INTELLIA THERAPEUTICS, INC.

2023 ANNUAL REPORT

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, 2023

☐ **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 001-37766

INTELLIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**36-4785571**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
40 Erie Street, Suite 130 Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip Code)**

(857) 285-6200

(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each Class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	NTLA	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 Section 15(d) of the Act. Yes ☐ No ☒

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

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

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

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

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

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

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

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $3,565,071,688 as of June 30, 2023 (based on a closing price of $40.78 per share as quoted by the Nasdaq Global Market as of such date). In determining the market value of non-affiliate common stock, shares of the registrant's common stock beneficially owned by officers, directors and affiliates have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The registrant had 96,106,405 shares of Common Stock, $0.0001 par value per share, outstanding as of February 16, 2024.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates by reference certain information from the registrant's definitive Proxy Statement for its 2024 annual meeting of shareholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end of December 31, 2023. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

Intellia Therapeutics, Inc.
Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2023

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Forward-looking Information

This Annual Report on Form 10-K contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by such forward-looking terminology as "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Our business and our forward-looking statements involve substantial known and unknown risks and uncertainties, including the risks and uncertainties inherent in our statements regarding:

- our ability to execute our clinical study strategy for NTLA-2001, our program for the treatment of transthyretin ("ATTR") amyloidosis, including the ability to successfully complete our global Phase 3 study, or the success of such program;
- our ability to execute our clinical study strategy for NTLA-2002, our program for the treatment of hereditary angioedema ("HAE"), including the ability to successfully complete our Phase 1/2 study and determine a recommended dose that can be advanced into later-stage studies, or the success of such program;
- our ability to initiate and complete our Phase 3 study for NTLA-2002 for HAE and file a biologics license application or comparable marketing application within a certain time period;
- our ability to execute our clinical study strategy for NTLA-3001, our program for the treatment of alpha-1 antitrypsin deficiency ("AATD")-associated lung disease, including the ability to successfully initiate our Phase 1 study, or the success of such program;
- our ability to use a modular platform capability or other strategies to efficiently discover and develop product candidates, including by applying learnings from one program to other programs;
- our ability to research, develop or maintain a pipeline of product candidates, including *in vivo* and *ex vivo* product candidates;
- our ability to manufacture or obtain materials for our preclinical and clinical studies, and our product candidates;
- our ability to advance any product candidates into, and successfully complete, clinical studies, including clinical studies necessary for regulatory approval and commercialization, and to demonstrate to the regulators that the product candidates are safe and effective and that their benefits outweigh known and potential risks for the intended patient population;
- our ability to advance our genome editing and therapeutic delivery capabilities, including our therapeutic delivery capabilities for tissues other than the liver;
- the scope of protection we are able to develop, establish and maintain for intellectual property rights, including patents, trade secrets and license rights, covering our product candidates and technology;
- our ability to operate, including commercializing products, without infringing or breaching the proprietary or contractual rights of others;
- the issuance or enforcement of, and compliance with, regulatory requirements and guidance regarding preclinical and clinical studies relevant to genome editing and our product candidates;
- the market acceptance, pricing and reimbursement of our product candidates, if approved;
- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic agreements, such as collaborations, co-development and co-commercialization, acquisitions, dispositions, mergers, joint ventures, and investment agreements, and our ability to establish and maintain strategic arrangements under favorable terms;

- our ability to acquire and maintain relevant intellectual property licenses and rights, and the scope and terms of such rights;
- developments relating to our licensors, licensees, third parties and ventures from which we derive or license rights, as well as collaborators, competitors and our industry; and
- other risks and uncertainties, including those listed under the caption "Risk Factors."

All of our express or implied forward-looking statements are as of the date of this Annual Report on Form 10-K only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Annual Report on Form 10-K or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission (the "SEC") could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Annual Report on Form 10-K, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Annual Report on Form 10-K that modify or impact any of the forward-looking statements contained in this Annual Report on Form 10-K will be deemed to modify or supersede such statements in this Annual Report on Form 10-K.

Summary of the Material Risks Associated with Our Business

- CRISPR/Cas9 genome editing technology has limited clinical validation and has only recently been approved for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics using CRISPR/Cas9 systems are unproven and may never lead to marketable products. If we are unable to develop viable product candidates, achieve regulatory approval for any such product candidate or market and sell any products, we may never achieve profitability.
- Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.
- Results, including data from our preclinical studies and clinical trials, that we announce from time to time, such as the interim data from our ongoing Phase 1 study of NTLA-2001 and our ongoing Phase 1/2 study of NTLA-2002, are not necessarily predictive of our other ongoing and future preclinical and clinical studies, and they do not guarantee or indicate the likelihood of approval of any potential product candidate by the United States Food and Drug Administration ("FDA") or any other regulatory agency. If we cannot replicate the positive results from any of our preclinical or clinical studies, we may be unable to successfully develop, obtain regulatory approval for and commercialize any potential product candidate.
- Negative public opinion and increased regulatory scrutiny of CRISPR/Cas9 use, genome editing or gene therapy generally may damage public perception of the safety of any product candidates that we develop and adversely affect our ability to conduct our business or obtain regulatory approvals for such product candidates.
- Even if we obtain regulatory approval of any product candidates, such candidates may not gain market acceptance among physicians, patients, hospitals, third party payors and others in the medical community.
- Under our license agreement with Caribou Biosciences, Inc. ("Caribou"), we sublicense a patent family from the Regents of the University of California and the University of Vienna that is co-owned by Dr. Emmanuel Charpentier (collectively, "UC/Vienna/Charpentier"). The outcome of ongoing legal proceedings, as well as potential future proceedings, related to this patent family may affect our rights under certain intellectual property sublicensed under our license agreement with Caribou.
- We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies.

- Third parties may have patent rights and other intellectual property rights that cover our product candidates, and we may be unable to avoid, obtain or invalidate patent rights owned by third parties that are necessary to develop, manufacture or commercialize our product candidates in one or more jurisdictions.
- Our ability to generate revenue from product sales and become profitable is dependent on the success of our application of CRISPR/Cas9 technology for human therapeutic use, which is at a clinical stage of development and will require significant additional discovery efforts, preclinical testing and clinical studies and manufacturing capabilities, as well as applicable regulatory guidance regarding preclinical testing and clinical studies from the FDA and other similar regulatory authorities, before we can seek regulatory approval and begin commercial sales of any potential product candidates.
- We have incurred net losses in each period since our inception, anticipate that we will continue to incur net losses in the future and may never achieve profitability.
- *In vivo* genome editing products and *ex vivo* engineered cell therapies based on CRISPR/Cas9 genome editing technology 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.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our ability to complete clinical trials or our receipt of necessary regulatory approvals could be delayed or prevented.
- Our technological advancements and any potential for revenue may be derived in part from our collaborations, including, for example, with Regeneron Pharmaceuticals, Inc. ("Regeneron"), and if the collaboration or co-development agreements related to a material collaboration were to be terminated or materially altered in an adverse manner, our business, financial condition, results of operations and prospects may be harmed.
- 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 operations and development efforts.
- We face significant competition in an environment of rapid technological change. The possibility that our competitors may achieve regulatory approval before we do or develop therapies that are more advanced or effective than ours may harm our business and financial condition or our ability to successfully market or commercialize our product candidates.
- The price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock.

