. We are also pursuing additional delivery technologies, including LNPs, for delivery to tissues beyond the liver, including hematopoietic stem cells and T cells.

siRNA-based Programs

Our siRNA-based portfolio includes clinical-stage programs in cardiovascular and thromboembolic diseases, developed in collaboration with Sirius Therapeutics and certain of its affiliates, or Sirius.

CTX611 (formerly known as SRSD107) is a novel double-stranded, long-acting siRNA, designed to target the human coagulation factor XI, or FXI, messenger RNA and inhibit FXI protein expression. Through modulation of the intrinsic coagulation pathway, CTX611 is intended to provide anticoagulant and antithrombotic effects. Supported by clinical experience conducted by Sirius in two Phase 1 clinical trials, CTX611 is being developed as a long-acting FXI inhibitor with the potential to support infrequent, including semi-annual, subcutaneous administration.

CTX611 is in an ongoing Phase 2 clinical trial in patients undergoing total knee arthroplasty.

CAR T

We believe CRISPR/Cas9 has the potential to create the next generation of CAR T cell therapies that may have a superior product profile and allow broader patient access compared to current autologous therapies. We are advancing cell therapy programs for autoimmune indications and oncology.

Zugocabtagene geleucel

Our lead next-generation product candidate, zugocabtagene geleucel (zugo-cel; formerly CTX112), incorporates edits designed to enhance CAR T potency, reduce CAR T exhaustion and evade the immune system. As a result of the next-generation edits, zugo-cel exhibits increased manufacturing robustness, with a higher and more consistent number of CAR T cells produced per batch. We are producing zugo-cel for clinical trials at our internal GMP manufacturing facility in Framingham, Massachusetts. Zugo-cel continues to advance in both autoimmune disease and hematologic malignancies.

In autoimmune disease, it is being investigated in an ongoing clinical trial designed to assess the safety and efficacy of the product candidate in adult patients with systemic lupus erythematosus, or SLE, systemic sclerosis, and inflammatory myositis, and a second clinical trial in immune thrombocytopenia purpura and warm autoimmune hemolytic anemia.

In oncology, the Phase 1/2 clinical trial in adult patients with relapsed or refractory B-cell malignancies who have received at least two prior lines of therapy is ongoing. Eligible disease subtypes include large B-cell lymphoma, or LBCL, follicular lymphoma grade 1-3a, marginal zone lymphoma, and mantle cell lymphoma. Initial positive clinical data generated through December 2025 support the advancement of zugo-cel into the Phase 2 portion of the ongoing Phase 1/2 trial. We have also established a collaboration and clinical supply agreement with Eli Lilly to evaluate zugo-cel together with pirtobrutinib in aggressive B-cell lymphomas, further expanding the program's development in oncology. Zugo-cel has been granted RMAT designation by the U.S. Food and Drug Administration for the treatment of relapsed or refractory follicular lymphoma and marginal zone lymphoma.

Additional candidates

Our CRISPR/Cas9 platform enables us to innovate continuously by incorporating incremental edits into next-generation products. We are advancing several additional investigational CAR T programs. In addition, we are developing both transient and integrated *in vivo* CAR T therapies by targeting T cells with LNPs and leveraging our delivery, mRNA, and gene editing expertise.

Regenerative Medicine

We continue to advance our regenerative medicine portfolio, including in diabetes. We are advancing CTX213, a deviceless beta cell replacement product candidate consisting of unencapsulated precursor islet cells derived from induced pluripotent stem cells for the treatment of T1D. To date, CTX213 has demonstrated preclinical efficacy data via direct administration. In addition, we have granted a non-exclusive license to certain of our CRISPR/Cas9 intellectual property to Vertex to accelerate Vertex's development of hypoimmune cell therapies for T1D in exchange for certain milestones and royalties.

Next-generation Editing Modalities

While we have made significant progress with our current portfolio of programs, we recognize that we may be able to bring transformative therapies to even more patients by continuing to innovate to unlock the full potential of gene editing. We are focused on innovating next-generation editing modalities. For example, we have developed a proprietary, next-generation, site-specific gene correction platform called SyNTase editing. In addition, we are also developing technologies to enable whole gene correction and insertion via non-viral DNA delivery and all-RNA systems.

Partnerships

Given the numerous potential therapeutic applications for CRISPR/Cas9, we have partnered strategically to broaden the indications we can pursue and accelerate development of programs by accessing specific technologies and/or disease-area expertise. We maintain broad partnerships to develop gene editing-based therapeutics in specific disease areas. For additional information regarding certain of these partnerships, please see "*Business—Strategic Partnerships and Collaborations*."

Hemoglobinopathies. In 2015, we partnered with Vertex and entered into a strategic collaboration, option and license agreement, which focused on the discovery and development of gene-based treatments for hemoglobinopathies and cystic fibrosis using CRISPR/Cas9 gene-editing technology. In 2017, Vertex exercised its option to co-develop and co-commercialize the hemoglobinopathies program and we entered into a joint development and commercialization agreement with Vertex, which we amended and restated in 2021, pursuant to which, among other things, we are co-developing and co-commercializing CASGEVY for TDT and SCD.

siRNA. In May 2025, we partnered with Sirius and entered into the Sirius Agreement pursuant to which, among other things, we and Sirius will collaborate on the research, development, manufacture, commercialization and use of the Sirius Collaboration Products, including co-development and co-commercialization of CTX611; and (2) Sirius granted us options to exclusively license Sirius siRNA technology to target up to two licensed targets from a list of seven reserved targets for the research, develop, manufacture and commercialization of siRNA Licensed Products, For the first Sirius Collaboration Product successfully developed, we will be the lead party responsible for commercialization efforts in the United States and Sirius will be the lead party responsible for commercialization efforts in Greater China.

Other Partnerships. We have entered into a number of additional collaborations, research and license agreements in other therapeutic areas, including additional agreements with Vertex including for the treatment of Duchenne muscular dystrophy and myotonic dystrophy type 1, as well as diabetes, and others, including to support and complement our hematopoietic stem cell, CAR T, *in vivo* and diabetes programs and platform.

Financial Overview

Since our inception in October 2013, we have devoted substantially all of our resources to our research and development efforts, identifying potential product candidates, undertaking drug discovery and preclinical development activities, building and protecting our intellectual property estate, establishing internal manufacturing capabilities, organizing and staffing our company, business planning, raising capital and providing general and administrative support for these operations. To date, we have primarily financed our operations through private placements of our preferred shares, common share issuances, convertible loans and payments related to certain of our license and collaboration agreements with strategic partners.

We have a history of recurring losses and expect to continue to incur losses for the foreseeable future; however, we have been in a net income position in certain previous years due to certain payments associated with our collaboration and license agreements with Vertex. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase as we continue our current research programs and development activities; seek to identify additional research programs and additional product candidates; conduct initial drug application supporting preclinical studies and initiate clinical trials for our product candidates; pursue business development activities; initiate preclinical testing and clinical trials for any other product candidates we identify and develop; seek regulatory approval for our product candidates; maintain, defend, protect and expand our intellectual property estate; further develop our gene editing platform; hire additional research, clinical and scientific personnel; incur facilities costs associated with such personnel growth; continue to develop internal manufacturing capabilities and infrastructure; and incur additional costs associated with operating as a public company.

Revenue Recognition

We have not generated any revenue to date from sales of any wholly-owned product. No collaboration revenue was recognized for the year ended December 31, 2025. During the years ended December 31, 2024 and 2023, we recognized $35.0 million and $370.0 million, respectively, of collaboration revenue, which is primarily related to our collaboration and license agreements with Vertex.

For the years ended December 31, 2025, 2024 and 2023, we generated $3.5 million, $2.3 million and $1.2 million, respectively, of grant revenue related to certain contracts with not-for-profit entities.

For additional information about our revenue recognition policy, see Note 2 and Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our product discovery efforts and the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits and equity-based compensation expense;
- costs of services performed by third parties that conduct research and development and preclinical and clinical activities on our behalf;
- costs of purchasing lab supplies and non-capital equipment used in our preclinical activities and in manufacturing preclinical study materials, as well as supplies and materials used to manufacture clinical drug material;
- consultant fees;
- facility costs, including rent, depreciation and maintenance expenses; and
- fees and other payments related to acquiring and maintaining licenses under certain of our third-party licensing agreements.

Our external research and development expenses support our various preclinical and clinical programs, and as such we do not break down external research and development expenses further. Our internal research and development expenses consist of payroll and benefits expenses, facilities expense, and other indirect research and development expenses incurred in support of overall research and development activities and as such are not allocated to a specific development stage or therapeutic area. Research and development costs are expensed as incurred. Nonrefundable advance payments for research and development goods or services to be received in the future are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. At this time, we cannot reasonably estimate or know the nature, timing or 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 and IND-enabling 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 the product, if and when approved, whether alone or in collaboration with others;

- acceptance of the 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 or the subsequent commercialization of any product candidates we may successfully develop could 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 to continue to incur research and development costs consistent with research and development at companies of our size and stage of development, which may increase in the foreseeable future as our current development programs progress, new programs are added and we continue to prepare regulatory filings. These increases will likely include the costs related to the implementation and expansion of clinical trial sites and related patient enrollment, monitoring, program management and manufacturing expenses for current and future clinical trials.

Acquired In-Process Research and Development Expenses

Asset acquisition costs related to acquired technology are expensed as acquired in-process research and development at the point that they have no established alternative future use. We classify asset acquisitions of acquired in-process research and development as investing activities on our consolidated statements of cash flows.

General and Administrative Expenses

General and administrative expenses consist primarily of employee related expenses, including salaries, benefits and equity-based compensation, for personnel in executive, finance, accounting, business development, human resources and other general and administrative functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

We expect to continue to incur general and administrative expenses consistent with general and administrative functions at research and development companies of our size and stage of development, which may increase in the future to support continued research and development activities, and potential commercialization of our product candidates. In addition, we anticipate ongoing expenses related to the reimbursements of third-party patent related expenses in connection with certain of our in-licensed intellectual property.

Collaboration Expense, Net

Collaboration expense, net, consists of operating expenses under our collaboration with Vertex for the hemoglobinopathies program.

Other Income (Expense), Net

Other income, net consists primarily of interest income earned on investments, as well as the change in fair value of corporate equity securities.

Critical Accounting Policies and Significant Judgments and Estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as critical because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates—which also would have been reasonable—could have been used. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue

Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers*, or ASC 606, applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases and collaboration arrangements. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps:

1) Identify the contract with the customer

A contract with a customer exists when (i) we enter into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance and (iii) we determine that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

2) Identify the performance obligations in the contract

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, we must apply judgment to determine whether promised goods and services are capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

3) Determine the transaction price

The transaction price is determined based on the consideration to which we will be entitled in exchange for transferring goods and services to the customer. To the extent the transaction price includes variable consideration, such as research, development, regulatory and commercial milestones, we determine if it is probable that we will receive such amounts and there is no risk of a significant revenue reversal. When we cannot conclude that receipt of such amounts is probable, we constrain the related variable consideration resulting in its exclusion from transaction consideration. In determining the portion of the transaction consideration to be constrained, we consider the probability and uncertainty that the related research, developmental, regulatory and commercial milestones will be achieved given the nature of research and clinical development and the stage of the underlying programs. This assessment is performed at each reporting period. In making this evaluation, we consider both internal and external information available, including information from industry publications and other relevant factors. Changes to the constraint of variable consideration can have a material effect on the amount of revenue recognized in the period.

4) Allocate the transaction consideration to performance obligations in the contract

If the contract contains a single performance obligation, the entire transaction consideration is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction consideration to each performance obligation on a relative standalone selling price basis unless the transaction consideration is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices. In determining these estimated standalone selling prices, we make a number of significant judgments including, for licenses, management's assumptions regarding probability weighted projected discounted cash flows for each of the collaboration development programs. The estimated standalone selling prices are sensitive to changes in assumptions, such as probabilities of scientific success, discount rate and certain assumptions that form the basis of forecasted cash flows. In developing these assumptions, management considers both internal and external information available, including information from other guideline companies within the same industry and other relevant factors. Changes to these assumptions can have a material effect on the allocation of the transaction consideration to performance obligations, as well as the amount and timing of revenue recognized.

5) Recognize revenue when or as we satisfy a performance obligation

We satisfy performance obligations over time or at a point in time, depending on the nature of the performance obligation. Revenue is recognized over time if the customer simultaneously receives and consumes the benefits provided by the entity's performance, the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

Collaboration Arrangements

We record the elements of our collaboration agreements that represent joint operating activities in accordance with Accounting Standards Codification Topic 808, *Collaborative Arrangements*, or ASC 808. Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the

significant risks and rewards that are dependent on the commercial success of the activities, are recorded as collaborative arrangements.

We evaluate the proper presentation of the commercial activities and the profit and loss sharing associated with the collaboration agreements. ASC 808 states that when payments between parties in a collaborative arrangement are not within the scope of other authoritative accounting literature, the income statement classification should be based on the nature of the arrangement, the nature of its business operations and the contractual terms of the arrangement. To the extent that these payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments shall be based on an analogy to authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational, and consistently applied accounting policy election.

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:

- CROs in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors in connection with preclinical development activities; and
- vendors related to development, manufacturing and distribution of clinical trial materials.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements are 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 vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical study 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 and adjust accordingly.

Recent Accounting Pronouncements

Refer to Note 2 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K for a discussion of recent accounting pronouncements.

Results of Operations

The following is a discussion of the components of results of operations. This section generally discusses 2025 and 2024 items and year-to-year comparisons between 2025 and 2024. Discussions of 2024 items and year-to-year comparisons between 2024 and 2023 that are not included in this Annual Report on Form 10-K can be found in "Management's Discussion and Analysis of Financial Condition and Results of Operations" Part II, Item 7 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 filed with the SEC on February 11, 2025.

Comparison of Years Ended December 31, 2025 and 2024

The following table summarizes our results of operations for the years ended December 31, 2025 and 2024, together with the dollar change in those items:

	Years Ended December 31,		Period to Period Change
	2025	2024	
		(in thousands)	
Revenue:			
Collaboration revenue	$ —	$ 35,000	$ (35,000)
Grant revenue	3,510	2,314	1,196
Total revenue	3,510	37,314	(33,804)
Operating expenses:			
Research and development	284,806	310,236	(25,430)

Acquired in-process research and development	96,253	—	96,253
General and administrative	73,542	72,977	565
Collaboration expense, net	213,480	120,667	92,813
Total operating expenses	668,081	503,880	164,201
Loss from operations	(664,571)	(466,566)	(198,005)
Other income, net	86,606	103,901	(17,295)
Net loss before income taxes	(577,965)	(362,665)	(215,300)
Provision for income taxes	(3,634)	(3,587)	(47)
Net loss	$ (581,599)	$ (366,252)	$ (215,347)

Collaboration Revenue

No collaboration revenue was recognized for the year ended December 31, 2025. Collaboration revenue was $35.0 million for the year ended December 31, 2024 and was related to Vertex's achievement of a $10.0 million research milestone and $25.0 million research milestone under the Non-Ex License Agreement with Vertex in 2024. Refer to Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K for a description of revenue recognized related to Vertex.

Grant Revenue

Grant revenue was $3.5 million and $2.3 million, respectively, for the years ended December 31, 2025 and 2024.

Research and Development Expenses

Research and development expenses were $284.8 million for the year ended December 31, 2025, compared to $310.2 million for the year ended December 31, 2024. The following table summarizes our research and development expenses for the years ended December 31, 2025 and 2024, together with the changes in those items in dollars (in thousands):

	Years Ended December 31,		Period to Period
	2025	2024	Change
External research and development expenses	$ 76,629	$ 80,197	$ (3,568)
Employee related expenses	63,786	76,029	(12,243)
Facility expenses	92,381	98,003	(5,622)
Stock-based compensation expenses	34,374	47,944	(13,570)
Other expenses	1,225	2,019	(794)
Sublicense and license fees	16,411	6,044	10,367
Total research and development expenses	$ 284,806	$ 310,236	$ (25,430)

The decrease of approximately $25.4 million was primarily attributable to the following:

- $25.8 million of decreased employee-related expenses, including stock-based compensation expenses, primarily driven by decreased headcount;
- $5.6 million of decreased facility expenses primarily driven by lower laboratory-related costs;
- $3.6 million of decreased external research and development costs, primarily associated with a decrease in variable external research and manufacturing costs; offset by
- $10.4 million of increased sublicense and license fees, primarily attributable to costs incurred related to a contingent liability as of December 31, 2025, as described in Note 9 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

Acquired In-Process Research and Development Expenses

Acquired in-process research and development expenses were $96.3 million for the year ended December 31, 2025. There were no acquired in-process research and development expenses for the year ended December 31, 2024. The $96.3 million acquired in-process research and development expense is attributable to the costs incurred upon entering the Sirius Agreement during the second quarter of 2025, as described in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

General and Administrative Expenses

General and administrative expenses were $73.5 million for the year ended December 31, 2025, compared to $73.0 million for the year ended December 31, 2024.