PART I

Item 1. Business

Overview

We are a leading clinical-stage gene editing company, focused on developing potentially curative therapeutics using CRISPR/Cas9-based technologies. CRISPR/Cas9, an acronym for Clustered, Regularly Interspaced Short Palindromic Repeats ("CRISPR")/CRISPR associated 9 ("Cas9"), is a technology for genome editing, the process of altering selected sequences of genomic deoxyribonucleic acid ("DNA"). To fully realize the transformative potential of CRISPR/Cas9-based technologies, we are building a full-spectrum gene editing company, by leveraging our modular platform, to advance *in vivo* and *ex vivo* therapies for diseases with high unmet need by pursuing two primary approaches. For *in vivo* applications to address genetic diseases, we deploy CRISPR/Cas9 as the therapy. Our *in vivo* programs use CRISPR/Cas9 to enable precise editing of disease-causing genes directly inside the human body. In addition, we are advancing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where we use CRISPR/Cas9 as the tool to create the engineered cell therapy. For our *ex vivo* programs, CRISPR/Cas9 is used to engineer human cells outside the body. Our deep scientific, technical and clinical development experience, along with our robust intellectual property ("IP") portfolio, have enabled us to unlock broad therapeutic applications of CRISPR/Cas9 and related technologies to create new classes of genetic medicine.

Treating—and potentially curing—a broad range of severe diseases will require multiple gene editing approaches. With proprietary CRISPR/Cas9-based technology at the core of our platform, we continue to add new capabilities to expand our current solutions for addressing a multitude of life-threatening diseases. These additions include our proprietary base editor and DNA writing technology, as well as novel CRISPR enzymes, which provide us with the capabilities to achieve multiple editing strategies.

We continue to advance our platform's modular solutions and research efforts on genome editing technologies as well as delivery and cell engineering capabilities to generate additional development candidates.

Our mission is to transform the lives of people with severe diseases by developing potentially curative genome editing treatments. We believe we can deliver on our mission and provide long-term benefits for all of our stakeholders by focusing on four key elements:

- Develop potentially curative CRISPR/Cas9-based medicines;
- Advance our science;
- Be the best place to make therapies; and
- Focus on long-term sustainability.

Our lead *in vivo* candidates, NTLA-2001 for the treatment of transthyretin ("ATTR") amyloidosis and NTLA-2002 for the treatment of hereditary angioedema ("HAE"), are the first CRISPR/Cas9-based therapy candidates to be administered systemically, via intravenous ("IV") infusion, for precision editing of a gene in a target tissue in humans. In addition, we are advancing multiple *ex vivo* programs, wholly owned and in collaboration with partners, for the treatment of immuno-oncology and autoimmune diseases.

CRISPR/Cas9 Technology

The Nobel Prize-winning CRISPR/Cas9 system developed by one of our scientific co-founders, Dr. Jennifer Doudna, and her collaborators, offers a revolutionary approach for therapeutic development due to its broad ability to precisely edit the genome. This system can be used to make three general types of edits: knockouts, repairs and insertions. Each of these editing strategies takes advantage of the Cas9 endonuclease, an enzyme which can be programmed to edit double-stranded DNA at specific locations using a ribonucleic acid ("RNA") molecule, called a guide RNA ("gRNA"). The desired edits result from naturally-occurring biological mechanisms that effect particular types of genetic alterations. CRISPR/Cas9 genome editing has the potential to make permanent, precisely targeted changes in a patient's chromosomes and repair the underlying genetic mutation, whereas more traditional gene therapy typically involves introducing a non-permanent copy of a gene into a patient's cells.

Strategy

Our strategy is to advance our full-spectrum gene editing company, focused on developing and commercializing curative CRISPR/Cas9-based therapeutics, by leveraging our modular platforms. Our approach to realizing the broad potential of genome editing includes:

Focusing on Indications that Enable Us to Fully Develop the Potential of the CRISPR/Cas9 System. To maximize our opportunity to rapidly develop clinically successful products, we have applied a risk-mitigated approach to selecting indications with significant unmet medical needs based on four primary criteria:

- the type of edit: knockout, repair or insertion;
- the delivery modality for *in vivo* and *ex vivo* applications;
- the existence of efficient regulatory pathways to approval; and
- the potential for the CRISPR/Cas9 system to provide improved therapeutic benefits over existing therapeutic options.

We believe these selection criteria position us to build a diversified pipeline, in which we are not reliant on any single delivery technology or editing approach for success. This approach has the potential to increase the probabilities of success in our initial indications and generate insights that will accelerate the development of additional therapeutic products. Specifically, we believe we can apply the learnings from our current programs to inform our selection of additional indications and targets of interest.

Aggressively Pursuing* In Vivo *Liver Indications to Develop Therapeutics with Our Proprietary Delivery System. For our *in vivo* indications, we select well-validated targets in diseases with significant unmet medical needs where there are predictive biomarkers, or measurable indicators of a biological condition or state, with strong disease correlation and where the CRISPR/Cas9 technology and our proprietary delivery tools can be applied towards developing novel therapeutics. Our current *in vivo* pipeline targets diseases of the liver. Our two lead clinical programs in development aim to treat ATTR amyloidosis and HAE. Both programs utilize our proprietary lipid nanoparticle ("LNP") delivery system to knockout a target gene to halt production of an unwanted protein. In addition, we are developing therapeutic candidates that leverage our modular gene insertion platform to restore native protein for the treatment of the lung manifestation of alpha-1 antitrypsin deficiency ("AATD"), hemophilia A, hemophilia B, and additional disease indications.

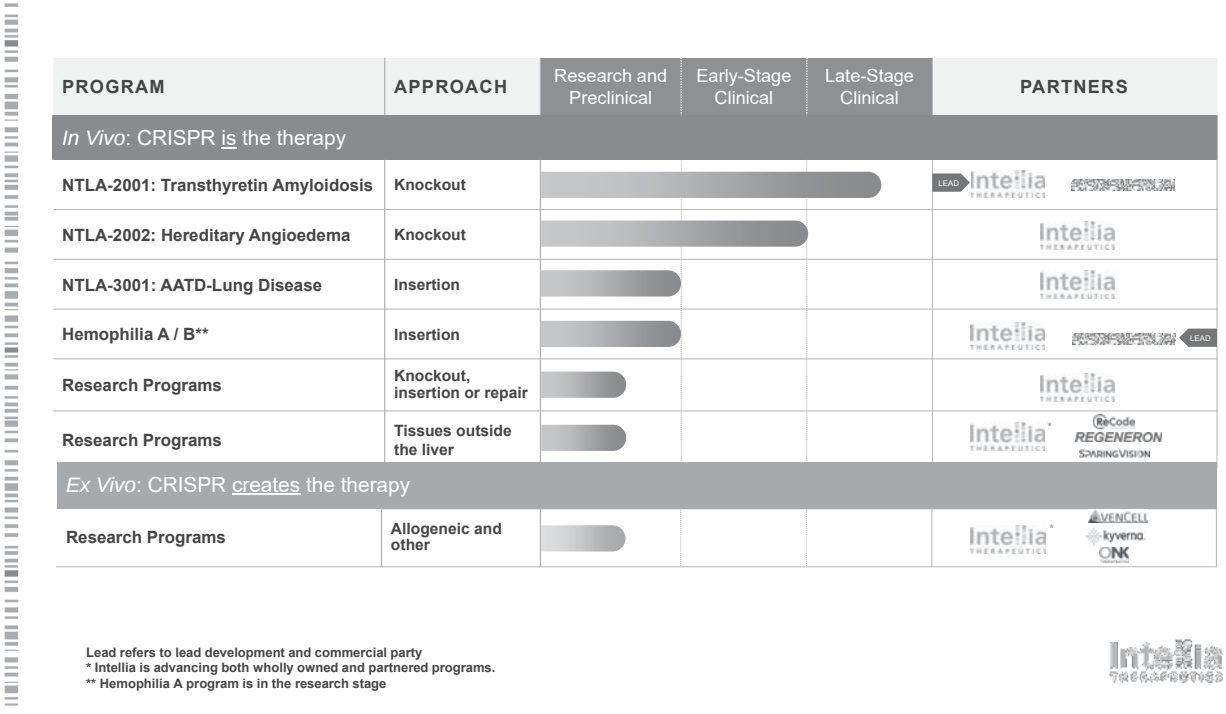
Progressing* Ex Vivo *Therapeutic Programs. We are independently researching proprietary engineered cell therapies to treat various cancers and autoimmune diseases. We are deploying our LNP-based cell engineering platform and allogeneic technology, a first-of-its-kind engineering solution designed to avoid both T cell and natural killer ("NK") cell-mediated rejection, to advance a pipeline of wholly owned and partnered *ex vivo* programs. We are pursuing targeting modalities, such as T cell receptors ("TCRs") and chimeric antigen receptors ("CARs"), with broad potential in multiple immuno-oncology and autoimmune indications.

Continuing to Leverage Strategic Partnerships to Accelerate Clinical Development. We view strategic partnerships as important drivers for accelerating the achievement of our goal of rapidly developing potentially curative therapies. The potential application of the CRISPR/Cas9 system and derivative technologies is extremely broad, and we plan to continue to identify partners who can contribute meaningful resources and technical expertise to our programs and allow us to more rapidly bring scientific innovation to a broader patient population. For example, we continue to collaborate on *in vivo* programs with Regeneron Pharmaceuticals, Inc. ("Regeneron"), a leader in genetics-driven drug discovery and development, and to advance our collaborations with AvenCell Therapeutics, Inc. ("AvenCell"), a company with a world-leading clinical-stage universal chimeric antigen receptor T ("CAR-T") cell platform; SparingVision SAS ("SparingVision"), a genomic medicine company developing vision saving treatments for ocular diseases; Kyverna Therapeutics, Inc. ("Kyverna"), a cell therapy company engineering a new class of therapies for autoimmune and inflammatory diseases; and ONK Therapeutics, Ltd. ("ONK"), a cell therapy company engineering a new class of NK cell therapies to treat cancer.

Growing Our Leadership Position in the Field of Genome Editing. We believe we have built the broadest and deepest gene editing toolbox, which enables us to select the best tools for each therapeutic application. We continue to invest internally in developing and deploying our platform capabilities, including innovative genome editing, delivery and cell engineering technologies to advance new therapeutic programs. We will also continue to explore accessing external technologies or opportunities to enhance our leadership position in developing innovative therapeutics.

Our Pipeline

The following table summarizes the status of our most advanced programs:



In Vivo *Programs*

Our selection criteria include identifying diseases that originate in the liver; have well-defined mutations that can be addressed by a knockout or insertion approach; have readily measurable therapeutic endpoints with observable clinical responses; and for which effective treatments are absent, limited or unduly burdensome. Our initial *in vivo* indications target genetic liver diseases, including our ATTR amyloidosis, HAE and AATD development programs. Our current efforts on *in vivo* delivery focus on the use of LNPs for delivery of the CRISPR/Cas9 complex to the liver.

Transthyretin ("ATTR") Amyloidosis Program

Background

ATTR amyloidosis is a progressive and fatal disorder resulting from deposition of insoluble amyloid fibrils into multiple organs and tissues leading to systemic failure. Blood-borne transthyretin ("TTR") protein is produced by hepatocytes and normally circulates as a soluble homotetramer that facilitates transport of vitamin A, via retinol binding protein, as well as the thyroid hormone, thyroxine. Mutations in the *TTR* gene lead to the production of TTR proteins that are destabilized in their tetramer form. These tetramers more readily dissociate into the monomeric form, and thence to an aggregative form that results in amyloid deposits in tissues. These deposits cause damage in those tissues, resulting in a disorder known as hereditary ATTR amyloidosis ("ATTRv"). Over 120 different genetic mutations are currently known to cause ATTRv.

Deposits of TTR amyloid in the heart, nerves and/or other tissues can lead to diverse disease manifestations, including two main hereditary forms – ATTRv with polyneuropathy ("ATTRv-PN"), and ATTRv with cardiomyopathy

("ATTRv-CM"). Typical onset of disease symptoms is during adulthood and can be fatal within two to 15 years. Estimates suggest that approximately 50,000 patients suffer from ATTRv worldwide.

In addition to the hereditary forms described above, ATTR amyloidosis can also develop spontaneously in the absence of any *TTR* gene mutation. This wild-type ATTR ("ATTRwt") is increasingly being recognized as a significant and often undiagnosed cause of heart failure in the elderly and is the subject of active investigation. Recent estimates suggest that, globally, between 200,000 and 500,000 people may suffer from ATTRwt with cardiomyopathy ("ATTRwt-CM").

Limitations of Current Treatment Options

Currently, there are four therapies for the treatment of ATTRv-PN approved in the United States ("U.S."), and five approved in most major markets outside of the U.S. While these therapies have shown the potential to slow or halt the progression of neuropathic symptoms, and in some patients lead to an improvement in symptoms, their approved prescribing instructions require them to be administered chronically for the life of the patient in order to sustain benefit. Additionally, patient response to these therapies varies. While some patients may experience symptomatic improvement after being treated with these therapies, the disease continues to progress in many of the treated patients, which highlights the continued need for efficacious and potentially curative therapies. At present, there is only one therapy approved for transthyretin amyloidosis with cardiomyopathy ("ATTR-CM") (including both ATTRv-CM and ATTRwt-CM) which has shown the ability to improve patient outcomes, though most patients still appear to have the progressive disease. As with the treatments for ATTRv-PN, chronic, lifetime dosing is required to sustain the therapeutic effects.

Our Approach

NTLA-2001 is the first investigational CRISPR-based therapy to be systemically delivered to edit a target gene inside the human body. NTLA-2001 has the potential to become the first single-dose treatment for ATTR amyloidosis. It is designed to inactivate the *TTR* gene that encodes for the TTR protein. Delivered with our *in vivo* LNP technology, NTLA-2001 offers the possibility of halting and reversing the disease by driving a deep, consistent and potentially lifelong reduction in TTR protein after a single dose. Using this approach, we aim to address ATTR amyloidosis regardless of the disease manifestation. It has been clinically validated that a significant correlation between TTR protein reduction and therapeutic benefit exists. Additionally, these studies suggest that loss of *TTR* gene expression from the liver would be well-tolerated in adult humans. We believe our approach may improve patient outcomes by significantly and consistently reducing TTR protein after a single dose, as opposed to life-long, chronic therapy.