Collaboration Expense, Net

Collaboration expense, net, was $213.5 million for the year ended December 31, 2025, compared to $120.7 million for the year ended December 31, 2024. In 2024, we exercised our option to defer specified costs under the CASGEVY program in excess of the $110.3 million deferral limit under the A&R Vertex JDCA, as amended. The increase of approximately $92.8 million in collaboration expense, net, was primarily attributable to reaching the deferral limit in 2024, as no such limit was applicable in 2025. Absent the deferral limit, the increase was primarily attributable to an increase in our share of CASGEVY operating expenses related to increased commercial and manufacturing costs for CASGEVY when compared to the prior period, which was partially offset by an increase in our share of CASGEVY revenue.

Other Income, Net

Other income, net, was $86.6 million for the year ended December 31, 2025, compared to $103.9 million for the year ended December 31, 2024. The decrease in other income, net, was primarily due to a decrease in interest income earned on cash, cash equivalents and marketable securities for the year ended December 31, 2025.

Liquidity and Capital Resources

Sources of Liquidity

We have predominantly incurred losses and cumulative negative cash flows from operations since our inception. As of December 31, 2025, we had $1,975.8 million in cash, cash equivalents and marketable securities, of which approximately $103.4 million was held outside of the United States, and an accumulated deficit of $1,947.6 million. We anticipate that we will continue to incur losses for at least the next several years. We expect to continue to incur research and development costs and general and administrative expenses, consistent with costs associated with research and development at companies of our size and stage of development, and, as a result, we will need additional capital to fund our operations, which we may raise through public or private equity or debt financings, strategic collaborations, or other sources.

At-the-Market Offerings (ATM)

We entered into an Open Market Sale Agreement[SM], or the Sales Agreement, with Jefferies LLC under which we, at our sole discretion, are able to offer and sell, from time to time at prevailing market prices, our common shares. The following are in connection with the Sales Agreement.

2021 ATM

In January 2021, we filed a prospectus supplement with the SEC to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $600.0 million, or, together with the subsequent prospectus supplements filed in July 2021 and August 2024 relating to the common shares remaining under the original prospectus supplement, the 2021 ATM. In 2025, we issued and sold an aggregate of 6.1 million common shares under the 2021 ATM at an average price of $59.63 per share for aggregate proceeds of $359.0 million, which were net of equity issuance costs of $4.7 million, excluding stamp taxes of $3.6 million.

In 2024, we issued and sold 0.4 million common shares under the 2021 ATM at an average price of $55.81 per share for aggregate proceeds of $21.7 million, which were net of equity issuance costs of $0.3 million, excluding stamp taxes of $0.2 million.

In 2023, we issued and sold 0.5 million common shares under the 2021 ATM at an average price of $72.32 per share for aggregate proceeds of $32.7 million, which were net of equity issuance costs of $0.4 million, excluding stamp taxes of $0.3 million.

As of December 31, 2025, we issued and sold an aggregate of 8.0 million common shares under the 2021 ATM at an average price of $74.77 per share for aggregate proceeds of $592.2 million, which were net of equity issuance costs of $7.8 million, excluding stamp taxes of $5.9 million. As of December 31, 2025, no common shares remain available under the 2021 ATM.

2025 ATM

In October 2025, we filed a new prospectus supplement with the SEC to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $600.0 million, referred to herein as the 2025 ATM. In 2025, we issued and sold an aggregate of 0.7 million common shares under the 2025 ATM at an average price of $60.81 per share for aggregate proceeds of $42.3 million, which were net of equity issuance costs of $0.5 million, excluding stamp taxes of $0.4 million. Common shares having aggregate gross proceeds up to $557.2 million remain available under the 2025 ATM.

Share Issuance Agreement with Sirius Therapeutics

As described in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K, we and Sirius entered into a share issuance agreement and we registered and issued 1,842,105 common shares to Sirius, nominal value CHF 0.03 per share, at an issue price of $38.00 per share as partial consideration for entering into the Sirius Agreement.

Additional Financings

In February 2024, we entered into an investment agreement for the sale of approximately $280.0 million of our common shares to a group of institutional investors in a registered direct offering, at a price per share of $71.50. We received net proceeds of $279.0 million, excluding stamp taxes due of $2.8 million.

Sources of Liquidity

Cash Flows

Discussions of 2024 items and year-to-year comparisons between 2024 and 2023 that are not included in this Annual Report on Form 10-K can be found in "Management's Discussion and Analysis of Financial Condition and Results of Operations" Part II, Item 7 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 filed with the SEC on February 11, 2025.

The following table provides information regarding our cash flows for each of the periods below:

	Years Ended December 31,	
	2025	2024
	(in thousands)	
Net cash used in operating activities	$ (345,014)	$ (142,774)
Net cash used in investing activities	(31,805)	(280,481)
Net cash provided by financing activities	426,026	331,984
Effect of exchange rate changes on cash	95	(21)
Increase (decrease) in cash and restricted cash	$ 49,302	$ (91,292)

Operating Activities

Net cash used in operating activities was $345.0 million for the year ended December 31, 2025, compared to net cash used in operating activities of $142.8 million for the year ended December 31, 2024. The $202.2 million increase in cash used in operating activities was primarily driven by the timing of receipt of milestone payments from Vertex which were recorded in accounts receivable as of the respective year-end periods and paid in the subsequent year ($200.0 million paid in the first quarter of 2024 compared to $25.0 million paid in the first quarter of 2025).

Investing Activities

Net cash used in investing activities for the year ended December 31, 2025 was $31.8 million, compared to net cash used in investing of $280.5 million for the year ended December 31, 2024. The decrease in net cash used in investing activities was primarily a result of the net purchase position for marketable debt securities for the year ended December 31, 2024, compared to a net maturity position for marketable debt securities for the year ended December 31, 2025.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2025 was $426.0 million, compared to net cash provided by financing of $332.0 million for the year ended December 31, 2024. Net cash provided by financing activities for the year ended December 31, 2025 consisted primarily of net proceeds of approximately $397.3 million from the sale of common shares issued in connection with our 2021 ATM and 2025 ATM, in the aggregate, as well as net proceeds of approximately $27.7 million from stock option exercise proceeds. Net cash provided by financing activities for the year ended December 31, 2024 primarily consisted of net proceeds of approximately $279.0 million from the issuance of common shares in connection with our registered direct offering, net proceeds of approximately $31.2 million from stock option exercises, and net proceeds of approximately $21.7 million from the issuance of common shares in connection with our 2021 ATM.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development activities, manufacturing activities, compensation and related expenses, laboratory and related supplies, legal and other regulatory expenses, patent prosecution filing, defense and intellectual property maintenance costs, business development activities and general overhead costs, including costs associated with operating as a public company. We expect to continue to incur operating expenses consistent with costs associated with research and development at companies of our size and stage of development, which may increase in the future to support continued research and development activities and potential commercialization of our product candidates.

Although we and our partner, Vertex, have received marketing approvals for CASGEVY in certain jurisdictions, we cannot guarantee we and Vertex will receive additional marketing approvals for CASGEVY or we will receive marketing approvals for our other product candidates in the future. Most of our programs are still in early stages of research and development and the outcome of our efforts is uncertain, and we cannot estimate the actual amounts necessary to successfully complete the development, manufacture and commercialization of any current or future product candidates, if approved, or whether, or when, we may achieve profitability.

Until such time as we can generate substantial product revenues, if ever, we expect to finance our cash needs through a combination of equity financings, debt financings and payments received in connection with our collaboration and license agreements. We intend to consider opportunities to raise additional funds through the sale of equity or debt securities when market conditions are favorable to us to do so. However, the trading prices for our common shares and other biopharmaceutical companies have been highly volatile. As a result, we may face difficulties raising capital through sales of our common shares or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event, including resulting from the uncertain geopolitical environment, global trade policy and global economic conditions, could materially and adversely affect our business and the value of our common shares. To the extent that we raise additional capital through the future sale of equity or debt securities, the ownership interests of our shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing shareholders. If we raise additional funds through license or collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or 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.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditures for at least the next 24 months without giving effect to any additional proceeds we may receive under our license agreements and collaborations, including with Vertex, and any other capital raising transactions we may complete. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Given our need for additional financing to support the long-term clinical development and future commercialization of our programs, as applicable, we intend to consider additional financing opportunities when market terms are favorable to us.

Our ability to generate revenue and achieve profitability depends significantly on our success in many areas, including: developing our delivery technologies and our gene editing technology platform; selecting appropriate product candidates to develop; completing research and preclinical and clinical development of selected product candidates; obtaining regulatory approvals and marketing authorizations for product candidates for which we complete clinical trials; developing a sustainable and scalable manufacturing process for product candidates; launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor; obtaining market acceptance of our product candidates, either directly or with a collaborator or distributor, if approved, including for CASGEVY; addressing any competing technological and market developments; negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter; maintaining good relationships with our collaborators and licensors; maintaining, defending, protecting and expanding our estate of intellectual property rights, including patents, trade secrets and know-how; and attracting, hiring and retaining qualified personnel.

Contractual and Other Obligations

Operating lease and sublease obligations

Our operating lease obligations primarily consist of lease payments on our office and laboratory facility in Boston, Massachusetts, as well as lease payments on our cell manufacturing facility in Framingham, Massachusetts, which are described in further detail in Note 7 of our consolidated financial statements included in this Annual Report on Form 10-K. Future contractual payments on operating lease and sublease obligations due within one year of December 31, 2025 are $29.7 million, and future contractual payments on operating lease and sublease obligations due greater than one year from December 31, 2025 are $235.9 million.

Other obligations

Under the A&R Vertex JDCA, as amended, for 2022, 2023 and 2024, the Company had an option to defer a portion of its share of costs if spending on the CASGEVY program exceeded specified amounts, which the Company exercised in each such year, resulting in deferred costs of $221.8 million, in the aggregate. Any deferred amounts are only payable to Vertex as an offset against future profitability of the CASGEVY program and the amounts payable are capped at a specified maximum amount per year. Deferred costs associated with the CASGEVY program have not been recognized as of December 31, 2025 because a reasonable estimate of future payments against future profitability cannot be made.

In the normal course of business, we enter into agreements with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes. These contracts are generally cancelable at any time by us upon less than 180 days' prior written notice. Certain of these agreements require us to pay milestones to such third parties upon achievement of certain development, regulatory or commercial milestones as further described in Note 9 of our consolidated financial statements included in this Annual Report on Form 10-K. Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory

approval and commercial milestones, which may not be achieved.

We also have obligations to make future payments to third parties that become due and payable on the achievement of certain milestones, including future payments to third parties with whom we have entered into research, development and commercialization agreements. We have not included these commitments on our balance sheet because the achievement and timing of these milestones is not fixed and determinable.

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

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. As of December 31, 2025, we had cash, cash equivalents and marketable securities of $1,975.8 million, primarily invested in U.S. Treasury securities and government agency securities, corporate bonds, commercial paper and money market accounts invested in U.S. government agency securities. Due to the conservative nature of these instruments, we do not believe that we have a material exposure to interest rate risk. If interest rates were to increase or decrease by 1%, the fair value of our investment portfolio would increase or decrease by an immaterial amount.

Foreign Currency Exchange Rate Risk

As a result of our foreign operations, we face exposure to movements in foreign currency exchange rates, primarily the Swiss Franc and British Pound, against the U.S. dollar. The current exposures arise primarily from cash, accounts payable and intercompany receivables and payables. Changes in foreign exchange rates affect our consolidated statement of operations and distort comparisons between periods. To date, foreign currency transaction gains and losses have not been material to our financial statements, and we have not engaged in any foreign currency hedging transactions.

Inflation

Inflation generally affects us by increasing our cost of labor, clinical trial and manufacturing costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2025, 2024 and 2023.

Item 8. Financial Statements and Supplementary Data.

The consolidated financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found in Item 15.

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 chief executive officer and chief financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) and Rule 15d-15(e) promulgated under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Annual Report on Form 10-K, have concluded that, based on such evaluation, our disclosure controls and procedures were effective. In designing and evaluating the disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management's Annual Report on Internal Control Over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and Rule 15d-15(f) promulgated under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel, 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. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of the assets;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our 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.

Our management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2025. In making this assessment, it used the criteria set forth in the Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework)(COSO). Based on its assessment, our management has concluded that, as of December 31, 2025, the Company's internal control over financial reporting is effective based on those criteria.

Our independent registered public accounting firm, Ernst & Young LLP, issued an attestation report on our internal control over financial reporting. See below.

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, during the fourth quarter of 2025 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of CRISPR Therapeutics AG

Opinion on Internal Control Over Financial Reporting

We have audited CRISPR Therapeutics AG's internal control over financial reporting as of December 31, 2025, 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, CRISPR Therapeutics AG (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2025, 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 the Company as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2025, and the related notes and our report dated February 12, 2026 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 and 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 12, 2026

Item 9B. Other Information.

From time to time, our officers (as defined in Rule 16a–1(f)) and directors may enter into Rule 10b5-1 or non-Rule 10b5-1 trading arrangements (as each such term is defined in Item 408 of Regulation S-K). During the three months ended December 31, 2025, our officers and directors took the following actions with respect to Rule 10b5-1 trading arrangements:

Name (Title)	Action Taken (Date of Action)	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
Katherine A. High, M.D. (Member of the Board of Directors)	Adoption (November 14, 2025)	Trading plan intended to satisfy the affirmative defense conditions of Securities Exchange Act Rule 10b5-1(c).	Sale of the Company's common stock pursuant to the terms of the plan.	Active through March 12, 2027	22,000
Simeon J. George, M.D. (Member of the Board of Directors)	Adoption (December 12, 2025)	Trading plan intended to satisfy the affirmative defense conditions of Securities Exchange Act Rule 10b5-1(c).	Sale of the Company's common stock pursuant to the terms of the plan.	Active through April 13, 2027	116,000
Naimish Patel, M.D. (Chief Medical Officer)	Adoption (December 16, 2025)	Trading plan intended to satisfy the affirmative defense conditions of Securities Exchange Act Rule 10b5-1(c).	Sale of the Company's common stock pursuant to the terms of the plan.	Active through December 31, 2026	6,068

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

Item 11. Executive Compensation.

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

Item 14. Principal Accountant Fees and Services.

The information required by this item is incorporated by reference to our Proxy Statement for our 2026 Annual General Meeting of Shareholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2025.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a)(1) Financial Statements.

See the "*Index to Consolidated Financial Statements*" on page F-1 below for the list of financial statements filed as part of this report.

(a)(2) Schedules other than that listed above have been omitted because of the absence of conditions under which they are required or because the required information is included in the financial statements or the notes thereto.

(a)(3) Exhibits.

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report are listed in the Exhibit Index below. The exhibits listed in the Exhibit Index below are filed or incorporated by reference as part of this Annual Report on Form 10-K.

(b) Exhibit Index.

Exhibit Number	Description
3.1	Amended and Restated Articles of Association of CRISPR Therapeutics AG, dated June 5, 2025 (incorporated herein by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on June 9, 2025).
4.1*	Description of Capital Shares.
10.1†	License Agreement, dated April 15, 2014, by and between CRISPR Therapeutics AG and Emmanuelle Marie Charpentier (incorporated herein by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.2†	License Agreement, dated April 15, 2014, by and between TRACR Hematology Limited and Emmanuelle Marie Charpentier (incorporated herein by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.3	Form of Indemnification Agreement (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 5, 2024).
10.4#	Second Amended and Restated Employment Agreement, dated October 2, 2017, by and between CRISPR Therapeutics, Inc. and Samarth Kulkarni (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on October 2, 2017).
10.5#	Employment Agreement, dated May 31, 2017, by and between CRISPR Therapeutics, Inc. and James R. Kasinger (incorporated herein by reference to Exhibit 10.16 to the Company's Annual Report on Form 10-K filed on March 8, 2018).
10.6#	Employment Agreement, dated May 23, 2024, by and between CRISPR Therapeutics, Inc. and Julianne Bruno (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on May 23, 2024).
10.7#	Employment Agreement, dated May 28, 2024, by and between CRISPR Therapeutics, Inc. and Naimish Patel, MD (incorporated herein by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 5, 2024).
10.8#	Employment Agreement, dated March 14, 2023, by and between CRISPR Therapeutics, Inc. and Raju Prasad, Ph.D. (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on March 14, 2023).
10.9#	Senior Executive Cash Incentive Bonus Plan (incorporated herein by reference to Exhibit 10.26 to the Company's Annual Report on Form 10-K filed on March 8, 2018).
10.10#	CRISPR Therapeutics AG Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 2, 2017).