About the NTLA-2001 Clinical Program

The global, pivotal Phase 3 MAGNITUDE trial is a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of NTLA-2001 in adults with ATTR-CM. We are actively enrolling patients, including in the U.S., and are on track to dose a first patient in the first quarter of 2024. The primary endpoint of the study is a composite of cardiovascular ("CV")-related mortality and events. Patients will be randomized 2:1 NTLA-2001:placebo, with a single 55 mg infusion of NTLA-2001 administered. MAGNITUDE trial enrollment is ongoing and we are also actively preparing for a global pivotal Phase 3 study of NTLA-2001 for the treatment of ATTRv-PN in 2024.

Advancing to a Phase 3 study was supported by a Phase 1 study of NTLA-2001, which was a two-part, open-label study in adults with ATTR amyloidosis, either ATTR-CM or ATTRv-PN.

For both the ATTR-CM and ATTRv-PN arms of the Phase 1 study, the primary objectives were to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of NTLA-2001. Patients received a single dose of NTLA-2001 via IV administration.

In November 2023, we announced new positive interim data from the Phase 1 study of NTLA-2001. Updated data from over 60 patients showed consistent, deep, and durable serum TTR reduction was achieved with a single dose of NTLA-2001, including in 29 patients who reached 12 months or more of follow-up as of the data cutoff date of May 11, 2023. Across all patients who received a dose of 0.3 mg/kg or higher (n=62), the median serum TTR reduction was 91% and the median absolute residual serum TTR concentration was 17 ug/mL at day 28. Across all patients and at all dose levels tested, NTLA-2001 was generally well tolerated, and the majority of adverse events were mild in

severity. These interim data were presented at the 4th International ATTR Amyloidosis Meeting, held in Madrid, Spain. We plan to present updated data from the ongoing Phase 1 study in 2024.

NTLA-2001 has received orphan drug designation for the treatment of ATTR amyloidosis by both the European Commission ("EC") and the U.S. Food and Drug Administration ("FDA").

NTLA-2001 is the subject of a co-development and co-promotion ("Co/Co") arrangement directed to our first collaboration target with Regeneron, ATTR (the "ATTR Co/Co"), for which we are the clinical and commercial lead party and Regeneron is the participating party. Regeneron shares in approximately 25% of worldwide development costs and commercial profits for the ATTR program. For more information regarding our collaboration with Regeneron, see the section below entitled "**Collaborations - *Regeneron Pharmaceuticals, Inc.*"**

Hereditary Angioedema ("HAE") Program

Background

HAE is a rare, genetic disease characterized by severe, recurring and unpredictable inflammatory attacks in various organs and tissues of the body, which can be painful, debilitating and life-threatening. The most common areas of the body to develop swelling are the limbs, face, intestinal tract and airway. Minor trauma or stress may trigger an attack but swelling often occurs without a known trigger. Episodes involving the intestinal tract cause severe abdominal pain, nausea and vomiting. Swelling in the airway can restrict breathing and lead to life-threatening obstruction of the airway. The disease is caused by increased levels of bradykinin, a protein which leads to swelling. Most patients with HAE have a deficiency of C1 esterase inhibitor ("C1-INH") protein, which normally prevents the overproduction of bradykinin that causes the recurring, debilitating and potentially fatal swelling attacks in people living with HAE. It is estimated that approximately one in 50,000 people are affected by HAE.

Limitations of Current Treatment Options

Current treatment options often include life-long therapies, which may require chronic IV or subcutaneous ("SC") administration as often as twice per week, or daily oral administration to ensure constant pathway suppression for disease control. Despite chronic administration, breakthrough attacks still occur. Kallikrein inhibition is a clinically validated strategy for the preventive treatment of HAE attacks.

Our Approach

NTLA-2002 is our wholly owned candidate for the treatment of HAE. NTLA-2002 is designed to knock out the *kallikrein B1* ("*KLKB1*") gene in the liver, with the potential to permanently reduce total plasma kallikrein protein and activity, a key mediator of HAE. This investigational approach aims to prevent attacks for people living with HAE by providing continuous reduction of plasma kallikrein activity following a single dose. It also aims to eliminate the significant treatment burden associated with currently available HAE therapies.

About the NTLA-2002 Clinical Program

Our multi-national Phase 1/2 study is evaluating the safety, tolerability, activity, pharmacokinetics and pharmacodynamics of NTLA-2002 in adults with Type I or Type II HAE. This includes the measurement of kallikrein protein levels and activity, as well as HAE attack rate. The Phase 1 portion of the study was an open-label, single-ascending dose design. Two dose levels of NTLA-2002 were identified from Phase 1 for further evaluation in the Phase 2, randomized, placebo-controlled portion of the study.

In January 2024, we announced that enrollment and dosing was completed in the Phase 2 portion of the study. Data from the Phase 2 study will inform the dose of NTLA-2002 selected for the pivotal Phase 3 study. We expect to initiate the global pivotal Phase 3 study, including U.S. patients, in the second half of 2024, subject to regulatory feedback.

In January 2024, we also announced that positive interim results from the Phase 1 portion of the Phase 1/2 study were published in the *New England Journal of Medicine*. These results were first reported in June 2023 at the European Academy of Allergy and Clinical Immunology Hybrid Congress. Across all ten patients, a 95% mean reduction in monthly attack rate was observed after a single dose of NTLA-2002 through the latest follow-up. The median duration of follow-up was 9.0 months (range of 5.6 - 14.1 months). At all three dose levels evaluated in the Phase 1 portion of

the study, NTLA-2002 was well tolerated, and the most frequent adverse events reported were mild, transient infusion-related reactions and fatigue. We plan to present updated data from the Phase 1 and new data from the Phase 2 portion of the study in 2024.

We have received five regulatory designations for NTLA-2002, including orphan designation in the European Union ("EU") granted by the EC in November 2023. NTLA-2002 was also granted orphan designation and Regenerative Medicine Advanced Therapy ("RMAT") designation by the FDA, the Innovation Passport by the United Kingdom ("U.K.") Medicines and Healthcare products Regulatory Agency ("MHRA") as well as access to the Priority Medicine ("PRIME") program by the European Medicines Agency ("EMA"). Access to the PRIME program is granted by the EMA to drug candidates that may offer a major therapeutic advantage over existing treatments or that benefit patients without treatment options.

Alpha-1 Antitrypsin Deficiency ("AATD") Program

Background

AATD is a genetic disorder that results in increased risk for lung and/or liver disease. Alpha-1 antitrypsin ("A1AT"), which is encoded by the *SERPINA1* gene, is a serine protease inhibitor that is primarily produced in the liver and has a wide range of biological functions, one of which is to inhibit neutrophil elastase. Patients with AATD have genetic variants of A1AT which cause the enzyme to accumulate in the liver, reducing the amount of functioning A1AT in the bloodstream. This has two prominent potential downstream clinical manifestations. The first is an increased risk for progressive liver disease, resulting from an accumulation of mutant A1AT enzyme in the liver. The second, and more common, effect is enhanced risk for emphysema resulting from reduced inhibition of neutrophil elastase in the lungs. Both clinical manifestations are progressive and potentially fatal.

It is estimated that there are approximately 250,000 individuals globally and greater than 60,000 individuals in the U.S. with the ZZ genotype, the genotype most associated with AATD and the downstream clinical manifestations. There are another 1.25 million individuals globally estimated to have the SZ genotype, who are also at enhanced risk of developing AATD. While augmentation therapy is available for the treatment of AATD, the effect on pulmonary exacerbations and on the progression of emphysema in AATD has not been conclusively demonstrated in randomized, controlled clinical trials.

Limitations of Current Treatment Options

There are multiple therapies approved by the FDA to treat patients with emphysema caused by hereditary AATD. All marketed therapies are plasma-derived alpha-1 proteinase inhibitors (alpha-1 antitrypsin) given through IV infusion, with the goal of augmenting naturally-occurring low levels of A1AT. To maintain benefit, current therapies are usually given weekly for the duration of a patient's lifetime. Currently marketed therapies may slow the progression of disease and lung dysfunction, but there remains high unmet need for more effective, and less burdensome, therapies that can further slow, halt, or even reverse disease progression.

Our Approach

NTLA-3001 is our wholly owned, first-in-class CRISPR-mediated *in vivo* targeted gene insertion development candidate for the treatment of AATD-associated lung disease. It is designed to precisely insert a healthy copy of the *SERPINA1* gene, which encodes the A1AT protein, with the potential to restore permanent expression of functional A1AT protein to therapeutic levels after a single dose. Our approach seeks to improve patient outcomes, including eliminating the need for weekly IV infusions of A1AT augmentation therapy or lung transplant in severe cases. In December 2023, we submitted a clinical trial application ("CTA") to initiate a first-in-human, Phase 1 study of NTLA-3001 and plan to dose the first patient in 2024.

In Vivo *Research Programs*

We continue to work on various liver-focused programs, such as hemophilia A and hemophilia B, which we are co-developing with Regeneron, as well as other liver targets, which we are working on both independently and in partnership with Regeneron, that would leverage our wide-ranging gene editing capabilities to knockout, insert and make consecutive edits to the genome.

We are further advancing editing and delivery strategies to expand the reach of CRISPR-based gene editing to tissues outside of the liver. For example, we have presented preclinical data establishing proof-of-concept for non-viral genome editing of bone marrow and hematopoietic stem cells ("HSCs") in mice. This represented our first demonstration of systemic *in vivo* genome editing in bone marrow using our proprietary non-viral delivery platform. We believe these results extend our modular *in vivo* capabilities to treat inherited blood disorders such as sickle cell disease. In September 2023, we entered into an expanded research collaboration with Regeneron to develop additional *in vivo* CRISPR-based gene editing therapies focused on neurological and muscular diseases. In addition, we are collaborating with SparingVision to develop novel genomic medicines utilizing CRISPR/Cas9 technology for the treatment of ocular diseases.

Ex Vivo *Programs*

We are advancing multiple preclinical programs, wholly owned and in collaboration with partners, utilizing our allogeneic platform for the treatment of immuno-oncology and autoimmune diseases. Our proprietary allogeneic cell engineering platform is designed to avoid both T cell- and NK cell-mediated rejection, a key unsolved challenge with other investigational allogeneic approaches.

- We are developing allogeneic cellular therapies, which are cells derived from unrelated donors and modified outside of the human body to allow them to be administered to an unrelated patient. These allogeneic cellular therapies could be used to treat both oncological and immunological diseases. Our proprietary technologies, including our LNP-based cell engineering platform and novel allogeneic solution, are designed to offer significant advantages over both autologous cell therapies and allogeneic approaches being investigated by others. Preclinical data presented on our differentiated allogeneic engineering platform showed allogeneic T cells were shielded from immune rejection, both host T and NK cell attack.

- We are advancing engineered CAR and TCR cells as immuno-oncological therapies.

- In addition, we strategically partner with others who possess complementary capabilities or technologies to bring forth innovative engineered cell therapy candidates outside of our core areas of focus. This includes collaborations with AvenCell and Kyverna, who are leveraging our *ex vivo* allogeneic cell engineering platform to develop novel CAR-T cell therapy candidates for a variety of therapeutic indications, as well as ONK to advance CRISPR-edited NK cell therapy candidates.

Ex Vivo *Research Programs*

We are researching engineered cell therapies to treat a range of hematological and solid tumors. We are pursuing modalities, such as TCRs and CARs, with broad potential in multiple indications. We are advancing efforts for allogeneic therapies to move from liquid to solid tumors. Our researchers are developing and improving cell-engineering manufacturing and delivery processes that, we believe, may allow us to deliver T cell therapies with high levels of editing, robust levels of cell expansion, desirable memory phenotypes, improved function and no translocations above background levels.

Our proprietary T cell engineering process using LNPs to engineer cell therapies enables multiple, sequential gene edits. We have shared preclinical data demonstrating that our LNP-based engineering technology is a significant improvement over electroporation, the standard engineering process used to introduce proteins and nucleic acids into cells. The resulting T cells engineered with LNPs had improved cell properties and performance both *in vitro* and *in vivo* as compared to electroporation. The data support the ability of our platform to be used for a variety of targeting modalities, including CARs and TCRs, and to support both autologous and allogeneic T cell candidates. The LNP-based approach has been used in multiple *ex vivo* candidates in development by us and our collaborators.

Our proprietary allogeneic solution to create engineered T cells with high anti-tumor activity may be uniquely capable of persisting in the patient to maintain durable responses. Notably, a novel combination of gene edits, including knockout of specific human leukocyte antigen ("HLA") Class II and some HLA proteins while retaining other HLA proteins, yielded T cells capable of avoiding rejection by host T and NK cells in preclinical models. With our approach, we are able to pursue a simplified HLA matching strategy between healthy donor T cells and recipient patients, allowing for the development of an "off-the-shelf" therapy that addresses the majority of the patient population with

only a small set of donors. Our allogeneic platform is being deployed for investigational TCR-T and CAR-T cell therapies.

Our genome editing capabilities include a novel, proprietary cytosine deaminase base editor technology. We have demonstrated the technology's potential for enhanced cell engineering, with multiple simultaneous gene knockouts achieving >90% T cell editing efficiency and no detectable increase in translocation above background levels.

Our Genome-Editing Platform

Our robust genome-editing platform forms the foundation of our full-spectrum therapeutic product pipeline based on CRISPR/Cas9 and derivative technologies. Our modular platform is based on our proprietary components that can serve both *in vivo* and *ex vivo* programs, as well as our delivery technologies that can be used in either program type. In addition to the components described below, we believe we have developed robust, high volume (high throughput) capabilities centering around enabling strategic target identification and validation that we believe will provide us with a competitive advantage in creating successful therapeutic products.

We are committed to staying at the forefront of the genome editing revolution and will continue to advance our technology platform through a mix of both internal research and development and external opportunities in order to potentially serve more patients across a broad set of diseases. With proprietary CRISPR/Cas9-based technology at the core of our platform, we have built a comprehensive set of editing and delivery tools to expand our current solutions for therapeutic application. These additions include our proprietary base editor, as well as novel CRISPR-derivative enzymes, which provide us with the capabilities to achieve multiple editing strategies.

Informatics

We have built a high throughput, scalable data processing and analysis, or informatics, infrastructure to support various aspects of our platform, including gRNA selection and evaluation of on- and off-target editing in cells. Depending on the desired editing strategy, we use proprietary bioinformatics methods to design candidate guides and select those that we believe are both highly specific and have high cutting efficiency. As we grow our experimental data set, we continue to incorporate gRNA performance into our algorithms to improve their predictive power.