10.10.1#	Form of Incentive Stock Option Agreement under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.2 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.10.2#	Form of Non-Qualified Stock Option Agreement for Company Employees under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.3 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.10.3#	Form of Non-Qualified Stock Option Agreement for Non-Employee Directors under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.4 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.10.4#	Form of Restricted Stock Award Agreement under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.5 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.10.5#	Form of Restricted Stock Award Agreement for Company Employees under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.6 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.10.6#	Form of Restricted Stock Award Agreement for Non-Employee Directors under CRISPR Therapeutics AG's Amended and Restated 2016 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 10.7 to the Company's Current Report on Form 10-Q filed on November 8, 2017).
10.11#	CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan and forms of agreements thereunder (incorporated herein by reference to Exhibit 99.1 to the Company's Registration Statement on Form S-8 filed on June 1, 2018).
10.11.1#	Form of Incentive Stock Option Agreement under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 99.2 to the Company's Registration Statement on Form S-8 filed on June 1, 2018).
10.11.2#	Form of Non-Qualified Stock Option Agreement for Company Employees under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 99.3 to the Company's Registration Statement on Form S-8 filed on June 1, 2018).
10.11.3#	Form of Non-Qualified Stock Option Agreement for Non-Employee Directors under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 99.4 to the Company's Registration Statement on Form S-8 filed on June 1, 2018).
10.11.4#	Form of Restricted Stock Award under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 99.5 to the Company's Registration Statement on Form S-8 filed on June 1, 2018).
10.11.5#	Form of Restricted Stock Award Agreement for Company Employees under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 99.6 to the Company's Registration Statement on Form S-8 filed on June 1, 2018).
10.11.6#	Form of Restricted Stock Award for Non-Employee Directors under CRISPR Therapeutics AG's 2018 Stock Option and Incentive Plan (incorporated herein by reference to Exhibit 99.7 to the Company's Registration Statement on Form S-8 filed on June 1, 2018).
10.12#	Amendment No. 1 to the 2018 Stock Option and Incentive Plan (incorporated herein by reference to Appendix A to the Company's Definitive Proxy Statement on Schedule 14A filed on April 30, 2019).
10.13#	Amendment No. 2 to the 2018 Stock Option and Incentive Plan (incorporated herein by reference to Appendix A to the Company's Definitive Proxy Statement on Schedule 14A filed on April 24, 2020).
10.14#	Amendment No. 3 to the 2018 Stock Option and Incentive Plan (incorporated herein by reference to Appendix A to the Company's Definitive Proxy Statement on Schedule 14A filed on April 25, 2022).
10.15#	Amendment No. 4 to the 2018 Stock Option and Incentive Plan (incorporated herein by reference to Appendix B to the Company's Definitive Proxy Statement on Schedule 14A filed on April 26, 2023).
10.16#	Amendment No. 5 to the 2018 Stock Option and Incentive Plan (incorporated herein by reference to Appendix A to the Company's Definitive Proxy Statement on Schedule 14A filed on April 9, 2024).

10.17#	CRISPR Therapeutics AG 2016 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1 filed on September 9, 2016).
10.18†	Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement for a Programmable DNA Restriction Enzyme for Genome Editing, dated December 15, 2016, by and among CRISPR Therapeutics AG, The Regents of the University of California, University of Vienna, Dr. Emmanuelle Charpentier, Intellia Therapeutics, Inc., Caribou Biosciences, Inc., ERS Genomics Ltd., and TRACR Hematology Ltd. (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 16, 2016).
10.19†	Strategic Collaboration, Option and License Agreement, dated October 26, 2015, by and among CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., TRACR Hematology Limited, Vertex Pharmaceuticals, Incorporated and Vertex Pharmaceuticals (Europe) Limited (incorporated herein by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 filed on October 7, 2016).
10.20†	Amendment No. 1 to the Strategic Collaboration, Option and License Agreement by and between, on the one hand, Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited, and on the other hand, CRISPR Therapeutics AG, CRISPR Therapeutics, Inc., CRISPR Therapeutics Limited and TRACR Hematology Ltd., dated as of December 12, 2017 (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on December 18, 2017).
10.21†	Amendment No. 2 to the Strategic Collaboration, Option and License Agreement by and between, on the one hand, Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited, and on the other hand, CRISPR Therapeutics AG, CRISPR Therapeutics, Inc., CRISPR Therapeutics Limited and TRACR Hematology Ltd., dated as of June 6, 2019 (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on July 29, 2019).
10.22†^	Amended and Restated Joint Development and Commercialization Agreement between, on the one hand, Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited, and on the other hand, CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., and TRACR Hematology Ltd., dated as of April 16, 2021 (incorporated herein by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on April 27, 2021).
10.23†^	Amendment No. 1 to the Amended and Restated Joint Development and Commercialization Agreement, dated December 12, 2023, by and between, on the one hand, Vertex Pharmaceuticals Incorporated and Vertex Pharmaceuticals (Europe) Limited, and on the other hand, CRISPR Therapeutics AG, CRISPR Therapeutics Limited, CRISPR Therapeutics, Inc., and TRACR Hematology Ltd. (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 13, 2023).
10.24†^	Non-Exclusive License Agreement, dated March 23, 2023, by and between Vertex Pharmaceuticals Incorporated and CRISPR Therapeutics AG (incorporated herein by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on March 27, 2023).
10.25^	Lease, dated May 5, 2020, by and between CRISPR Therapeutics, Inc. and CRP/KING 33 NY AVE. OWNER, L.L.C. (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on April 27, 2021).
10.26^	First Amendment to Lease dated December 2, 2020, by and between CRISPR Therapeutics, Inc. and CRP/KING 33 NY AVE. OWNER, L.L.C. (incorporated herein by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on April 27, 2021).
10.27^	Second Amendment to Lease dated April __, 2021, by and between CRISPR Therapeutics, Inc. and 33 NYA OWNER (DE) LLC, as successor in interest to CRP/KING 33 NY AVE. OWNER, L.L.C. (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on July 29, 2021).
10.28†	Lease, dated July 24, 2020, by and between CRISPR Therapeutics, Inc. and 105 W First Street Owner, L.L.C. (incorporated herein by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on July 27, 2020).
10.29	Letter Agreement dated January 6, 2022, by and between CRISPR Therapeutics, Inc. and 105 W First Street Owner, L.L.C. (incorporated herein by reference to Exhibit 10.37 to the Company's Annual Report on Form 10-K filed on February 15, 2022).

10.30	Lease Commencement Date Agreement, dated May 1, 2022, by and between CRISPR Therapeutics AG and 105 W First Street Owner, L.L.C. (incorporated herein by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 8, 2022).
10.31	CRISPR Therapeutics AG Organizational Rules.
19.1	CRISPR Therapeutics AG Insider Trading Policy.
21.1*	Subsidiaries of the Registrant.
23.1*	Consent of Ernst & Young LLP.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1+	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1	CRISPR Therapeutics AG Policy Relating to Recovery of Erroneously Awarded Compensation (incorporated herein by reference to Exhibit 97.1 to the Company's Annual Report on Form 10-K filed on February 21, 2024).
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File as its XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

* Filed herewith.
+ Furnished herewith.
† Certain portions of this exhibit have been omitted because they are not material and the registrant customarily and actually treats that information as private or confidential.
# A management contract or compensatory plan or arrangement required to be filed as an exhibit pursuant to Item 15(a)(3) of Form 10-K.
^ Certain exhibits and schedules to these agreements have been omitted pursuant to Item 601 of Regulation S-K. The registrant will furnish copies of any of the exhibits and schedules to the Securities and Exchange Commission upon request.

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**.**

CRISPR Therapeutics AG

Date: February 12, 2026

By: /s/ Samarth Kulkarni
Samarth Kulkarni
Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned directors and officers of CRISPR Therapeutics AG (the "Company"), hereby severally constitute and appoint Samarth Kulkarni, Raju Prasad and James R. Kasinger, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Samarth Kulkarni Samarth Kulkarni	Chief Executive Officer, Chairman and Director (Principal Executive Officer)	February 12, 2026
/s/ Raju Prasad Raju Prasad	Chief Financial Officer (Principal Financial and Accounting Officer)	February 12, 2026
/s/ Ali Behbahani Ali Behbahani	Director	February 12, 2026
/s/ Maria Fardis Maria Fardis	Director	February 12, 2026
/s/ H. Edward Fleming, Jr. H. Edward Fleming, Jr.	Director	February 12, 2026
/s/ Simeon J. George Simeon J. George	Director	February 12, 2026
/s/ John Greene John Greene	Director	February 12, 2026
/s/ Katherine A. High Katherine A. High	Director	February 12, 2026
/s/ Sandesh Mahatme Sandesh Mahatme	Director	February 12, 2026
/s/ Briggs Morrison Briggs Morrison	Director	February 12, 2026
/s/ Christian Rommel Christian Rommel	Director	February 12, 2026
/s/ Douglas A. Treco Douglas A. Treco	Director	February 12, 2026

/s/ Raju Prasad Raju Prasad	Authorized Representative in the United States	February 12, 2026

CRISPR Therapeutics AG

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of CRISPR Therapeutics AG

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of CRISPR Therapeutics AG (the Company) as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2025, 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, 2025 and 2024, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2025, 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, 2025, 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 12, 2026 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 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.

Collaboration Expense, Net, Related to the Vertex Hemoglobinopathy Agreements

Description of the Matter

As discussed in Note 8 to the consolidated financial statements, the Company accounts for elements of its Vertex Hemoglobinopathy Agreements with Vertex Pharmaceuticals, Inc. (or "Vertex") under ASC 808. The Company records its share of the net profits and net losses, as applicable, for elements of such agreements as collaboration expense, net on the consolidated statement of operations and comprehensive loss. For the year ended December 31, 2025, the Company reported $213.5 million of collaboration expense, net, related to the Vertex Hemoglobinopathy Agreements.

Auditing the recognition of collaboration expense, net required a greater extent of audit effort to test the completeness and accuracy of the Company's recognition of the net expense incurred during the year and payable to Vertex as of December 31, 2025.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's process to record collaboration expense, net. For example, we tested controls over management's review and assessment of the completeness and accuracy of the information used to record collaboration expense, net.

Our audit procedures included, among others, inspecting collaboration cost information provided by Vertex to the Company related to collaboration expense, net. We performed analytical procedures surrounding period-over-period changes in activity. We tested that the Company's recognition of collaboration expense, net was in accordance with the provisions of the Vertex Hemoglobinopathy Agreements. We also tested settled payments made by the Company throughout the year. In addition, we confirmed directly with Vertex the total shared costs incurred under the Vertex Hemoglobinopathy Agreements for the year, the amount allocated to the Company, and the amount due from the Company to Vertex as of December 31, 2025.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.
Boston, Massachusetts
February 12, 2026

CRISPR Therapeutics AG
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 347,559	$ 298,257
Marketable securities	1,628,269	1,605,569
Accounts receivable	—	25,000
Prepaid expenses and other current assets	9,843	8,306
Total current assets	1,985,671	1,937,132
Property and equipment, net	115,851	134,093
Restricted cash	7,629	11,519
Operating lease assets	131,724	143,461
Other non-current assets	24,368	15,829
Total assets	$ 2,265,243	$ 2,242,034
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	$ 11,138	$ 14,709
Accrued expenses	89,407	41,072
Deferred revenue, current	15,771	3,845
Accrued tax liabilities	1,113	451
Operating lease liabilities	18,578	17,288
Other current liabilities	13,113	10,417
Total current liabilities	149,120	87,782
Deferred revenue, non-current	—	12,323
Operating lease liabilities, net of current portion	188,168	206,405
Other non-current liabilities	6,142	3,444
Total liabilities	343,430	309,954
Commitments and contingencies (Note 9)		
Shareholders' equity:		
Common shares, CHF 0.03 nominal value, 132,477,166 shares authorized at December 31, 2025 and December 31, 2024, 96,009,657 and 85,912,297 shares issued at December 31, 2025 and December 31, 2024, respectively, 95,894,341 and 85,741,981 shares outstanding at December 31, 2025 and December 31, 2024, respectively	3,087	2,698
Treasury shares, at cost, 115,316 and 170,316 shares at December 31, 2025 and December 31, 2024, respectively	(60)	(62)
Additional paid-in capital	3,861,516	3,293,556
Accumulated deficit	(1,947,551)	(1,365,952)
Accumulated other comprehensive income	4,821	1,840
Total shareholders' equity	1,921,813	1,932,080
Total liabilities and shareholders' equity	$ 2,265,243	$ 2,242,034

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

	Years Ended December 31,		
	2025	2024	2023
Revenue:			
Collaboration revenue	$ —	$ 35,000	$ 370,000
Grant revenue	3,510	2,314	1,206
Total revenue	3,510	37,314	371,206
Operating expenses:			
Research and development	284,806	310,236	387,332
Acquired in-process research and development	96,253	—	—
General and administrative	73,542	72,977	76,162
Collaboration expense, net	213,480	120,667	130,250
Total operating expenses	668,081	503,880	593,744
Loss from operations	(664,571)	(466,566)	(222,538)
Other income:			
Other income, net	86,606	103,901	71,816
Total other income, net	86,606	103,901	71,816
Net loss before income taxes	(577,965)	(362,665)	(150,722)
Provision for income taxes	(3,634)	(3,587)	(2,888)
Net loss	(581,599)	(366,252)	(153,610)
Foreign currency translation adjustment	95	(21)	73
Unrealized gain (loss) on marketable securities	2,886	(52)	17,487
Comprehensive loss	$ (578,618)	$ (366,325)	$ (136,050)
Net loss per common share — basic	$ (6.47)	$ (4.34)	$ (1.94)
Basic weighted-average common shares outstanding	89,925,109	84,359,126	79,220,930
Net loss per common share — diluted	$ (6.47)	$ (4.34)	$ (1.94)
Diluted weighted-average common shares outstanding	89,925,109	84,359,126	79,220,930

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Shareholders' Equity
(In thousands, except share and per share data)

	Common Shares		Treasury Shares					
	Shares	CHF 0.03 Par Value	Shares	Amount, at cost	Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive (Loss) Income	Total Shareholders' Equity
Balance at December 31, 2022	78,512,450	$ 2,441	180,316	$ (63)	$ 2,734,838	$ (846,090)	$ (15,647)	$ 1,875,479
Issuance of common shares, net of issuance costs of $2.9 million	458,547	15	—	—	32,379	—	—	32,394
Vesting of restricted shares	277,808	10	—	—	—	—	—	10
Exercise of vested options, net of issuance costs of $0.5 million	742,291	31	(10,000)	1	28,071	—	—	28,103
Purchase of common stock under ESPP	53,282	—	—	—	1,839	—	—	1,839
Stock-based compensation expense	—	—	—	—	81,028	—	—	81,028
Other comprehensive income	—	—	—	—	—	—	17,560	17,560
Net loss	—	—	—	—	—	(153,610)	—	(153,610)
Balance at December 31, 2023	80,044,378	$ 2,497	170,316	$ (62)	$ 2,878,155	$ (999,700)	$ 1,913	$ 1,882,803
Issuance of common shares, net of issuance costs of $4.0 million	4,309,521	145	—	—	297,557	—	—	297,702
Vesting of restricted shares	450,701	16	—	—	—	—	—	16
Exercise of vested options, net of issuance costs of $0.8 million	900,136	40	—	—	29,539	—	—	29,579
Purchase of common stock under ESPP	37,245	—	—	—	1,738	—	—	1,738
Stock-based compensation expense	—	—	—	—	86,567	—	—	86,567
Other comprehensive loss	—	—	—	—	—	—	(73)	(73)
Net loss	—	—	—	—	—	(366,252)	—	(366,252)
Balance at December 31, 2024	85,741,981	$ 2,698	170,316	$ (62)	$ 3,293,556	$ (1,365,952)	$ 1,840	$ 1,932,080
Issuance of common shares, net of issuance costs of $9.9 million	8,645,598	332	—	—	467,711	—	—	468,043
Vesting of restricted shares	736,238	28	—	—	—	—	—	28
Exercise of vested options, net of issuance costs of $0.7 million	726,396	29	(55,000)	2	26,275	—	—	26,306
Purchase of common stock under ESPP	44,128	—	—	—	1,475	—	—	1,475
Stock-based compensation expense	—	—	—	—	72,499	—	—	72,499
Other comprehensive loss	—	—	—	—	—	—	2,981	2,981
Net loss	—	—	—	—	—	(581,599)	—	(581,599)
Balance at December 31, 2025	95,894,341	3,087	115,316	(60)	3,861,516	(1,947,551)	4,821	1,921,813

See accompanying notes to these consolidated financial statements.

CRISPR Therapeutics AG
Consolidated Statements of Cash Flows
(In thousands)

	Years Ended December 31,		
	2025	**2024**	**2023**
Operating activities			
Net loss	$ (581,599)	$ (366,252)	$ (153,610)
Reconciliation of net loss to net cash used in operating activities:			
Depreciation and amortization	19,479	19,259	19,837
Stock-based compensation expense	72,499	86,567	81,028
Other non-cash items, net	(23,528)	(38,618)	(16,545)
Acquired in-process research and development	96,253	—	2,500
Changes in:			
Accounts receivable	25,000	175,000	(200,000)
Prepaid expenses and other assets	3,337	5,285	23,219
Accounts payable and accrued expenses	44,894	(27,283)	(20,247)
Deferred revenue	(397)	(1,949)	5,794
Operating lease assets and liabilities	(5,210)	(4,407)	(2,461)
Other liabilities, net	4,258	9,624	110
Net cash used in operating activities	(345,014)	(142,774)	(260,375)
Investing activities			
Purchase of property, plant and equipment	(914)	(1,901)	(9,470)
Purchase of in-process research and development	(25,000)	—	(2,500)
Investment in equity securities	(9,700)	(23,183)	—
Sale of equity securities	702	—	—
Purchases of marketable debt securities	(1,008,170)	(1,463,196)	(1,065,911)
Maturities of marketable debt securities	1,011,277	1,207,799	1,452,528
Net cash used in (provided by) investing activities	(31,805)	(280,481)	374,647
Financing activities			
Proceeds from issuance of common shares, net of issuance costs	398,090	300,695	32,721
Proceeds from exercise of options and ESPP contributions, net of issuance costs	27,936	31,289	29,943
Net cash provided by financing activities	426,026	331,984	62,664
Effect of exchange rate changes on cash	95	(21)	73
Increase (decrease) in cash	49,302	(91,292)	177,009
Cash, cash equivalents and restricted cash, beginning of period	309,776	401,068	224,060
Cash, cash equivalents and restricted cash, end of period	$ 359,078	$ 309,776	$ 401,068
Supplemental disclosure of non-cash investing and financing activities			
Property and equipment purchases in accounts payable and accrued expenses	$ 394	$ 154	$ 725
Equity issuance costs in accounts payable and accrued expenses	$ 4,799	$ 3,371	$ 417
Acquired in-process research and development expense related to issuance of common shares	$ 71,253	$ —	$ —

Reconciliation to amounts within the consolidated balance sheets	As of December 31,		
	2025	**2024**	**2023**
Cash and cash equivalents	347,559	298,257	389,477
Restricted cash included in prepaid expenses and other current assets	3,890	—	—
Restricted cash	7,629	11,519	11,591
Total	$ 359,078	$ 309,776	$ 401,068

See accompanying notes to these consolidated financial statements.