Guide RNA Qualification

As part of the process to identify gRNAs for potential development candidates, we screen numerous gRNAs for their ability to generate the required edit at the genomic site of interest, called on-target activity, as well as any potential propensity to generate unwanted events at other sites in the genome, also known as off-target activity. To evaluate on-target activity, we use high throughput sequencing methods to analyze the genomes of edited cells, allowing us to assess overall editing efficiency and to examine the nature of the editing events, such as specific insertions or deletions.

For gRNAs selected through our primary on-target screens, we perform a variety of analyses to look for possible off-target editing events, including bioinformatic evaluations and experimental methods. Part of our approach involves identifying candidates with no or few off-target sites based on experimental measurements of genome-wide DNA breaks, as well as targeted sequencing of such candidate sites to evaluate actual off-target editing events in relevant cell types. We continue to optimize our gRNA qualification capability over time by increasing our throughput, improving our off-target activity detection accuracy and increasing our bioinformatics predictive accuracy.

Guide RNA Format

CRISPR/Cas9 systems can function with gRNAs having a variety of modifications, such as changes to the gRNA sequence or chemical modifications of nucleotides. As part of our development of CRISPR/Cas9 therapeutics, we have engineered modified gRNAs to, for example, improve editing efficiency, specificity and stability inside cells, as well as to reduce the likelihood of an immune response. We believe our work in this area will allow us to develop the most appropriate gRNAs for therapeutic applications.

Nuclease

Our current preferred Cas9 protein is derived from a species of bacteria called *S. pyogenes* ("*Spy*"), which is the Cas9 used in the vast majority of published CRISPR/Cas9 literature to date. We are exploring other naturally occurring

Cas9 proteins and nucleases from other bacteria, which may differ from *Spy* Cas9 in aspects such as specificity, size or mechanism of DNA recognition, binding and cutting. We are pursuing these alternative Cas9 forms and other nucleases through ongoing internal work, collaborations with our existing partners and scientific founders, and in-licensing opportunities. We also are investigating targeted modifications of Cas9 that can modulate DNA activity by mechanisms other than cleavage. We believe that different therapeutic applications may be best addressed using different forms of Cas9 or other nucleases, depending on the target cell or tissue of interest, the delivery method and the desired type of edit.

Types of Edits

Knockout

The CRISPR/Cas9 system, by itself, primarily functions to cut DNA, while the resulting desired therapeutic editing events are performed by the cell, subsequent to the cut, as the cell seeks to rejoin the cut ends. One type of edit is caused by a DNA repair mechanism that is prone to losing or adding short lengths of DNA around the cut site. The resulting changes in the DNA impair the function of any encoded protein, causing a knockout edit. Using a combination of our informatics, gRNA qualification and format, and nuclease platform capabilities, we have developed an efficient process to identify gRNAs that create this kind of edit at high frequency while possessing high specificity for the on-target site and no substantial off-target effects.

Based on both NHP and rodent disease models, we have demonstrated the ability to knockout multiple targets in the liver, including *TTR*, *KLKB1*, *SERPINA1*, hydroxyacid oxidase 1 (*"HAO1")* and lactate dehydrogenase A (*"LDHA")*. We believe these data demonstrate the modular nature of our proprietary LNP delivery system.

Gene Insertion

While knockout edits can be made using solely a Cas9 protein and gRNA, other kinds of editing, involving repair and insertion, additionally require a template DNA that contains a desired genomic sequence that may be inserted or used to correct a patient's original sequence. For *ex vivo* applications, in addition to delivering a Cas9-gRNA complex to cleave the cellular DNA sequence at the desired location, the desired DNA template may be delivered by physical means such as LNP in combination with a Cas9-gRNA complex, or by other means such as viral vectors or chemical means. For *in vivo* applications, we have developed combination approaches for delivering the editing machinery by LNP, and the repair and insertion templates by adeno-associated virus ("AAV") vectors. We are independently advancing our *in vivo* gene insertion platform for multiple genes of interest to treat a variety of diseases, such as AATD, and working closely with Regeneron to advance programs for the treatment of hemophilia A and hemophilia B. We have demonstrated in NHP and rodent preclinical models the ability to precisely insert a gene, including *SERPINA1* and *Factor 9 ("F9"*) , to produce normal human levels of the missing protein.

In February 2024, Regeneron and Intellia announced the clearance by the FDA of an investigational new drug ("IND") application to initiate a clinical trial for our investigational *in vivo* CRISPR-based *F9* gene insertion program for people living with hemophilia B. A Phase 1, first-in-human study is expected to begin in mid-2024. Regeneron leads development and commercialization of hemophilia A and B programs in collaboration with us.

DNA Writing Technology

Our DNA writing technology may enable a range of precise editing strategies. These strategies include targeted corrections, insertions, deletions, and the full range of single-nucleotide changes, which could provide new ways to edit disease-causing genes and broaden the therapeutic potential for genomic medicines.

In Vivo *Delivery*

We are focusing our initial *in vivo* applications in the liver, where we deliver the CRISPR/Cas9 therapy intravenously to patients using our proprietary LNP platform.

Our proprietary LNPs encapsulate the therapeutic cargo, providing it with stability, selective delivery, improved pharmacologic properties and controlled circulation time. Our therapeutic cargo is designed to degrade relatively quickly, resulting in transient expression of Cas9. We see multiple advantages of using LNPs as an *in vivo* delivery vehicle, particularly as optimized by us for delivery of the CRISPR/Cas9 system or its components. First, LNPs have

been clinically validated as an effective delivery vehicle of therapeutic nucleic acids to the liver after IV administration. LNPs have shown to have favorable tolerability in humans, with toxicities being dose-dependent, monitorable and reversible. Additionally, LNPs are chemically well-defined and have a completely synthetic route of manufacture, which permits greater scalability, product quality and controls. LNPs are tunable, do not exhibit cargo size limitations and can co-formulate different nucleic acid components, such as messenger RNA and gRNAs. There is no pre-existing immunity to the LNP or limiting de novo immunity after dosing, allowing for repeat dosing as required by the therapeutic approach. We are currently advancing our programs using our proprietary LNP delivery system, which uses a set of biodegradable, well-tolerated lipids, based on lipids originally developed by Novartis Institutes for BioMedical Research, Inc. ("Novartis") and in-licensed by us for use with all genome editing technologies, including CRISPR/Cas9 products. To date, we have successfully demonstrated well-tolerated *in vivo* editing in various animal models, including in mouse, rat and NHP livers, with a single dose of systemically delivered LNPs. In addition, we have moved into late-stage human clinical trials using LNPs as the delivery mechanism. Based on interim data reported from the first-in-human study of NTLA-2001, we have also successfully demonstrated that LNP delivery of CRISPR/Cas9 is well-tolerated in humans.

We plan to continue to further improve on our LNP system to optimize delivery of a variety of CRISPR/Cas9 therapeutic components, including templates for repair and insertion edits. In parallel, we are exploring additional delivery vehicles, including synthetic particles and viral vectors. We also are developing delivery strategies that we believe will allow us to target other tissues.

Ex Vivo *Delivery*

Cellular therapies are based on the administration of engineered human cells that are modified to provide or restore necessary functions in the cells of patients, or to target and eliminate cells with harmful attributes, such as cancer cells. The cells to be modified *ex vivo* can come from the individual patient (autologous source) or from another individual (allogeneic source). The CRISPR/Cas9 system can be used to modify cells outside the body using clinically proven delivery methods, such as electroporation. We are exploring these standard methods in parallel with our own newly-developed proprietary LNP-based delivery methods, which may provide advantages such as increased delivery efficiency and cell viability.

Ex Vivo *Allogeneic Platform*

We have developed a proprietary allogeneic cell engineering platform to overcome one of the key challenges to current allogeneic approaches employed by others, which is host rejection of the adoptive cell therapy. In preclinical studies, our allogeneic technology demonstrated the ability to create T cells with high anti-tumor activity capable of avoiding host T and NK cells, and thereby persisting to maintain durable responses. Our proprietary approach leverages a novel combination of sequential edits, including knockout of HLA Class II and HLA-A while retaining HLA-B and HLA-C proteins. With our approach, we can pursue a simplified HLA matching strategy between healthy donor T cells and recipient patients, allowing for the development of an "off-the-shelf" therapy that addresses the majority of the patient population with only a small set of donors. Our allogeneic platform is being deployed for investigational TCR-T and CAR-T cell therapies.

Collaborations and Other Arrangements

To accelerate the development and commercialization of CRISPR/Cas9-based products in multiple therapeutic areas, we have formed, and intend to seek other opportunities to form, strategic alliances with collaborators who can augment our leadership in CRISPR/Cas9 therapeutic development.

Regeneron Pharmaceuticals, Inc. ("Regeneron")

In April 2016, we entered into a license and collaboration agreement with Regeneron (as amended from time to time, the "2016 Regeneron Agreement"). The 2016 Regeneron Agreement has two principal components: (i) a product development component under which the parties will research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver, and (ii) a technology collaboration component, pursuant to which we and Regeneron will engage in research-related activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas technology to enhance our genome editing platform. Under this agreement, we also may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of our liver programs.

We amended the 2016 Regeneron Agreement in May 2020 to, among other things, (a) extend the technology collaboration, and related target selection rights, until April 2024, which Regeneron has since further extended to April 2026; (b) increase the number of exclusive *in vivo* targets to which Regeneron may develop CRISPR/Cas-based therapeutic products to fifteen; and (c) grant Regeneron a non-exclusive license under certain of our IP to independently develop and commercialize up to 10 CRISPR/Cas-based *ex vivo* gene edited products made using certain defined cell types. In September 2023, we further amended the 2016 Regeneron Agreement (the "2023 Regeneron Amendment") to expand the research and development collaboration to develop additional *in vivo* CRISPR-based gene editing therapies focused on neurological and muscular diseases. The expanded research and development collaboration will leverage our proprietary Nme2 CRISPR/Cas9 genome editing systems adapted for viral vector delivery and designed to precisely modify a target gene and Regeneron's proprietary antibody-targeted AAV vectors and delivery systems. Under the 2023 Regeneron Amendment, the companies will collaborate to research and develop products directed to two *in vivo* non-liver targets initially; each party will have the opportunity to lead potential development and commercialization for one product candidate, and the party that is not leading development and commercialization will have the option to enter into a co-development and co-commercialization agreement for the target.

We also have entered into three co-development and co-funding agreements with Regeneron, specifically the ATTR Co/Co and co-development and co-funding agreements for the treatment of hemophilia A and hemophilia B (the "Hemophilia Co/Co") agreements. Our collaboration with Regeneron under the ATTR Co/Co and Hemophilia Co/Co agreements is described above in the section entitled "**Our Pipeline – In Vivo *Research Programs***".

In October 2023, Regeneron notified us that it was exercising its one-time option to extend the technology collaboration term for an additional two years (the "2024 Technology Collaboration Extension"), until April 2026, in exchange for a nonrefundable payment of $30.0 million due in April 2024. Refer to Note 9 to our consolidated financial statements of this Annual Report on Form 10-K for a detailed description of the terms related to the 2016 Regeneron Agreement and the 2020 Regeneron Amendment.

AvenCell Therapeutics, Inc. ("AvenCell")

AvenCell was formed in July 2021 as a joint venture between us, Cellex Cell Professionals GmbH ("Cellex") and funds managed by Blackstone Life Sciences Advisors L.L.C. ("BXLS"). As part of our contribution to AvenCell, we entered into a license and collaboration agreement (the "AvenCell LCA"), under which we are collaborating with AvenCell to develop allogeneic universal CAR-T cell therapies and which granted AvenCell a license to develop and commercialize genome edited universal CAR-T cell therapies (limited to its use with their switchable, universal CAR-T cell UniCAR and RevCAR platforms). In exchange for the license, we received a 33.33% equity interest in AvenCell at the time of the initial closing.

In July 2021, we also entered into a co-development and co-funding agreement to co-develop and co-commercialize allogeneic universal CAR-T cell products for an immuno-oncology indication (the "AvenCell Co/Co"), which we terminated in November 2022 as a result of re-prioritizing our *ex vivo* programs. Our obligations under the terminated agreement were completed in the second quarter of 2023. We have one option to enter into an additional co-development and co-funding agreement for a payment of $30.0 million to AvenCell.

Refer to Notes 9 and 10 to our consolidated financial statements of this Annual Report on Form 10-K for additional information related to the terms of the agreements between us and AvenCell.

SparingVision SAS ("SparingVision")

In October 2021, we entered into a license and collaboration agreement with SparingVision, a genomic medicine company developing vision saving treatments for ocular diseases, to develop novel genomic medicines utilizing CRISPR/Cas9 technology for the treatment of ocular diseases. We granted SparingVision exclusive rights to our proprietary *in vivo* CRISPR/Cas9-based genome editing technology for up to three ocular targets addressing diseases with significant unmet medical need. In addition, the parties are collaborating to research and develop novel self-inactivating AAV vectors and LNP-based product candidates to address delivery of CRISPR/Cas9 genome editing reagents to the retina. SparingVision will lead and fund the preclinical and clinical development for the genome editing product candidates pursued under the collaboration. We will also be eligible to receive certain research, development and commercial milestone cash payments (up to approximately $200.0 million per product) as well as royalties on

potential future sales of products arising from the collaboration. We will have an option to obtain exclusive U.S. commercialization rights for product candidates arising from two of three collaboration targets.

Refer to Notes 9 and 10 to our consolidated financial statements of this Annual Report on Form 10-K for additional information related to the terms of the agreement between us and SparingVision.

Kyverna Therapeutics, Inc. ("Kyverna")

In December 2021, we entered into a licensing and collaboration agreement with Kyverna, a cell therapy company engineering a new class of therapies for autoimmune and inflammatory diseases, for the development of an allogeneic CD19 CAR-T cell therapy for the treatment of a variety of B cell-mediated autoimmune diseases. We granted Kyverna rights to our proprietary *ex vivo* CRISPR/Cas9-based allogeneic platform for the development of KYV-201, an allogeneic CD19 CAR-T cell investigational candidate for the treatment of select autoimmune diseases. Kyverna will lead and fund preclinical and clinical development for KYV-201 and we will be eligible to receive certain development and commercial milestone payments, as well as low-to-mid-single-digit royalties on potential future sales. We may also exercise an option to lead U.S. commercialization for KYV-201 under a co-development and co-commercialization agreement. If we choose to co-develop and co-commercialize KYV-201, we will pay an opt-in fee of $5.0 million and share in 50% of development costs and future net profit and/or loss arising from commercializing KYV-201 in the U.S. Kyverna would retain all rights outside of the U.S., and we would receive low-to-mid-single-digit royalties on net sales generated outside of the U.S.