1. Organization and Operations

CRISPR Therapeutics AG ("CRISPR" or the "Company") was incorporated on October 31, 2013 in Basel, Switzerland. The Company was established to translate CRISPR/Cas9, a genome editing technology, into transformative gene-based medicines for the treatment of serious human diseases. The foundational intellectual property underlying the Company's operations was licensed to the Company in April 2014. The Company devotes substantially all of its efforts to product research and development activities, initial market development and raising capital. The Company's principal offices are in Zug, Switzerland, with the U.S. headquarters for research and development in Boston, Massachusetts, additional research and development based in San Francisco, California, and a cell therapy manufacturing facility in Framingham, Massachusetts.

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, third party collaborations, 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.

The Company had an accumulated deficit of $1,947.6 million as of December 31, 2025 and has financed its operations to date from a series of preferred shares and convertible loan issuances, proceeds obtained from its initial public offering, or IPO, subsequent public offerings of its common shares, at-the-market offerings, as well as upfront fees and milestones received under its collaboration, license and joint venture arrangements. The Company will require additional capital to fund its research and development and ongoing operating expenses.

As of December 31, 2025, the Company had cash, cash equivalents and marketable securities of $1,975.8 million. While the Company was in a net income position in certain previous years due to upfront payments associated with the Company's collaborations and license agreements with Vertex Pharmaceuticals Incorporated and certain of its subsidiaries, or Vertex, the Company has a history of recurring losses and expects to continue to incur losses for the foreseeable future. The Company expects its cash and cash equivalents and marketable securities will be sufficient to fund current planned operations for at least the next twenty-four months.

2. Summary of Significant Accounting Policies and Basis of Presentation

Basis of Presentation and Use of Estimates

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, or GAAP, and include the accounts of the Company and its wholly-owned subsidiaries as of December 31, 2025. All intercompany accounts and transactions have been eliminated. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification, or ASC, and Accounting Standards Updates, or ASUs, of the Financial Accounting Standards Board, or FASB.

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, revenue recognition, equity-based compensation expense and reported amounts of research and development expenses during the period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Certain items in the prior year's consolidated financial statements have been reclassified to conform to the current presentation. Specifically, the Company reclassified certain collaboration costs related to the Vertex Hemoglobinopathy Agreements, as defined in Note 8, which were classified in research and development expense for the year ended December 31, 2024 and reclassified to collaboration expense, net in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2025. As a result, no subtotals in the prior year consolidated financial statements were impacted.

Segment Information

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or CODM, in deciding how to allocate resources and in assessing performance. The CODM is the Company's Chief Executive Officer. The Company views its operations as and manages its business in one operating segment, which is the business of discovering, developing and commercializing therapies derived from or incorporating genome-editing technology. Segment information is further described in Note 15 of the notes to the consolidated financial statements included in this

Annual Report on Form 10-K.

Foreign Currency Translation and Transactions

The majority of the Company's operations occur in entities that have the U.S. dollar as their functional currency. Non-U.S. dollar denominated functional currency subsidiaries have assets and liabilities translated into U.S. dollars at rates of exchange in effect at the end of the year. Revenue and expense amounts are translated using the average exchange rates for the period. Net unrealized gains and losses resulting from foreign currency translation are included in "Accumulated other comprehensive income" on the Company's consolidated balance sheets. Net foreign currency exchange transaction gains or losses are included in "Other income, net" on the Company's consolidated statement of operations, the impact of which is not significant.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less from the purchase date to be cash equivalents. As of December 31, 2025 and 2024, the Company had $347.6 million and $298.3 million in cash and cash equivalents, respectively.

Restricted Cash

As of December 31, 2025, the Company had $11.5 million in restricted cash, which was unchanged from December 31, 2024, representing letters of credit securing the Company's obligations under certain leased facilities. The letters of credit are secured by cash held in a restricted depository account, with $3.9 million included in prepaid expenses and other current assets and $7.6 million included in restricted cash in the accompanying consolidated balance sheets as of December 31, 2025.

Marketable Securities

As of December 31, 2025 and 2024, the Company had $1,628.3 million and $1,605.6 million, respectively, in marketable securities. The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the credit quality standards outlined in the Company's investment policy. The Company classifies marketable securities with a remaining maturity, when purchased, of greater than three months as available-for-sale. Marketable securities are classified as current assets on the consolidated balance sheets if the marketable securities are available to be converted into cash to fund current operations. Marketable securities in an unrealized loss position for greater than one year with a remaining maturity date greater than one year are classified as non-current assets.

Marketable securities classified as Level 1 within the valuation hierarchy consist of corporate equity securities with quoted prices in active markets. Marketable securities classified as Level 2 within the valuation hierarchy generally consist of U.S. Treasury securities and government agency securities, corporate bonds, commercial paper and prefunded warrants. 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 arising at purchase is amortized to interest expense over the period of the earliest call date, and any discount arising at purchase is accreted to interest income over the life of the instrument. Realized gains and losses on debt securities are determined using the specific identification method and are included in other income, net.

The Company assesses its available-for-sale debt securities under the available-for-sale debt security impairment model in ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Statements*, or ASC 326, as of each reporting date in order to determine if a portion of any decline in fair value below carrying value recognized on its available-for-sale debt securities is the result of a credit loss. The Company records credit losses in the consolidated statements of operations and comprehensive loss as credit loss expense within other income, net, which is limited to the difference between the fair value and the amortized cost of the security. To date, the Company has not recorded any credit losses on its available-for-sale debt securities.

Concentrations of Credit Risk and Off-balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents and marketable securities. The Company's cash is held in accounts with financial institutions that management believes are creditworthy. 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. The Company has no financial instruments with off-balance sheet risk of loss.

Fair Value of Financial Instruments

The Company has certain financial assets and liabilities recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements:

Level 1 — Quoted prices in active markets that are accessible at the market date for identical unrestricted assets or liabilities.

Level 2 — Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs for which all significant inputs are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

To the extent that 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.

Items measured at fair value on a recurring basis include marketable securities (see Note 3, *Marketable Securities*, and Note 4, *Fair Value Measurement*). The carrying amount of accounts receivable, other receivables, accounts payable and accrued expenses as reported on the consolidated balance sheets as of December 31, 2025 and 2024 approximate fair value, due to the short-term duration of these instruments.

Property and Equipment

Property and equipment are recorded 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. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

Asset	Estimated useful life
Computer equipment	3 years
Furniture, fixtures and other	5 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term

Impairment of Long-lived Assets

The Company reviews long-lived assets when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the book values of the assets to 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 value of the assets exceed their fair value, which is measured based on the projected discounted future net cash flows arising from the assets.

Revenue Recognition

The Company records revenue in accordance with ASC 606, *Revenue from Contracts with Customers,* or ASC 606. ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases and collaboration arrangements. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps:

1) Identify the contract with the customer

A contract with a customer exists when (i) the Company enters into an enforceable contract with a customer that defines each party's rights regarding the goods or services to be transferred and identifies the related payment terms, (ii) the contract has commercial substance and (iii) the Company determines that collection of substantially all consideration for goods and services that are transferred is probable based on the customer's intent and ability to pay the promised consideration.

2) Identify the performance obligations in the contract

Performance obligations promised in a contract are identified based on the goods and services that will be transferred to the customer that are both capable of being distinct, whereby the customer can benefit from the good or service either on its own or together with other available resources, and are distinct in the context of the contract, whereby the transfer of the good or service is separately identifiable from other promises in the contract. To the extent a contract includes multiple promised goods and services, the Company must apply judgment to determine whether promised goods and services are capable of being distinct and distinct in the context of the contract. If these criteria are not met, the promised goods and services are accounted for as a combined performance obligation.

3) Determine the transaction price

The transaction price is determined based on the consideration to which the Company will be entitled in exchange for

transferring goods and services to the customer. To the extent the transaction price includes variable consideration such as research, development, regulatory and commercial milestones, the Company determines if it is probable that it will receive such amounts and there is no risk of a significant revenue reversal. When the Company cannot conclude that receipt of such amounts is probable, the Company constrains the related variable consideration resulting in its exclusion from transaction consideration. In determining the portion of the transaction consideration to be constrained, the Company considers the probability and uncertainty that the related research, developmental, regulatory and commercial milestones will be achieved given the nature of research and clinical development and the stage of the underlying programs. This assessment is performed at each reporting period. In making this evaluation, the Company considers both internal and external information available, including information from industry publications and other relevant factors. Changes to the constraint of variable consideration can have a material effect on the amount of revenue recognized in the period.

4) Allocate the transaction consideration to performance obligations in the contract

If the contract contains a single performance obligation, the entire transaction consideration is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction consideration to each performance obligation on a relative standalone selling price basis unless the transaction consideration is variable and meets the criteria to be allocated entirely to a performance obligation or to a distinct service that forms part of a single performance obligation. The consideration to be received is allocated among the separate performance obligations based on relative standalone selling prices. In determining these estimated standalone selling prices, the Company makes a number of significant judgments including, for licenses, management's assumptions regarding probability weighted projected discounted cash flows for each of the collaboration development programs. The estimated standalone selling prices are sensitive to changes in assumptions, such as probabilities of scientific success, discount rate and certain assumptions that form the basis of forecasted cash flows. In developing these assumptions, management considers both internal and external information available, including information from other guideline companies within the same industry and other relevant factors. Changes to these assumptions can have a material effect on the allocation of the transaction consideration to performance obligations, as well as the amount and timing of revenue recognized.

5) Recognize revenue when or as the Company satisfies a performance obligation

The Company satisfies performance obligations over time or at a point in time, depending on the nature of the performance obligation. Revenue is recognized over time if the customer simultaneously receives and consumes the benefits provided by the entity's performance, the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or the entity's performance does not create an asset with an alternative use to the entity and the entity has an enforceable right to payment for performance completed to date. If the entity does not satisfy a performance obligation over time, the related performance obligation is satisfied at a point in time by transferring the control of a promised good or service to a customer.

Accounts Receivable

The Company's accounts receivable consists primarily of milestones due under its licensing and collaboration agreements accounted for under ASC 606. No such milestones were due as of December 31, 2025. As of December 31, 2024, accounts receivable was $25.0 million related to the achievement of milestones under the Company's license and collaboration agreements with Vertex, which was collected in 2025. Vertex is a creditworthy entity that maintains an ongoing relationship with the Company and as such, the Company does not have an allowance for estimated credit losses recorded related to these other receivables.

Contract Balances

The Company recognizes a contract asset when the Company transfers goods or services to a customer before the customer pays consideration or before payment is due, excluding any amounts presented as an accounts receivable. A contract asset is an entity's right to consideration in exchange for goods or services that the entity has transferred to a customer. Contract liabilities, or deferred revenue, primarily relate to contracts where the Company has received payment, but the Company has not yet satisfied the related performance obligations.

Collaboration Arrangements

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC 808, *Collaborative Agreements*, or ASC 808. Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities, are recorded as collaborative arrangements.

The Company evaluates the proper presentation of the commercial activities and the profit and loss sharing associated with the collaboration agreements. ASC 808 states that when payments between parties in a collaborative arrangement are not within the scope of other authoritative accounting literature, the income statement classification should be based on the nature of the arrangement, the nature of its business operations and the contractual terms of the arrangement. To the extent that these payments are not within the scope of other authoritative accounting literature, the income statement classification for the payments shall be based on an analogy to

authoritative accounting literature or if there is no appropriate analogy, a reasonable, rational and consistently applied accounting policy election.

Collaboration costs specific to the Vertex Hemoglobinopathy Agreements (as defined in Note 8) accounted for under ASC 808 are presented within "collaboration expense, net" in the consolidated statements of operations and comprehensive loss. Refer to Note 8 to these consolidated financial statements for further discussion on the Vertex Hemoglobinopathy Agreements.

Research and Development Expenses

Research and development costs are charged to expense as costs are incurred in performing research and development activities, including salaries and benefits, facilities costs, overhead costs, clinical study and related clinical manufacturing costs, license and milestone fees, contract services and other related costs. Research and development costs, including up-front fees and milestones paid to collaborators, are also expensed as incurred. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense. The Company accrues costs for clinical trial activities based upon estimates of the services received and related expenses incurred that have yet to be invoiced by the contract research organizations, clinical study sites, laboratories, consultants or other clinical trial vendors that perform the activities. The Company recognizes the reimbursement associated with collaborative activities to its collaborative partners, excluding collaboration costs under the Vertex Hemoglobinopathy Agreements accounted for under ASC 808, as a reduction to research and development expense in the period the services are provided. Costs associated with collaborative activities to collaborative partners accounted for under ASC 808 and included in research and development expense was not significant for the years ended December 31, 2025, 2024 and 2023.

Acquired In-process Research and Development Expenses

In-process research and development that is associated to a product that has not yet achieved regulatory approval and is acquired in a transaction that does not qualify as a business combination under U.S. GAAP is recorded as "Acquired in-process research and development" in the Company's consolidated statements of operations and comprehensive loss in accordance with ASC 730, *Research and development costs*, or ASC 730, as the asset acquired does not have an alternative future use. The Company classifies asset acquisitions of acquired in-process research and development as investing activities on its consolidated statements of cash flows.

Contingent Liabilities

The Company accounts for its contingent liabilities in accordance with ASC 450, *Contingencies*, or ASC 450. The Company accrues for loss contingencies when losses become probable and can be reasonably estimated. The Company recognizes contingent liabilities within accrued expenses, accrued income taxes, and other current and non-current liabilities in the consolidated balance sheets, as applicable, depending on if the contingency is expected to be resolved within one year or more. If the reasonable estimate of the loss is a range and no amount within the range is a better estimate, the minimum amount of the range is recognized as a liability. The Company does not accrue for contingent losses that, in its judgment, are considered to be reasonably possible but not probable; however, it discloses the range of such reasonably possible losses, if material, or a statement that such an estimate cannot be made. Legal costs related to a loss contingency are expensed as incurred and are classified as general and administrative expenses in the Company's consolidated statements of operations and comprehensive loss.

Leases

The Company accounts for its leases in accordance with ASC 842, *Leases*, or ASC 842. At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not have any material financing leases.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Prospectively, the Company will adjust the right-of-use assets for straight-line rent expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company has elected not to recognize leases with an original term of one year or less on its consolidated balance sheets. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty of renewal.

Assumptions made by the Company at the commencement date are re-evaluated upon occurrence of certain events, including a lease modification. A lease modification results in a separate contract when the modification grants the lessee an additional right of

use not included in the original lease and when lease payments increase commensurate with the standalone price for the additional right of use. When a lease modification results in a separate contract, it is accounted for in the same manner as a new lease.

Equity Based Compensation Expense

The Company's share-based compensation programs grant awards that have included stock options, restricted stock units and restricted stock awards. Grants are awarded to employees and non-employees, including directors.

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees and non-employee directors, including grants of employee stock options and restricted stock units and modifications to existing stock options, to be recognized in the consolidated statements of operations and comprehensive loss based on their fair values. The Company uses the Black-Scholes option pricing model to determine the fair value of options granted.

The Company accounts for forfeitures as they occur instead of estimating forfeitures at the time of grant and revising those estimates in subsequent periods if actual forfeitures differ from its estimates. Stock-based compensation expense recognized in the financial statements is based on awards for which performance or service conditions are expected to be satisfied.

The Company's stock-based awards are subject to service or performance-based vesting conditions. Compensation expense related to awards to employees, directors and non-employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Compensation expense related to awards to employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

The Company expenses restricted stock unit awards to employees based on the fair value of the award on a straight-line basis over the associated service period of the award.

The Company estimates the fair value of its option awards to employees, directors and non-employees using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (i) the expected stock price volatility, (ii) the calculation of expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. The Company computed the historical volatility data using the daily closing prices of the Company's publicly traded stock during the equivalent period of the calculated expected term of its stock-based awards. The Company has estimated the expected term of its employee stock options using the "simplified" method, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option, due to its lack of sufficient historical data. The risk-free interest rates for periods within the expected term of the option are based on the U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The Company has never paid, and does not expect to pay, dividends in the foreseeable future.

Patent Costs

Costs to secure and prosecute patent applications and other legal costs related to the protection of the Company's intellectual property are expensed as incurred and are classified as general and administrative expenses in the Company's consolidated statements of operations.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, or 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 tax reporting basis of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has evaluated available evidence and concluded that the Company may not realize all the benefit of its deferred tax assets; therefore, a valuation allowance has been established for the amount of the deferred tax assets that the Company does not believe is more likely than not to 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. As of December 31, 2025 and 2024, the Company does not have any significant uncertain tax positions. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. Income taxes are further described in Note 14 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

Comprehensive Loss

Comprehensive loss consists of net loss and other comprehensive loss. Other comprehensive loss consists of foreign currency translation adjustments and unrealized gains and losses on marketable debt securities.

Net Loss Per Share Attributable to Common Shareholders

Basic net loss per share is calculated by dividing net loss attributable to common shareholders by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is calculated by dividing the net loss attributable to common shareholders by the weighted-average number of common equivalent shares outstanding for the period, including any dilutive effect from outstanding stock options and restricted stock units using the treasury stock method. See Note 12 for further details.

New and Recently Adopted Accounting Pronouncements

In December 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures*, which requires entities, on an annual basis, to disclose disaggregated information about their effective tax rate reconciliation and income taxes paid. The disclosure requirements will be applied on a prospective basis, with the option to apply them retrospectively. The standard is effective for fiscal years beginning after December 15, 2024, with early adoption permitted. The Company has adopted ASU 2023-09 and applied the guidance prospectively to the period ended December 31, 2025 in the disclosures contained in the consolidated financial statements.

In November 2024, the FASB issued ASU 2024-03, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures*, or ASU 2024-03, and in January 2025, the FASB issued ASU 2025-01, *Income Statement—Reporting Comprehensive Income—Expense Disaggregation Disclosures: Clarifying the Effective Date,* or ASU 2025-01. ASU 2024-03 requires disclosure of additional information about specific expense categories in the notes to the financial statements on an interim and annual basis. ASU 2024-03, as clarified by ASU 2025-01, is effective for fiscal years beginning after December 15, 2026, and for interim periods beginning after December 15, 2027, with early adoption permitted. The Company is currently evaluating the disclosure requirements related to this new standard.

3. Marketable Securities

A summary of the Company's cash equivalents and marketable securities as of December 31, 2025 and 2024, which are recorded at fair value (and excludes $295.4 million and $193.9 million of cash at December 31, 2025 and 2024, respectively) is shown below (in thousands):

December 31, 2025	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 37,255	$ —	$ —	$ 37,255
Commercial paper	14,896	—	(4)	14,892
Total cash equivalents	52,151	—	(4)	52,147
Marketable securities:				
Corporate debt securities	1,152,319	3,827	(181)	1,155,965
Certificates of deposit	101,100	—	—	101,100
Government-sponsored enterprise securities	304,259	1,054	(15)	305,298
Commercial paper	49,432	28	—	49,460
Total marketable debt securities	1,607,110	4,909	(196)	1,611,823
Corporate equity securities	7,500	8,946	—	16,446
Total marketable securities	1,614,610	13,855	(196)	1,628,269
Total cash equivalents and marketable securities	$ 1,666,761	$ 13,855	$ (200)	$ 1,680,416

December 31, 2024	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash equivalents:				
Money market funds	$ 74,155	$ —	$ —	$ 74,155
Corporate debt securities	882	—	—	882
U.S. Treasury securities	29,271	—	(9)	29,262
Total cash equivalents	104,308	—	(9)	104,299
Marketable securities:				
U.S. Treasury securities	5,936	2	—	5,938
Corporate debt securities	1,136,255	3,442	(1,592)	1,138,105
Certificates of deposit	52,372	—	—	52,372
Government-sponsored enterprise securities	266,877	482	(497)	266,862
Commercial paper	127,805	34	(39)	127,800
Total marketable debt securities	1,589,245	3,960	(2,128)	1,591,077
Corporate equity securities	10,387	4,600	(495)	14,492
Total marketable securities	1,599,632	8,560	(2,623)	1,605,569
Total cash equivalents and marketable securities	$ 1,703,940	$ 8,560	$ (2,632)	$ 1,709,868

The following table summarizes the net unrealized gain (loss) recorded on marketable debt and equity securities during year ended December 31, 2025 and 2024 (in millions):

	Years Ended December 31,		
	2025	2024	2023
Unrealized gain (loss) recorded on marketable debt securities	$ 2.9	$ (0.1)	$ 17.5
Unrealized gain (loss) recorded on marketable equity securities	4.8	4.1	—

Unrealized gains and losses on the Company's marketable debt securities are included in comprehensive loss in the consolidated statements of operations and comprehensive loss. Unrealized gains and losses due to the change in fair value of the Company's marketable equity securities are included in other income (expense), net, in the consolidated statements of operations and comprehensive loss.

The following table summarizes the net unrealized gain (loss) position of the Company's marketable debt and equity securities as of December 31, 2025 and 2024 (in millions):

	December 31, 2025	December 31, 2024
Unrealized gain position of marketable debt securities	$ 4.7	$ 1.8
Unrealized gain position of marketable equity securities	8.9	4.1

The following table summarizes the aggregate fair value of marketable debt securities that were in an unrealized loss position as of December 31, 2025 and 2024 by the length of time the security has been in a loss position (in millions):

	December 31, 2025	December 31, 2024
Debt securities in an unrealized loss position for 12 months or less	$ 193.8	$ 451.9
Debt securities in an unrealized loss position for more than 12 months	—	31.8
Total debt securities in an unrealized loss position	$ 193.8	$ 483.7

As of December 31, 2025, there were no marketable debt securities in an unrealized loss position for more than twelve months with maturities beyond one year. As of December 31, 2024, no marketable debt securities in an unrealized loss position for more than twelve months had maturities beyond one year.

The Company determined that there was no material credit risk of the above investments as of December 31, 2025 and 2024. The Company has the intent and ability to hold such securities until recovery. As a result, the Company did not record any charges for credit-related impairments for its marketable securities for the years ended December 31, 2025 and 2024. No available-for-sale debt securities held as of December 31, 2025 had remaining maturities greater than thirty months.

Equity Investments Without Readily Determinable Fair Value

The Company holds investments in privately-held companies in the form of equity securities without readily determinable fair values and in which the Company does not have a controlling interest or significant influence. These investments had a net carrying value of $22.6 million and $12.9 million as of December 31, 2025 and 2024, respectively, and are classified within other non-current assets on the consolidated balance sheets. There were no upward or downward adjustments for observable price changes or impairment charges recorded for the year ended December 31, 2025 and 2024 related to these equity securities.

4. Fair Value Measurement

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicate the fair value hierarchy classification of such fair values as of December 31, 2025 and 2024 (in thousands):

	Fair Value Measurements at December 31, 2025			
	Total	Level 1	Level 2	Level 3
Cash and cash equivalents:				
Cash	$ 295,412	$ 295,412	$ —	$ —
Money market funds	37,255	37,255	—	—
Commercial paper	14,892	—	14,892	—
Marketable securities:				
Corporate debt securities	1,155,965	—	1,155,965	—
Certificates of deposit	101,100	—	101,100	—
Government-sponsored enterprise securities	305,298	—	305,298	—
Commercial paper	49,460	—	49,460	—
Corporate equity securities	16,446		16,446	—
Total	$ 1,975,828	$ 332,667	$ 1,643,161	$ —

	Fair Value Measurements at December 31, 2024			
	Total	Level 1	Level 2	Level 3
Cash and cash equivalents:				
Cash	$ 193,958	$ 193,958	$ —	$ —
Money market funds	74,155	74,155	—	—
Corporate debt securities	882	—	882	—
U.S. Treasury securities	29,262	—	29,262	—
Marketable securities:				
U.S. Treasury securities	5,938	—	5,938	—
Corporate debt securities	1,138,105	—	1,138,105	—
Certificates of deposit	52,372	—	52,372	—
Government-sponsored enterprise securities	266,862	—	266,862	—
Commercial paper	127,800	—	127,800	—
Corporate equity securities	14,492	2,391	12,101	—
Total	$ 1,903,826	$ 270,504	$ 1,633,322	$ —

Marketable securities classified as Level 1 within the valuation hierarchy consist of corporate equity securities with quoted prices in active markets. Marketable securities classified as Level 2 within the valuation hierarchy generally consist of U.S. Treasury securities and government agency securities, corporate bonds, commercial paper and warrants to purchase common shares of publicly traded companies. The Company estimates the fair values of these marketable securities by taking into consideration valuations obtained from third-party pricing sources.

5. Property and Equipment, net

Property and equipment, net, consists of the following (in thousands):

	As of December 31,	
	2025	2024
Computer equipment	$ 4,152	$ 3,833
Furniture, fixtures, and other	8,554	8,554
Laboratory equipment	43,575	42,008
Leasehold improvements	146,667	145,852
Construction work in process	3,955	6,118
Total property and equipment, gross	206,903	206,365
Accumulated Depreciation	(91,052)	(72,272)
Total property and equipment, net	$ 115,851	$ 134,093

Depreciation expense for the year ended December 31, 2025, 2024 and 2023 was $19.4 million, $19.2 million, and $19.8 million, respectively.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31,	
	2025	2024
Payroll and employee-related costs	12,966	18,443
Research costs	16,247	15,549
Collaboration costs	53,567	—
Licensing fees	874	1,850
Professional fees	3,749	3,086
Intellectual property costs	1,382	1,513
Other	622	631
Total	$ 89,407	$ 41,072

7. Leases

In May 2020, the Company entered into a lease agreement for a cell therapy manufacturing facility in Framingham, Massachusetts, or the Framingham Lease, for clinical and commercial production of the Company's investigational cell therapy product candidates. The Framingham Lease expires in March 2036 and the Company has an option to extend the term of the lease for two additional seven-year periods. The right-of-use asset and corresponding lease liability does not include the additional seven-year periods under the renewal option as the Company is not reasonably certain to exercise that option.

In July 2020, the Company entered into a lease agreement for an office and laboratory facility in Boston, Massachusetts, with a commencement date of June 1, 2021, or the 2020 Lease. At lease commencement, the Company recorded a right-of-use asset of $149.8 million and a corresponding operating lease liability of $147.9 million. Tenant incentives of $49.2 million were recorded as a reduction to the operating lease asset and liability at lease commencement. The lease expires in March 2034 and the Company has an option to extend the term of the lease for two additional five-year periods. The right-of-use asset and corresponding lease liability does not include the additional five-year periods under the renewal option as the Company is not reasonably certain to exercise that option.

The Company also rents certain office space in Zug, Switzerland, on a short-term basis for which a right-of-use asset and liability are not recorded, in accordance with the practical expedient elected.

The Company has embedded leases in certain research and license agreements for which the Company has recorded a right of use asset and liability. These arrangements are not significant in comparison to the Company's total operating lease assets and liabilities.

The Company identified and assessed the following estimates in recognizing the right-of-use asset and corresponding liability:

- *Expected lease term*: The expected lease term includes noncancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise that option.

- *Incremental borrowing rate*: As the discount rates in the Company's leases are not implicit, the Company estimated the incremental borrowing rate based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term.

The following table summarizes the lease assets and liabilities as of December 31, 2025 and 2024 (in thousands):

	As of December 31,	
	2025	2024
Assets		
Operating lease assets	$ 131,724	$ 143,461
Total lease assets	131,724	143,461
Liabilities		
Current		
Operating lease liabilities	18,578	17,288
Non-current		
Operating lease liabilities, net of current portion	188,168	206,405
Total lease liabilities	$ 206,746	$ 223,693

The following table summarizes operating lease costs included in research and development and general and administrative expense, as well as sublease income for the years ended December 31, 2025, 2024 and 2023 (in thousands):

	Years Ended December 31,		
	2025	2024	2023
Operating lease costs	$ 23,843	$ 24,417	$ 25,870
Short-term lease costs	46	40	—
Variable lease costs	13,500	12,364	14,387
Sublease income	(930)	(573)	(137)
Net lease cost	$ 36,459	$ 36,248	$ 40,120

The following table summarizes the maturity of undiscounted payments due under lease liabilities and the present value of those liabilities as of December 31, 2025 (in thousands):

	Total
2026	29,684
2027	28,798
2028	28,206
2029	27,314
2030	28,035
Thereafter	123,535
Total	$ 265,572
Present value adjustment	(58,826)
Present value of lease liabilities	$ 206,746

The following table summarizes the lease term (in years) and discount rate for operating leases as of December 31, 2025 and 2024:

	As of December 31,	
	2025	2024
Weighted-average remaining lease term	8.9	9.8
Weighted-average discount rate	5.9%	5.9%

The following table summarizes the cash paid for amounts included in the measurement of lease liabilities for the years ended December 31, 2025, 2024 and 2023 (in thousands):

	Years Ended December 31,		
	2025	2024	2023
Cash paid for amounts included in measurement of lease liabilities:			
Operating cash flows used in operating leases	$ (29,217)	$ (28,949)	$ (27,310)

Operating lease non-cash items:			
Right-of-use assets increased through lease modifications and reassessments	375	525	2,660
Right-of-use assets obtained in exchange for operating lease liabilities	—	243	7,552

8. Significant Contracts

Agreements with Vertex

For purposes of this Note 8 and Note 9, CASGEVY (exagamglogene autotemcel [exa-cel]) is referred to as "CASGEVY".

2015 collaboration

In 2015, the Company entered into a strategic collaboration, option and license agreement, or the 2015 Collaboration Agreement, with Vertex. The 2015 Collaboration Agreement is focused on the use of the Company's CRISPR/Cas9 gene editing technology to discover and develop potential new treatments aimed at the underlying genetic causes of human disease. The Company and Vertex amended the 2015 Collaboration Agreement in 2017 and 2019 with Amendment No. 1 and Amendment No. 2, respectively, namely to clarify Vertex's option rights under the 2015 Collaboration Agreement and to modify certain definitions and provisions of the 2015 Collaboration Agreement to make them consistent with the JDA (as defined below) and a strategic collaboration and license agreement from 2019 for the development and commercialization of products for the treatment of Duchenne muscular dystrophy, or DMD, and myotonic dystrophy Type 1, or DM1. In 2017, Vertex exercised an option granted to it under the 2015 Collaboration Agreement to obtain a co-exclusive license to develop and commercialize hemoglobinopathy and beta-globin targets, and in 2019, Vertex exercised the remaining options granted to it under the 2015 Collaboration Agreement to exclusively license certain collaboration targets developed under the 2015 Collaboration Agreement.

Hemoglobinopathies collaboration

In 2017, following Vertex's exercise of its option to obtain a co-exclusive license to develop and commercialize hemoglobinopathy and beta-globin targets, the Company and Vertex entered into a joint development and commercialization agreement, or the JDA, and agreed for potential hemoglobinopathy treatments, including CASGEVY, the Company and Vertex would share equally all research and development costs and worldwide revenues. In 2021, the Company and Vertex amended and restated the JDA, or the A&R Vertex JDCA (as amended and in effect, from time to time), pursuant to which the parties agreed to, among other things, (a) adjust the governance structure for the collaboration and adjust the responsibilities of each party thereunder, whereby Vertex leads and has all decision making (i.e., control) in relation to the CASGEVY program prospectively; (b) adjust the allocation of net profits and net losses between the parties with respect to CASGEVY only, which will be allocated 40% to the Company and 60% to Vertex, prospectively; and (c) exclusively license (subject to the Company's reserved rights to conduct certain activities) certain intellectual property rights to Vertex relating to the specified product candidates and products (including CASGEVY) that may be researched, developed, manufactured and commercialized on a worldwide basis under the A&R Vertex JDCA. Additionally, for 2022, 2023, and 2024, the Company had an option to defer a portion of its share of costs under the A&R Vertex JDCA if spending on the CASGEVY program exceeded specified amounts. Any deferred amounts under the A&R Vertex JDCA, as amended, are only payable to Vertex as an offset against future profitability of the CASGEVY program and the amounts payable are capped at a specified maximum amount per year.

In December 2023, the Company entered into an amendment to the A&R Vertex JDCA, or Amendment No. 1 to the A&R Vertex JDCA, with Vertex related to the global development, manufacturing, and commercialization of CASGEVY. Pursuant to Amendment No. 1 to the A&R Vertex JDCA, among other things, the Company and Vertex agreed to (a) allocate certain costs arising from a license agreement with a third party, resulting in a current payment due to Vertex by the Company of $20.0 million upon an event specified in Amendment No. 1 to the A&R Vertex JDCA, and (b) adjust, under certain specified circumstances, the timing of and portion of the Company's share of costs it is permitted to defer under the agreement.

In connection with the closing of the transaction contemplated by the A&R Vertex JDCA, the Company received a $900.0 million up-front payment from Vertex. Additionally, in December 2023, the Company and Vertex received approval of CASGEVY by the U.S. Food and Drug Administration, or the FDA. The FDA's approval of CASGEVY triggered Vertex's obligation to make a $200.0 million milestone payment to the Company.

Letter Agreement

In May 2024, Vertex and the Company entered into a letter agreement, or the Letter Agreement, with respect to the priority review voucher issued by the U.S. Food and Drug Administration to Vertex as the sponsor of the rare pediatric disease product application for CASGEVY. Vertex and the Company agreed that if Vertex utilizes or transfers the priority review voucher prior to the

first calendar year in which the CASGEVY program generates a net profit, Vertex will pay the Company $43.0 million or an amount equal to 42% of the net proceeds from such transfer, as applicable. If the CASGEVY program begins generating calendar-year net profits prior to such utilization or transfer, Vertex will instead pay the Company up to $43.0 million, set-off by deductions Vertex would otherwise be eligible to take against the CASGEVY program's net profits due to the Company related to amounts deferred previously by the Company.

Collaboration in the field of diabetes

In 2021, the Company and ViaCyte, Inc., or ViaCyte, entered into a joint development and commercialization agreement, or the ViaCyte JDCA, to jointly develop and commercialize product candidates and shared products for the diagnosis, treatment or prevention of diabetes type 1, diabetes type 2 or insulin dependent / requiring diabetes throughout the world. In the third quarter of 2022, Vertex acquired ViaCyte, and ViaCyte became a wholly-owned subsidiary of Vertex. In March 2023, (1) the Company and ViaCyte entered into an amendment to the ViaCyte JDCA, or the ViaCyte JDCA Amendment, and adjusted certain rights and obligations of the Company and ViaCyte under the ViaCyte JDCA, and (2) the Company and Vertex entered into a non-exclusive license agreement, or the Non-Ex License Agreement, pursuant to which the Company agreed to license to Vertex, on a non-exclusive basis, certain of its gene editing intellectual property to exploit certain products for the diagnosis, treatment or prevention of diabetes type 1, diabetes type 2 or insulin dependent / requiring diabetes throughout the world. Subsequently, ViaCyte elected to opt-out of the ViaCyte JDCA. Per the opt-out terms, the on-going collaboration assets are now wholly-owned by the Company, subject to a royalty on future sales owed to ViaCyte. The opt-out became effective in early February 2024.

In connection with entering into the Non-Ex License Agreement in 2023, the Company received a $100.0 million upfront payment from Vertex and subsequently received a $70.0 million research milestone achieved in the second quarter of 2023. In 2024, the Company received a $10.0 million research milestone achieved in the fourth quarter of 2024 and recorded a receivable of $25.0 million as of December 31, 2024 related to an additional research milestone achieved under the Non-Ex License Agreement in the fourth quarter of 2024. The Company is eligible to receive additional milestone payments under the Non-Ex License Agreement of $125.0 million in aggregate, which are dependent on the achievement of pre-determined research, development and commercial milestones for certain products utilizing the licensed intellectual property. Additionally, the Company is eligible to receive tiered royalties on the sales of certain products in the low to mid-single digits.

Accounting Analysis

For purposes of this Note 8, the 2015 Collaboration Agreement, Amendment No. 1, Amendment No. 2, A&R Vertex JDCA, and Amendment No. 1 to the A&R Vertex JDCA are collectively referred to as the "Vertex Hemoglobinopathy Agreements" and the Non-Ex License Agreement and ViaCyte JDCA Amendment are collectively referred to as the "March 2023 Diabetes Agreements."

The Vertex Hemoglobinopathy Agreements and the March 2023 Diabetes Agreements include components of a customer-vendor relationship as defined under ASC 606, collaborative arrangements as defined under ASC 808, and research and development costs as defined under ASC 730. Specifically, with regards to the March 2023 Diabetes Agreements, the Company concluded that the non-exclusive license is a performance obligation under ASC 606 and the ongoing research and development services under the ViaCyte JDCA Amendment are a unit of account under ASC 808.

The Company has determined that recognition criteria for the Letter Agreement has not been met and will not be met until the priority review voucher is (i) utilized or (ii) there is sufficient profitability such that Vertex is obligated to pay the Company under the Letter Agreement.

Accounting Analysis Under ASC 606

March 2023 Diabetes Agreements

Identification of the Contract

The March 2023 Diabetes Agreements were negotiated as a package with a single commercial objective and, as such, the March 2023 Diabetes Agreements were combined for accounting purposes and treated as a single arrangement. The Company determined for accounting purposes that the combined contract terminated the original ViaCyte JDCA and created a new contract.

Identification of Performance Obligations

The Company concluded the transfer of the non-exclusive license, including certain modified rights and obligations provided as part of the ViaCyte JDCA Amendment to support the delivery of the license, was both capable of being distinct and distinct within the context of the contract.

Determination of Transaction Price

The initial transaction price was comprised of the upfront payment of $100.0 million.

In the second quarter of 2023, the Company adjusted the transaction price to include $70.0 million in previously constrained variable consideration related to a research milestone which was achieved in the second quarter of 2023. In the fourth quarter of 2024, the Company adjusted the transaction price to include $35.0 million in previously constrained variable considerations related to two research milestones that were achieved in the fourth quarter of 2024. The Company determined that all other possible variable consideration resulting from milestones and royalties discussed below was fully constrained as of December 31, 2025. The Company will re-evaluate the transaction price in each reporting period.

Allocation of Transaction Price to Performance Obligations

The Company identified one performance obligation for the March 2023 Diabetes Agreements and, as a result, no allocation of the transaction price was required.

Recognition of Revenue

The Company determined the non-exclusive license, including certain modified rights and obligations provided as part of the ViaCyte JDCA Amendment to support the delivery of the license, represented functional intellectual property, as the intellectual property provides Vertex with the ability to perform a function or task in the form of research and development in the field of diabetes.

In 2023, the Company recognized revenue of $100.0 million for the non-exclusive license at the onset of the arrangement, as this was the point in time in which the non-exclusive license was delivered, as well as revenue of $70.0 million from previously constrained variable consideration related to a research milestone achieved in the second quarter of 2023. Revenue recognized under the March 2023 Diabetes Agreements for the year ended December 31, 2023 and 2024 was $170.0 million and $35.0 million, respectively. No revenue was recognized under the March 2023 Diabetes Agreements for the year ended December 31, 2025.

Milestones under the Non-Ex License Agreement

As of December 31, 2025, the Company is eligible to receive potential future milestone payments from Vertex of up to $125.0 million in the aggregate under the Non-Ex License Agreement depending on the achievement of pre-determined research, development and commercial milestones for certain products utilizing the licensed intellectual property. Additionally, the Company is eligible to receive tiered royalties on the sales of certain products in the low to mid-single digits.

Each of the remaining milestones under the Non-Ex License Agreement are fully constrained as of December 31, 2025. There is uncertainty as to whether the events to obtain the research and developmental milestones will be achieved given the nature of clinical development and the stage of the CRISPR/Cas9 technology. The remaining research, development and regulatory milestones will be constrained until it is probable that a significant revenue reversal will not occur. Commercial milestones and royalties relate predominantly to a license of intellectual property and are determined by sales or usage-based thresholds. The commercial milestones and royalties are accounted for under the royalty recognition constraint and will be accounted for as constrained variable consideration. The Company applies the royalty recognition constraint for each commercial milestone and will not recognize revenue for each until the subsequent sale of a licensed product (achievement of each) occurs.

Accounting for the Vertex Hemoglobinopathy Agreements

Recognition of Revenue

Revenue recognized under the Vertex Hemoglobinopathy Agreements for the year ended December 31, 2023 was $200.0 million of previously constrained variable consideration related to a milestone that was achieved upon approval of CASGEVY by the Food and Drug Administration, or FDA, in December 2023. No revenue was recognized under the Vertex Hemoglobinopathy Agreements for the years ended December 31, 2024 and 2025.

Milestones under the Vertex Hemoglobinopathy Agreements

The Company has evaluated the milestones that may be received in connection with the Vertex Hemoglobinopathy Agreements.

Under the 2015 Collaboration Agreement and subsequent amendments, the Company is eligible to receive up to $410.0 million in additional development, regulatory and commercial milestones and royalties on net product sales for each of the three collaboration targets that Vertex licensed in 2019. Each milestone is payable only once per collaboration target, regardless of the number of products directed to such collaboration target that achieve the relevant milestone event.

The Company has the option to conduct research at its own cost in certain defined areas. If such research is beneficial to the CASGEVY program and CASGEVY ultimately achieves regulatory approval in such areas, the Company could be entitled to receive from Vertex certain milestone payments aggregating to high eight digits.

Each of the remaining milestones described above are fully constrained as of December 31, 2025. There is uncertainty that the events to obtain the research and developmental milestones will be achieved given the nature of clinical development and the stage of the CRISPR/Cas9 technology. The remaining research, development and regulatory milestones will be constrained until it is probable

that a significant revenue reversal will not occur. Commercial milestones and royalties relate predominantly to a license of intellectual property and are determined by sales or usage-based thresholds. The commercial milestones and royalties are accounted for under the royalty recognition constraint and will be accounted for as constrained variable consideration. The Company applies the royalty recognition constraint for each commercial milestone and will not recognize revenue for each until the subsequent sale of a licensed product (achievement of each) occurs.

Accounting Analysis under ASC 808

Vertex Hemoglobinopathy Agreements

In connection with the Vertex Hemoglobinopathy Agreements, the Company identified the following collaborative elements, which are accounted for under ASC 808: (i) development and commercialization services for shared products, including any transition services related to CASGEVY under the A&R Vertex JDCA; (ii) R&D Services for follow-on products; and (iii) committee participation. The related impact of the cost sharing is included within collaboration expense, net, in the consolidated statements of operations and comprehensive loss.

During the years ended December 31, 2025, 2024 and 2023, the Company recognized $213.5 million, $120.7 million and $130.3 million of collaboration expense, net, related to the CASGEVY program, respectively. Collaboration expense, net, for the year ended December 31, 2024 and 2023 reflects the Company's exercise of its option to defer specified costs on the CASGEVY program in excess of the deferral limit under A&R Vertex JDCA, as amended, which is further described in Note 9 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K. Collaboration expense, net, during the years ended December 31, 2025, 2024 and 2023 was net of $1.9 million, $3.2 million, and $18.0 million of reimbursements from Vertex related to the CASGEVY program, respectively.

Additional Accounting Considerations

The Company is eligible to receive potential future payments of up to $775.0 million under a strategic collaboration and license agreement from 2019 for the development and commercialization of products for the treatment of DMD and DM1. The Company is also eligible to receive tiered royalties on future net sales on any products that may result from this collaboration; however, the Company has the option to forego the DM1 milestones and royalties to co-develop and co-commercialize all DM1 products globally.

Each of the remaining milestones are fully constrained as of December 31, 2025. There is uncertainty that the events to obtain the research and developmental milestones will be achieved given the nature of clinical development and the stage of the CRISPR/Cas9 technology. The remaining research, development and regulatory milestones will be constrained until it is probable that a significant revenue reversal will not occur. Commercial milestones and royalties relate predominantly to a license of intellectual property and are determined by sales or usage-based thresholds. The commercial milestones and royalties are accounted for under the royalty recognition constraint and will be accounted for as constrained variable consideration. The Company applies the royalty recognition constraint for each commercial milestone and will not recognize revenue for each until the subsequent sale of a licensed product (achievement of each) occurs.

As of December 31, 2025, there was $12.3 million of current deferred revenue and no non-current deferred revenue related to the strategic collaboration and license agreement from Vertex from 2019 for the development and commercialization of products for the treatment of DMD and DM1. As of December 31, 2024, there was no current deferred revenue and $12.3 million of non-current deferred revenue related to the strategic collaboration and license agreement from Vertex from 2019 for the development and commercialization of products for the treatment of DMD and DM1. The transaction price allocated to the remaining performance obligations was $12.3 million.

Agreement with Sirius Therapeutics

On May 19, 2025, the Company entered into a collaboration, option and license agreement, or the Sirius Agreement, with Sirius Therapeutics and certain of its affiliates, or Sirius, pursuant to which, among other things, (1) Sirius and the Company will collaborate on the research, development, manufacture, commercialization and use of certain collaboration products utilizing Sirius' siRNA technology for targeting Factor XI, including CTX611 (formerly SRSD107), collectively, the Sirius Collaboration Products; and (2) Sirius granted to the Company options to exclusively license Sirius siRNA technology to target up to two licensed targets from a list of seven reserved targets for the research, development, manufacture and commercialization of licensed products, collectively the siRNA Licensed Products, in exchange for the potential to receive certain option fees, milestone payments and royalties.

In connection with entering into the Sirius Agreement, the Company made an upfront cash payment to Sirius of $25.0 million and also entered into a share issuance agreement with Sirius, pursuant to which the Company registered and issued to Sirius 1,842,105 common shares equal to approximately $70.0 million based on a price per common share equal to $38.00, nominal value CHF 0.03 per share, or the Sirius Shares.

With respect to Sirius Collaboration Products, the Company and Sirius will share equally all development and

commercialization costs. For the first collaboration product candidate successfully developed, the Company will be the lead party responsible for commercialization efforts in the United States and Sirius will be the lead party responsible for commercialization efforts in Greater China. The parties will determine the lead party responsible for commercialization in the rest of the world at a future date. The Company and Sirius will share equally net profits and net losses incurred under the Sirius Agreement with respect to all Sirius Collaboration Products, except in the event that a party opts out of the joint development and commercialization. The Company will pay Sirius certain specified future development and regulatory milestones of up to an aggregate of $87.5 million for the first Sirius Collaboration Products to achieve the applicable milestone events. At the Company's sole election, such milestone payments may be paid in cash, common shares of the Company, or a combination thereof.

With respect to the siRNA Licensed Products, if the Company elects to exercise its option to a licensed target to research, develop, manufacture and commercialize siRNA Licensed Products, the Company will make a one-time $10.0 million payment per option exercise, each, a Sirius Option Payment, to Sirius. The Sirius Option Payment is payable up to two times. In addition, the Company will pay Sirius certain specified future development, regulatory and sales milestones of up to an aggregate of $300.0 million for the first siRNA Licensed Product relating to each licensed target to achieve the applicable milestone events, as well as tiered royalty payments in the mid-single digits to low double digits range on future sales of a commercialized siRNA Licensed Product. The royalty payments are subject to reduction under certain specified conditions set forth in the Sirius Agreement. In addition, at the Company's sole election, such milestones may be paid in cash, common shares of the Company, or a combination thereof. The Company is solely responsible for all research, development, manufacturing and global commercialization activities and associated costs for the siRNA Licensed Products, as well as all associated costs related to Sirius activities set forth in any applicable research plan relating thereto.

Accounting for the Sirius Agreement

The Company determined that substantially all the fair value of the upfront payment under the Sirius Agreement was attributable to acquired in-process research and development for which there was no alternative future use and that no substantive processes were acquired that would constitute a business. As a result, the Company recorded $96.3 million to acquired in-process research and development in the consolidated statements of operations and comprehensive loss. The $96.3 million represented the $25.0 million upfront cash payment to Sirius, as well as $71.3 million in expense related to the issuance of the Sirius Shares at a fair value of $38.68 per share, which was the fair value of the Company's common shares on the effective date of the Sirius Agreement.

The Sirius Agreement includes components of collaborative arrangements as defined under ASC 808 and research and development costs as defined under ASC 730.

Specifically, development and commercialization costs for the Sirius Collaboration Products contain collaborative elements accounted for under ASC 808, and the related impact of cost sharing for the Sirius Collaboration Products under the Sirius Agreement is included within research and development expenses in the consolidated statements of operations and comprehensive loss. Costs related to siRNA Licensed Products under the Sirius Agreement are included within research and development expenses in the consolidated statements of operations and comprehensive loss.

Research and development costs under the Sirius Agreement were not material for the twelve months ended December 31, 2025.

9. Commitments and Contingencies

Intellectual Property Agreements

Charpentier License Agreements

In April 2014, the Company entered into certain technology license agreements with Dr. Emmanuelle Charpentier pursuant to which the Company licensed certain intellectual property rights under joint ownership from Dr. Charpentier to develop and commercialize products for the treatment or prevention of human diseases. In connection therewith, Dr. Charpentier is entitled to receive nominal clinical milestone payments, low single digit percentage of sublicensing payments received under any sublicense agreement with a third party, and low single-digit percentage royalties based on annual net sales of licensed products and services by the Company and its affiliates and sublicensees.

Research, Manufacturing and License Agreements

The Company has engaged several research institutions and companies to identify new delivery strategies and applications of the Company's gene editing technology. The Company is also a party to a number of license agreements which require significant upfront payments and may be required to make future royalty payments and potential milestone payments from time to time. In addition, the Company is also a party to intellectual property agreements, which require maintenance and milestone payments from time to time. Further, the Company is a party to a number of manufacturing agreements that require upfront payments for the future performance of services.

In connection with these agreements, on a product-by-product basis, the counterparties are eligible to receive up to low eight-digit potential payments upon specified research, development and regulatory milestones. In addition, on a product-by-product basis, the counterparties are eligible to receive potential commercial milestone payments based on specified annual sales thresholds. The potential payments are low-single digit percentages of the specified annual sales thresholds. The counterparties are also eligible to receive low single-digit royalties on future net sales.

In the second quarter of 2025, a third-party licensor formally engaged with the Company regarding certain matters under their intellectual property contracts with the Company that may lead to further actions that could result in additional amounts being owed by the Company to such third party. Based on the status of ongoing negotiations with the third-party licensor, the Company has determined that it is probable that a loss was incurred as of December 31, 2025, and, based on the Company's best estimate of loss, the Company recorded incremental research and development expenses of $13.0 million for the year ended December 31, 2025. The total liability associated with the contingent loss as of December 31, 2025 was $14.5 million, which is primarily included within other current liabilities on the consolidated balance sheets as of December 31, 2025. The Company is unable to provide an estimate of a range of loss, and the ultimate resolution of the matter could result in a material charge in excess of the amount accrued as of December 31, 2025. The Company will reassess the contingent liability in each reporting period.

Under certain circumstances and if certain contingent future events occur, Vertex is eligible to receive up to $395.0 million in potential specified research, development, regulatory and commercial milestones and tiered single-digit percentage royalties on future net sales related to a specified target under an amendment to the 2015 Collaboration Agreement (as such term is defined in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K). In addition, Vertex has the option to conduct research at its own cost in certain defined areas that, if beneficial to the CASGEVY program and ultimately achieves regulatory approval, could result in the Company owing Vertex certain milestone payments aggregating to high eight digits, subject to certain limitations on the profitability of the CASGEVY program.

Under the A&R Vertex JDCA, as amended, for 2022, 2023 and 2024, the Company had an option to defer a portion of its share of costs if spending on the CASGEVY program exceeded specified amounts, which the Company exercised in each such year, resulting in deferred costs of $221.8 million, in the aggregate. Any deferred amounts under the A&R Vertex JDCA, as amended, are only payable to Vertex as an offset against future profitability of the CASGEVY program and the amounts payable are capped at a specified maximum amount per year. These deferred costs on the CASGEVY program will be recognized by the Company when recoverability of such deferred amounts by Vertex is probable and the amount can be reasonably estimated. As of December 31, 2025, no contingent payments have been accrued to date. The Company's arrangements with Vertex are further described in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

The Company may be required to make future potential payments to Sirius under the Sirius Agreement defined and described in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K. Potential payments to Sirius include (i) up to $20.0 million in Sirius Option Payments, (ii) up to $300.0 million in certain specified future development, regulatory and sales milestones for the first siRNA Licensed Product relating to each licensed target to achieve the applicable milestones, as well as tiered royalty payments in the mid-single digits to low double digits range on future sales of a commercialized siRNA Licensed Product, and (iii) up to $87.5 million in certain specified future development and regulatory milestones related to the Sirius Collaboration Products.

Litigation

In the ordinary course of business, the Company is from time to time involved in lawsuits, investigations, proceedings and threats of litigation related to, among other things, the Company's intellectual property estate (including certain in-licensed intellectual property), commercial arrangements and other matters. Such proceedings may include quasi-litigation, *inter partes* administrative proceedings in the U.S. Patent and Trademark Office, the European Patent Office and patent offices in other countries involving the Company's intellectual property estate including certain in-licensed intellectual property. For example, in the fourth quarter of 2025, ToolGen, Inc., or ToolGen, initiated a lawsuit against the Company and other third parties alleging patent infringement by CASGEVY of a ToolGen patent relating to CRISPR/Cas9 gene editing technology. The outcome of any of the foregoing is inherently uncertain. In addition, litigation and related matters are costly and may divert the attention of Company's management and other resources that would otherwise be engaged in other activities. If the Company is unable to prevail in any such proceedings, the Company's business, results of operations, liquidity and financial condition could be adversely affected.

10. Share Capital

All of the Company's common shares are issued under Swiss corporate law with a nominal value of 0.03 CHF per share. Though the nominal value of common shares is stated in Swiss francs, the Company continues to use U.S. dollars as its reporting currency for preparing the consolidated financial statements.

As of December 31, 2025, the Company's share capital consists of 96,747,997 registered common shares with a nominal value of CHF 0.03 per share, 8,202,832 registered common shares reserved for potential issuance of bonds or similar instruments and

19,537,850 registered common shares reserved for the Company's employee equity incentive plans. In addition, our board of directors is authorized to conduct one or more increases of the share capital at any time until June 8, 2028, or the expiration of the capital band if earlier, up to an upper limit of CHF 3,142,094.52 by issuing a corresponding number of registered shares with a nominal value of CHF 0.03 each to be fully paid in. As of December 31, 2025, the number of shares that may be issued under the capital band is 7,988,487 registered common shares.

Common Share Issuances

At-the-Market Offerings

The Company has entered into an Open Market Sale Agreement[SM], or the Sales Agreement, with Jefferies LLC under which the Company, at its sole discretion, is able to offer and sell, from time to time at prevailing market prices, its common shares. The following are in connection with the Sales Agreement.

2021 ATM

In January 2021, the Company filed a prospectus supplement with the SEC to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $600.0 million, or, together with the subsequent prospectus supplements filed in July 2021 and August 2024 relating to the common shares remaining under the original prospectus supplement, the 2021 ATM. In 2025, the Company issued and sold an aggregate of 6.1 million common shares under the 2021 ATM at an average price of $59.63 per share for aggregate proceeds of $359.0 million, which were net of equity issuance costs of $4.7 million, excluding stamp taxes of $3.6 million.

In 2024, the Company issued and sold 0.4 million common shares under the 2021 ATM at an average price of $55.81 per share for aggregate proceeds of $21.7 million, which were net of equity issuance costs of $0.3 million, excluding stamp taxes of $0.2 million.

In 2023, the Company issued and sold 0.5 million common shares under the 2021 ATM at an average price of $72.32 per share for aggregate proceeds of $32.7 million, which were net of equity issuance costs of $0.4 million, excluding stamp taxes of $0.3 million.

As of December 31, 2025, the Company has issued and sold an aggregate of 8.0 million common shares under the 2021 ATM at an average price of $74.77 per share for aggregate proceeds of $592.2 million, which were net of equity issuance costs of $7.8 million, excluding stamp taxes of $5.9 million. As of December 31, 2025, no common shares remain available under the 2021 ATM.

2025 ATM

In October 2025, the Company filed a new prospectus supplement with the SEC to offer and sell, from time to time, common shares having aggregate gross proceeds of up to $600.0 million, or the 2025 ATM. In 2025, the Company has issued and sold an aggregate of 0.7 million common shares under the 2025 ATM at an average price of $60.81 per share for aggregate proceeds of $42.3 million, which were net of equity issuance costs of $0.5 million, excluding stamp taxes of $0.4 million. Common shares having aggregate gross proceeds up to $557.2 million remain available under the 2025 ATM.

Share Issuance Agreement with Sirius Therapeutics

As described in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K, in 2025, the Company and Sirius entered into a share issuance agreement, and, in connection therewith, the Company registered and issued 1,842,105 of the Company’s common shares to Sirius, nominal value CHF 0.03 per share, at an issue price of $38.00 per share, as partial consideration for entering into the Sirius Agreement.

Additional Financings

In February 2024, the Company entered into an investment agreement for the sale of approximately $280.0 million of its common shares to a group of institutional investors in a registered direct offering, at a price per share of $71.50. The Company received net proceeds of $279.0 million, excluding stamp taxes due of $2.8 million.

Common Share Characteristics

The Common Shares have the following characteristics:

Voting Rights

The holders of common shares are entitled to one vote for each common share held at all meetings of shareholders.

Dividends

The holders of common shares are entitled to receive dividends, if and when resolved upon by the general meeting of shareholders based on a respective proposal by our board of directors and provided that the Company disposes of sufficient freely

distributable reserves. As of December 31, 2025, no dividends have been declared or paid since the Company's inception.

Liquidation

The holders of the common shares are entitled to share ratably in the Company's assets available for distribution to shareholders in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a deemed liquidation event.

11. Equity-based Compensation

Option and Grant Plans

In April 2015, the Company's shareholders approved the 2015 Stock Option and Grant Plan, or the 2015 Plan, and in July 2016, the Company's shareholders approved the 2016 Stock Option and Incentive Plan, or the 2016 Plan. In May 2018, the Company's shareholders approved the 2018 Stock Option and Incentive Plan, or the 2018 Plan (collectively, the "Plans"). Subsequent to the IPO, no further options were granted under the 2015 Plan. The Plans provide for the issuance of equity awards in the form of restricted shares, options to purchase common shares which may constitute incentive stock options, or ISOs, or non-statutory stock options, or NSOs, unrestricted stock unit grants, and qualified performance and market-based awards to eligible employees, officers, directors, non-employee consultants and other key personnel. Terms of the equity awards, including vesting requirements, are determined by our board of directors, subject to the provisions of the Plans. Options granted by the Company typically vest over four years and have a contractual life of ten years. Restricted stock unit grants typically vest over two to four years. At December 31, 2025, the Company had 29,405,365 common shares authorized for issuance under the 2018 Plan and 9,254,175 common shares available for future grant under the 2018 Plan.

Equity-Based Compensation Expense

The Company recognized stock-based compensation expense totaling $72.5 million, $86.6 million, and $81.0 million during the years ended December 31, 2025, 2024 and 2023, respectively. Stock-based compensation expense by classification within the consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Years Ended December 31,		
	2025	2024	2023
Research and development	$ 34,374	$ 47,944	$ 46,356
General and administrative	38,125	38,623	34,672
Total	$ 72,499	$ 86,567	$ 81,028

As of December 31, 2025, there was $61.7 million and $76.3 million of unrecognized compensation expense related to unvested stock options and restricted stock units, respectively, that is expected to be recognized over a weighted-average period of 2.5 and 2.5 years, respectively.

Stock Options

The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Years Ended December 31,		
	2025	2024	2023
Options granted	1,391,380	1,566,536	1,860,485
Weighted-average exercise price	$ 47.76	$ 62.40	$ 45.47
Weighted-average grant date fair value	$ 28.51	$ 38.63	$ 28.39
Assumptions:			
Expected volatility	60.9%	63.9%	65.1%
Expected term (in years)	6.0	6.0	6.0
Risk-free interest rate	4.0%	4.2%	4.1%
Expected dividend yield	0.0%	0.0%	0.0%

The following table summarizes stock option activity under the Company's equity award plans (intrinsic value in thousands):

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value

Outstanding at December 31, 2024	7,288,883	$ 58.07	6.6	$ 14,050
Granted	1,391,380	47.76		
Exercised	(726,396)	37.23		
Cancelled or forfeited	(1,206,032)	65.74		
Outstanding at December 31, 2025	6,747,835	$ 56.82	6.3	$ 42,270
Exercisable at December 31, 2025	4,709,497	$ 58.57	5.2	$ 31,455
Vested and expected to vest at December 31, 2025	6,747,835	$ 56.82	6.3	$ 42,270

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during the year ended December 31, 2025, 2024 and 2023 was $15.3 million, $32.2 million, and $13.9 million, respectively.

As of December 31, 2025, options to purchase 150,000 common shares subject to market-based vesting conditions were vested, as market conditions were satisfied in prior years. 100,000 options to purchase common shares subject to market-based vesting conditions were outstanding as of December 31, 2025.

The Company did not grant stock options subject to performance-based or market-based vesting conditions during 2025, 2024, and 2023.

Restricted Stock Units

The following table summarizes the restricted stock unit activity under the Company's equity award plans:

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance at December 31, 2024	2,397,643	$ 59.21
Granted	958,921	46.86
Vested	(736,238)	60.99
Cancelled or forfeited	(654,759)	58.55
Unvested balance at December 31, 2025	1,965,567	$ 52.16

During the years ended December 31, 2025, 2024 and 2023, the total fair value of restricted stock units vested was $36.6 million, $30.0 million, and $14.1 million, respectively.

During 2022, the Company granted 150,000 performance stock units with market-based vesting conditions in which the recipient is eligible to receive between zero and 150,000 common shares at the end of a three-year service period based upon achieving a specified average stock price. Expense for these awards was recognized over the requisite service period. As of December 31, 2025, 150,000 of previously unvested performance stock units were forfeited during 2025 as the market-based vesting conditions were not achieved. Activity related to stock units subject to market-based vesting conditions is included in the table above.

The Company did not grant restricted stock units subject to performance-based or market-based vesting conditions during 2025, 2024, and 2023.

Employee Stock Purchase Plan

On July 19, 2016, our board of directors adopted its 2016 Employee Stock Purchase Plan, or the ESPP Plan, which was subsequently approved by its shareholders and became effective on October 19, 2016. The ESPP Plan authorizes the initial issuance of up to a total of 413,226 shares of the Company's common stock to participating employees. The Company activated its ESPP Plan on January 1, 2020. The Company issued 44,128, 37,245, and 53,282 shares under the ESPP Plan during the years ended December 31, 2025, 2024 and 2023, respectively.

12. Net Loss Per Share Attributable to Common Shareholders

Basic net loss per share is calculated by dividing net loss attributable to common shareholders by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is calculated by adjusting weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period using the treasury stock method. For purposes of the diluted net loss per share calculation, stock options, unvested restricted common shares and ESPP shares are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share, as their effect would be

anti-dilutive; therefore, basic and diluted net loss per share were the same for all periods presented as a result of the Company's net loss. The Company's net loss is net loss attributable to common shareholders for all periods presented.

The Company did not include the securities in the following table in the computation of the net loss per share calculations for the years ended December 31, 2025, 2024 and 2023 because the effect would have been anti-dilutive during each period:

	Year ended December 31,		
	2025	2024	2023
Outstanding options	6,747,835	7,288,883	7,204,372
Unvested restricted common shares	1,965,567	2,397,643	1,781,415
ESPP	11,426	19,522	16,026
Total	8,724,828	9,706,048	9,001,813

13. 401(k) Savings Plan

The Company established a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code, or the "401(k) Plan", in November 2016. 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. The Company contributed $1.7 million, $2.7 million, and $3.0 million to the 401(k) Plan for the years ended December 31, 2025, 2024 and 2023, respectively.

14. Income Taxes

The Company is subject to U.S. federal and various state corporate income taxes as well as taxes in foreign jurisdictions for the foreign parent and where foreign subsidiaries have been established.

Net loss before taxes

For the years ended December 31, 2025, 2024 and 2023, the net loss before income taxes consist of the following (in thousands):

	Years Ended December 31,		
	2025	2024	2023
Domestic	$ 32,527	$ 41,232	$ 30,357
Foreign	(610,492)	(403,897)	(181,079)
Total	$ (577,965)	$ (362,665)	$ (150,722)

The provision for income taxes consist of the following (in thousands):

	Years Ended December 31,		
	2025	2024	2023
Current income taxes:			
Federal	$ (1,658)	$ (2,592)	$ (2,318)
State	(1,061)	(1,479)	(994)
Foreign	—	—	—
Total current income taxes	(2,719)	(4,071)	(3,312)
Deferred income taxes:			
Federal	$ (933)	$ 492	$ 424
State	18	(8)	—
Foreign	—	—	—
Total deferred income taxes	(915)	484	424
Total income tax provision	$ (3,634)	$ (3,587)	$ (2,888)

A reconciliation of income tax expense computed at the statutory corporate income tax rate to the effective income tax rate after the adoption of ASU 2023-09 for the year ended December 31, 2025 is as follows (amounts in thousands):

	Year Ended December 31, 2025	
	Amount	Percent
Statutory federal tax rate	44,966	(7.8)%
State and local income tax, net of federal income tax effect[1]	—	0.0%
Foreign Tax Effects		
United States		
Statutory rate difference between the U.S. and Switzerland	(4,300)	0.7%
State and local income tax, net of federal income tax effect[2]	(1,937)	0.3%
Research and development tax credits	7,775	(1.3)%
Change in valuation allowances	1,957	(0.4)%
Non-taxable or non-deductible items	(3,467)	0.6%
Other	(85)	0.0%
Other Foreign Jurisdictions	(3)	0.0%
Changes in valuation allowances	(39,082)	6.8%
Non-taxable or non-deductible items		
Equity issuance for in-process research and development	(5,543)	1.0%
Other	(910)	0.2%
Changes in unrecognized tax benefits	(1,046)	0.2%
Other adjustments	(1,959)	0.3%
Effective income tax rate	(3,634)	0.6%

(1) State taxes in the Swiss Canton of Zug made up the majority (greater than 50 percent) of the tax effect in this category.
(2) State taxes in Massachusetts made up the majority (greater than 50 percent) of the tax effect in this category.

A reconciliation of income tax expense computed at the statutory corporate income tax rate to the effective income tax rate prior to the adoption of ASU 2023-09 for the years ended December 31, 2024 and 2023 is as follows:

	Years Ended December 31,	
	2024	2023
Income tax expense at statutory rate	11.9%	11.9%
State income tax, net of federal benefit	1.1%	2.3%
Non-deductible expenses	0.0%	(0.2)%
Foreign rate differential	(1.0)%	(2.1)%
Statutory to U.S. GAAP permanent differences	0.0%	0.0%
Stock-based compensation	(0.4)%	(4.0%)
Impact of deferred rate change	(0.1)%	0.1%
Research credits	2.7%	8.2%
Change in valuation allowance	(15.2)%	(17.2)%
Other Rate Items	0.0%	(0.9)%
Effective income tax rate	(1.0%)	(1.9%)

The federal statutory rate reflects the Switzerland mixed company service rate.

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company’s deferred tax assets are comprised of the following (in thousands):

	Years Ended December 31,	
	2025	2024
Deferred tax assets:		
Net operating loss carryforwards	$ 241,462	$ 178,061
Accruals and reserves	3,393	4,479
Operating lease liabilities	56,594	60,570
Other deferred tax assets	12,337	17,809
Stock-based compensation	18,801	20,553
Research credit	77,901	74,012
Total deferred tax assets	410,488	355,484
Less valuation allowance	(345,395)	(282,739)
Net deferred tax assets	65,093	72,745
Deferred tax liabilities:		
Depreciation	(30,128)	(34,078)
Operating lease assets	(36,058)	(38,845)
Other deferred tax liabilities	(37)	(36)
Total deferred tax liabilities	(66,223)	(72,959)
Long term deferred taxes	$ (1,130)	$ (214)

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of worldwide operating losses, the Company has concluded that it is more-likely-than-not that the benefit of its U.S. and non-U.S. deferred tax assets will not be realized. Accordingly, as of December 31, 2025 and 2024, the Company has provided a full valuation allowance against its net deferred tax assets in Switzerland and the United Kingdom. The Company has also provided a valuation allowance against the U.S. deferred tax assets that cannot be realized by existing deferred tax liabilities based upon when they are scheduled to reverse. The valuation allowance increased by $62.7 million during 2025, which is primarily attributable to increase in net operating loss carryforwards as a result of current year net loss.

As of December 31, 2025, the Company had no available U.S. federal net operating loss carryforwards. As of December 31, 2025, the Company had available U.S. state net operating loss carryforward of $9.4 million that begin to expire in 2045. As of December 31, 2025, the Company had available non-U.S. net operating loss carryforwards of $4,037.2 million of which $2,017.4 million relate to Switzerland, $2,017.4 million relate to the Canton of Zug, and $2.4 million relate to the Company's wholly-owned subsidiary in the United Kingdom. The net operating losses generated in Switzerland and the Canton of Zug begin to expire in 2027 and the net operating losses generated in the United Kingdom can be carried forward indefinitely.

As of December 31, 2025, the Company had U.S. domestic federal research and development credit carryforwards of $31.1 million that begin to expire in 2041 for federal purposes, which are net of uncertain tax positions of $24.4 million. As of December 31, 2025, the Company had U.S. domestic federal orphan drug credit carryforwards of $27.0 million which begin to expire in 2040 for federal purposes, which are net of uncertain tax positions of $11.5 million. As of December 31, 2025, the Company had U.S. domestic state research and development credit carryforwards of $25.1 million which begin to expire in 2035, which are net of uncertain tax positions of $13.0 million.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statement by prescribing the minimum recognition threshold and measurement of a tax position taken or expected to be taken in a tax return.

As of December 31, 2025, the Company had gross unrecognized tax benefits of $50.7 million of which $46.7 million would favorably impact the effective tax rate if recognized. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2025 and 2024, interest and penalties recognized in the Company's financial statements related to uncertain tax positions were not material. As of December 31, 2023, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts had been recognized in the Company's consolidated statements of operations and comprehensive loss.

The aggregate changes in gross unrecognized tax benefits were as follows (in thousands):

	Years Ended December 31,		
	2025	2024	2023
Balance at beginning of year	$ 49,959	$ 44,148	$ 34,536
Increases for tax positions taken during current period	2,900	5,777	9,703
Increases for tax positions taken in prior periods	51	34	—
Decreases for tax positions taken during current period	—	—	—
Decreases for tax positions taken in prior periods	(2,201)	—	(91)
Balance at end of year	$ 50,709	$ 49,959	$ 44,148

The Company files income tax returns in the U.S. federal, state, and certain non-U.S. jurisdictions. The Company is subject to U.S. federal, Massachusetts, California and non-U.S. income tax examinations by authorities for tax years ending after December 31, 2021. Research credits generated in prior tax years that are closed for examination may still be adjusted upon future examination if they have or will be used in a future period. The Company is subject to income tax examinations by authorities in its non-U.S. jurisdictions for all years.

A summary of income taxes paid by jurisdiction, net of refunds, after the adoption of ASU 2023-09 for the year ended December 31, 2025 is as follows (in thousands):

	Years Ended December 31, 2025
Foreign	
U.S. Federal	$ 1,720
Massachusetts	1,264
Other	1
Total	2,985

15. Segment Information

The Company operates and manages its business as one reportable segment and one operating segment, which is the business of discovering, developing and commercializing therapies derived from or incorporating genome-editing technology. The determination of a single business segment is consistent with the consolidated financial information regularly provided to the Company's chief operating decision maker, or CODM. The Company's chief executive officer, as the CODM, uses consolidated, single-segment financial information for purposes of evaluating performance, making operating decisions, allocating resources and planning and forecasting for future periods.

The CODM assesses performance and decides how to allocate resources based on consolidated net loss. The measure is used to monitor budget versus actual results to evaluate the performance of the segment.

The measure of segment assets is reported on the consolidated balance sheets as total consolidated assets. All material long-lived assets are located in the United States. Long-lived assets consist of property and equipment, net, and operating lease right-of-use assets. The accounting policies of the segment are the same as those described in Note 2 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

The following table summarizes information about segment revenue, significant segment expenses and segment operating loss for the periods presented (in thousands):

	Years Ended December 31,		
	2025	2024	2023
Revenue[1]:			
Collaboration revenue	—	$ 35,000	$ 370,000
Grant revenue	3,510	2,314	1,206
Less[2]:			
Research and development expense[3]	239,872	252,010	330,121
Acquired in-process research and development[4]	96,253	—	—
General and administrative expense[5]	26,570	25,453	32,589
Collaboration expense, net	213,480	120,667	130,250
Stock-based compensation expense	72,499	86,567	81,028
Depreciation expense	19,407	19,183	19,756
Other segment items[6]	(82,972)	(100,314)	(68,928)
Segment net loss	(581,599)	(366,252)	(153,610)
Reconciliation of profit or loss:			
Adjustments or reconciling items	—	—	—
Consolidated net loss	(581,599)	(366,252)	(153,610)

(1) Collaboration revenue for the years ended December 31, 2025, 2024 and 2023 is related to our license agreements and collaborations with Vertex, as further described in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K. Collaboration revenue is attributed to the CRISPR Therapeutics AG entity, which is domiciled in Switzerland.

(2) The significant expense categories and amounts align with the segment-level information that is regularly provided to the CODM.

(3) Research and development expense for the years ended December 31, 2025, 2024 and 2023 is net of $34.4 million, $47.9 million, and $46.4 million of stock-based compensation expense, respectively, and $10.6 million, $10.3 million, and $10.9 million of depreciation expense, respectively. For the year ended December 31, 2024, the Company recorded a non-cash adjustment of $4.8 million related to an option expiration which was recognized as a benefit to research and development expense.

(4) Acquired in-process research and development expense for the year ended December 31, 2025 relates to expense of $25.0 million related to the upfront cash payment to Sirius in the second quarter of 2025, as well as expense of $71.3 million related to the issuance of the Company's common shares issued to Sirius as part of the Sirius Agreement in the second quarter of 2025, as described further in Note 8 of the notes to the consolidated financial statements included in this Annual Report on Form 10-K.

(5) General and administrative expense for the years ended December 31, 2025, 2024 and 2023 is net of $38.1 million, $38.6 million, and $34.7 million of stock-based compensation expense, respectively, and $8.8 million, $8.9 million, and $8.9 million of depreciation expense, respectively.

(6) Other segment items include interest income, net, the change in fair value of corporate equity securities and income tax expense.

Exhibit 4.1

DESCRIPTION OF THE REGISTRANT'S SECURITIES

REGISTERED PURSUANT TO SECTION 12 OF THE

SECURITIES EXCHANGE ACT OF 1934

As of February 12, 2026, CRISPR Therapeutics AG has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

The following description of our common shares is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our Amended and Restated Articles of Association (the "Articles of Association"), which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.1 is a part. We encourage you to read our Articles of Association and the applicable provisions of the Swiss Code of Obligations, or CO, for additional information.

Description of Capital Shares

The Company has one class of common shares. Our share capital recorded in the commercial register as of February 12, 2026 is CHF 2,902,439.91 and is fully paid-in. It is divided into 96,747,997 common shares with a nominal value of CHF 0.03 each. The issued common shares are fully paid, non-assessable, and rank pari-passu with each other and all other shares.

The shares are registered in book-entry form in DTC under the ISIN CH0334081137. The Company's Transfer Agent and Registrar is Equiniti Trust Company, LLC, and its address is 48 Wall Street, Floor 23, New York, NY 10005.

Stock Exchange Listing

The shares are listed on the Nasdaq Global Market under the symbol "CRSP".

Capital Band

As of February 12, 2026, our Articles of Association authorize the board of directors to conduct one or more increases of the share capital at any time until June 8, 2028, or the expiry of the capital band if earlier, up to an upper limit of CHF 3,142,094.52, by issuing a corresponding number of registered shares with a nominal value of CHF 0.03 each to be fully paid in.

Conditional Share Capital

As of February 12, 2026, our Articles of Association provide for a conditional capital for bonds and similar debt instruments. For such purposes, as per our current Articles of Association, our share capital may be increased by a maximum amount of CHF 246,084.96 through the issue of a maximum of 8,202,832 common shares, payable in full, each with a nominal value of CHF 0.03 through the exercise of conversion and/or option rights granted in connection with bonds or similar instruments, issued or to be issued by us or by our subsidiaries, including convertible debt instruments. In addition, our Articles of Association provide for a conditional capital for employee benefit plans. For such purposes, as per our current Articles of Association, our share capital may be increased by an amount not exceeding CHF 586,135.50 through the issue of a maximum of 19,537,850 common shares, payable in full, each with a nominal value of CHF 0.03, in connection with the exercise of option rights granted to any of our employees or a subsidiary of us, and any consultant, members of the board of directors, or other person providing services to us or a subsidiary.

Pre-Emptive Rights

Pursuant to the Swiss Code of Obligations, or CO, shareholders have pre-emptive rights (*Bezugsrechte*) to subscribe for new issuances of shares. With respect to conditional capital in connection with the issuance of

conversion rights, convertible bonds or similar debt instruments, shareholders have advance subscription rights (*Vorwegzeichnungsrechte*) for the subscription of conversion rights, convertible bonds or similar debt instruments.

A resolution passed at a general meeting of shareholders by two-thirds of the share votes represented and the absolute majority of the nominal value of the shares represented may authorize our board of directors to withdraw or limit pre-emptive rights or advance subscription rights in certain circumstances.

If pre-emptive rights are granted, but not exercised, the board of directors may allocate the pre-emptive rights as it elects.

With respect to our capital band, the board of directors is authorized by our Articles of Association to withdraw or to limit the pre-emptive rights of shareholders, and to allocate them to third parties, in the event that the newly issued shares are used for the following purposes:

- if the issue price of the new registered shares is determined by reference to the market price;
- for the acquisition of an enterprise, part(s) of an enterprise or participations, or for the financing or refinancing of any of such transactions, or in the event of share placement for the financing or refinancing of such transactions;
- for purposes of broadening the shareholder constituency of the Company in certain financial or investor markets, for purposes of the participation of strategic partners, or in connection with the listing or registration of new registered shares on domestic or foreign stock exchanges;
- for purposes of granting an over-allotment option of up to 20% of the total number of registered shares in a placement or sale of registered shares to the respective initial purchaser(s) or underwriter(s);
- for raising of capital (including private placements) in a fast and flexible manner as such transaction would probably be difficult to carry out, or could be carried out only at less favorable terms, without the exclusion of the statutory pre-emptive right of the existing shareholders;
- following a shareholder or a group of shareholders acting in concert having accumulated shareholdings in excess of 15% of the share capital registered in the commercial register without having submitted to the other shareholders a takeover offer recommended by the board of directors, or for the defense of an actual, threatened or potential takeover bid, in relation to which the board of directors, upon consultation with an independent financial adviser retained by it, has not recommended to the shareholders acceptance on the basis that the board of directors has not found the takeover bid to be financially fair to the shareholders; or
- for other valid grounds in the sense of Article 652b para. 2 of the Swiss Code of Obligations, or CO.

With respect to our conditional share capital, the shareholders' advance subscription rights with regard to the new bonds or similar instruments may be restricted or excluded by our board of directors in order to finance or refinance the acquisition of companies, parts of companies or holdings, or new investments planned by us, or in order to issue convertible bonds or similar instruments on the international capital markets or through private placement. If advance subscription rights are excluded, then (1) the instruments are to be placed at market conditions, (2) the exercise period is not to exceed ten years from the date of issue of option rights and twenty years for conversion rights and (3) the conversion or exercise price for the new shares is to be set at least in line with the market conditions prevailing at the date on which the instruments are issued.

Voting Rights

The shareholders exercise their voting rights at the general meetings of shareholders in proportion to the nominal value of the shares belonging to them. The holders of shares are entitled to one vote for each share held at all meetings of shareholders. The holders of our common shares do not have cumulative voting rights in the election of directors, as cumulative voting is not permitted under Swiss law. The shares are not divisible. The right to vote and the other rights of share ownership may only be exercised by shareholders (including any nominees) or

usufructuaries who are entered in our share register at the cut-off date determined by the board of directors and by persons who are entitled by law to the voting right of a share. Each shareholder may be represented by the independent proxy holder (annually elected by the general meeting of shareholders), another registered shareholder or third person with written authorization to act as proxy or the shareholder's legal representative. The requirements regarding powers of attorney and instructions are determined by the board of directors.

According to our Articles of Association, when exercising voting rights, no person or entity can accumulate voting rights over its shares of more than 15% of the registered share capital recorded in the commercial register of the Canton of Zug, Switzerland. This restriction on exercise of voting rights does not apply to the exercise of voting rights by the independent proxy holder.

Our Articles of Association further contain provisions that prevent shareholders from acquiring voting rights over its shares that exceed 5% or more of the registered share capital recorded in the commercial register of the Canton of Zug, Switzerland. Specifically, no individual or legal entity shall be registered with voting rights over its shares (held directly or indirectly) that exceed 5% or more of the registered share capital recorded in the commercial register of the Canton of Zug, Switzerland; the common shares exceeding the limit of 15% shall be entered in our share register as shares without voting rights. The board of directors may in special cases approve exceptions to the above regulations.

Our Articles of Association contain provisions that persons who do not expressly declare in the registration application that they are holding the shares on their own account (thereafter: nominees) shall forthwith be entered on the share register as shareholders with voting rights up to a maximum of 3% of the share capital. Beyond that limit, registered shares of nominees shall only be entered as voting if the nominees in question disclose the names, addresses and shareholdings of the persons on whose account they hold 0.5% or more of the share capital. The board of directors concludes agreements with nominees that among other things govern the representation of shareholders and the voting rights.

Dividends

The holders of shares are entitled to receive dividends, if and when resolved upon by the general meeting of shareholders based on a respective proposal by the board of directors and provided that the Company disposes of sufficient freely distributable reserves.

Treasury Shares

The Swiss Code of Obligations, or CO, limits the Company's ability to hold or repurchase shares. The Company and its subsidiaries may only repurchase shares if and to the extent that sufficient freely distributable reserves are available. The aggregate par value of all shares held by the Company and its subsidiaries may not exceed 10% of the registered share capital, safe for the purpose of cancellation, subject to the approval of the general meeting of shareholders. Repurchased shares held by the Company or its subsidiaries do not carry any rights to vote at a general meeting of shareholders, but are entitled to the economic benefits generally associated with the shares.

Profit Participation Certificates

As of February 12, 2026, we have not issued any profit participation certificates (*Genussscheine*).

Exhibit 21.1

Subsidiaries of the Registrant

Name of Subsidiary	Jurisdiction of Incorporation or Organization
CRISPR Therapeutics, Inc.	Delaware
TRACR Hematology Ltd	United Kingdom
CTX Financing GmbH	Switzerland
CTX Securities Corporation	Massachusetts

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-281262) of CRISPR Therapeutics AG,

(2) Registration Statement (Form S-8 No. 333-221427) pertaining to the CRISPR Therapeutics AG Amended and Restated 2016 Stock Option and Incentive Plan,

(3) Registration Statement (Form S-8 No. 333-214184) pertaining to the CRISPR Therapeutics AG 2015 Stock Option and Grant Plan, the CRISPR Therapeutics AG 2016 Stock Option and Incentive Plan, the CRISPR Therapeutics AG 2016 Employee Stock Purchase Plan, the Non-Qualified Option Agreement with Megan Menner, the Non-Qualified Option Agreement with Paul Schneider, and the Non-Qualified Option Agreement with Pablo Cagnoni, and

(4) Registration Statements (Form S-8 Nos. 333-225369, 333-232877, 333-240120, 333-266636, 333-273764, 333-281247) pertaining to the CRISPR Therapeutics AG 2018 Stock Option and Incentive Plan;

of our reports dated February 12, 2026, with respect to the consolidated financial statements of CRISPR Therapeutics AG and the effectiveness of internal control over financial reporting of CRISPR Therapeutics AG included in this Annual Report (Form 10-K) of CRISPR Therapeutics AG for the year ended December 31, 2025.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 12, 2026

Exhibit 31.1

CERTIFICATIONS

I, Samarth Kulkarni, certify that:

1. I have reviewed this Annual Report on Form 10-K of CRISPR Therapeutics AG;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 12, 2026

/s/ Samarth Kulkarni
Samarth Kulkarni
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Raju Prasad, certify that:

1. I have reviewed this Annual Report on Form 10-K of CRISPR Therapeutics AG;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 12, 2026

/s/ Raju Prasad
Raju Prasad
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

SECTION 906 CEO/CFO CERTIFICATION

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Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code) each of the undersigned officers of CRISPR Therapeutics AG (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2025 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 12, 2026

/s/ Samarth Kulkarni
Samarth Kulkarni
Chief Executive Officer
(Principal Executive Officer)

Date: February 12, 2026

/s/ Raju Prasad
Raju Prasad
Chief Financial Officer
(Principal Financial and Accounting Officer)