Refer to Notes 9 and 10 to our consolidated financial statements of this Annual Report on Form 10-K for additional information related to the terms of the agreement between us and Kyverna.

ONK Therapeutics, Ltd ("ONK")

In February 2022, we announced a license, collaboration and option agreement with ONK for the development of engineered NK cell therapies to cure patients with cancer. The agreement grants ONK a non-exclusive license to our proprietary *ex vivo* CRISPR/Cas9-based genome editing platform and our LNP-based delivery technologies for development of up to five allogeneic NK cell therapies. ONK will be responsible for preclinical and clinical development for the engineered NK cell therapies enabled by the agreement. We will be eligible to receive up to $184.0 million per product in development and commercial milestone payments, as well as up to mid-single-digit royalties on potential future sales. In addition, the agreement grants us options to co-develop and co-commercialize up to two products worldwide with rights to lead commercialization in the U.S. Refer to Notes 9 and 10 to our consolidated financial statements of this Annual Report on Form 10-K for additional information related to the terms of the agreement between us and ONK.

Rewrite Therapeutics Inc. ("Rewrite")

On February 2, 2022, we entered into an Agreement and Plan of Merger with, *inter alia*, Rewrite Therapeutics, Inc. (the "Rewrite Merger Agreement"). Under the Rewrite Merger Agreement, we agreed to pay Rewrite's former stockholders and option holders (the "Rewrite Holders") (a) upfront consideration in an aggregate amount of approximately $45.0 million payable in cash, excluding customary purchase price adjustments, and (b) up to an additional $155.0 million in milestone payments, including $55.0 million upon the achievement of certain pre-specified research milestones and $100.0 million upon achievement of a certain regulatory approval milestone, payable through a mixture of $130.0 million in cash and $25.0 million in shares of common stock. In September 2022, Rewrite merged into Intellia, with Intellia as the surviving entity. In January 2023, a $25.0 million research milestone was achieved and, in February 2023, we paid the Rewrite Holders a mixture of cash and 567,045 shares of common stock in order to fulfill this obligation.

ReCode Therapeutics, Inc. ("ReCode")

On February 15, 2024, we announced a strategic collaboration with ReCode Therapeutics, Inc. ("ReCode"), a clinical-stage genetic medicines company, to develop novel genomic medicines for the treatment of cystic fibrosis ("CF"). CF is a genetic disease caused by mutations in the *CFTR* gene, leading to the accumulation of thick mucus in the lungs,

digestive systems and other organs. CF can result in life-threatening infections, respiratory failure and other serious complications.

Potential Future Collaborations

We view strategic partnerships as important drivers for helping accelerate our goal of rapidly treating patients. The potential application of CRISPR/Cas9 is extremely broad, and we plan to continue to identify partners who can contribute meaningful resources and insights to our programs and allow us to more rapidly bring scientific innovation to a broader patient population.

Intellectual Property

We believe we are well positioned in terms of our IP because we:

- have built, and intend to expand, a broad worldwide portfolio of IP, including patents and patent applications, in areas relevant to the development and commercialization of human therapeutic products using CRISPR/Cas9 technology;
- protect our IP by maintaining trade secrets relating to our proprietary technology innovations and know-how; and
- intend to take additional steps, where appropriate, to further protect our IP rights, including, for example, through the use of copyright protection, trademark and regulatory protections available via orphan drug designations, data exclusivity, market exclusivity and patent term extensions.

Our licensed patent portfolio encompasses foundational filings on the use of CRISPR/Cas9 systems for genome editing, improvement modifications of these CRISPR systems, including base editor and DNA writing technologies, LNP technologies, TCRs for specific targets, and cell expansion technology relevant to stem cell-based therapies. We access these patent estates from licensors, including Caribou Biosciences, Inc. ("Caribou") and others.

In addition to our in-licensed IP, our IP portfolio includes over 70 patent families filed since 2015 covering solely or jointly owned technologies that we have developed independently or through our collaboration with Regeneron. The patent families claim inventions relating to CRISPR/Cas9 improvements, methods for delivering CRISPR/Cas9 complexes, methods of treating diseases using CRISPR/Cas9 genome editing, and methods for analyzing editing events, among others. Patents resulting from our internal portfolio, if issued, would expire no earlier than 2036.

We actively apply for, maintain, and plan to defend and enforce, as needed, our internally developed and externally licensed patent rights. Furthermore, we continue to search for and evaluate opportunities to in-license IP relevant to our therapeutic programs and platforms and to develop and acquire new IP in collaboration with third parties.

Caribou Biosciences In-Licensed Intellectual Property ("Caribou")

In July 2014, we entered into a license agreement with Caribou (the "Caribou License"), as subsequently amended and supplemented, for an exclusive, worldwide license for human therapeutic, prophylactic, and palliative uses, except for anti-fungal and anti-microbial uses, defined in the license agreement as our field of use, of any CRISPR/Cas9-related patents and applications owned, controlled or licensed by Caribou as well as companion diagnostics to our product or product candidates.

The licensed Caribou patent portfolio includes several U.S. and foreign patents and patent applications owned or licensed by Caribou, including over 50 patent applications in the U.S. and internationally, related to the CRISPR/Cas platform and an exclusive sublicense in our field of use to the Regents of the University of California ("UC") and University of Vienna's ("Vienna") rights in U.S. and foreign patents and patent applications covering the CRISPR/Cas9 technology, which they co-own with Dr. Emmanuelle Charpentier (collectively, the "UC/Vienna/Charpentier IP"). In July 2015, we exercised our option to include in the licensed Caribou patent portfolio the U.S. and foreign patent and patent applications owned or controlled by Pioneer Hi-Bred International ("Pioneer") and its affiliates. We have the right to grant sublicenses to the licensed Caribou patent portfolio to third parties in our field of use. Caribou retains the right to practice the licensed IP in all other fields, including for its own specific therapeutic product candidates outside our field of use. The UC/Vienna/Charpentier IP and Pioneer IP, and our rights to the same, are further described below.

We have agreed to pay 30.0% of Caribou's patent prosecution, filing and maintenance costs for the IP included in the license agreement, which has amounted to a total of $9.1 million incurred through December 31, 2023. Any patents that grant or have granted from these applications will expire in or after 2034, assuming payment of necessary maintenance fees. We also granted Caribou an exclusive, royalty-free, worldwide license, with the right to sublicense, to any CRISPR/Cas9 patents, patent applications and know-how in Caribou's retained fields of use owned or developed by us between July 16, 2014 and January 30, 2018. Caribou, which is obligated to pay a portion of our patent filing, prosecution and maintenance costs for any such licensed IP, also has an option to sublicense any CRISPR/Cas9 IP in-licensed by us for uses and activities in its retained field of use.

The Caribou License terminates on the expiration of the last-to-expire patent right that is licensed to either party. We must use commercially reasonable and diligent efforts to research, develop, manufacture and commercialize at least one product covered by the licensed IP. Either party may terminate the agreement in the event of the other party's uncured material breach, bankruptcy or insolvency-related events, or breach of its obligations with respect to the included in-licenses.

In June 2021, we executed a Leaseback Agreement ("Leaseback") with Caribou, concluding an arbitration between us and Caribou in which an arbitration panel found that Caribou had violated the terms of the Caribou License. The arbitration panel required us to grant Caribou an equitable "leaseback" to use certain IP exclusively licensed to us in Caribou's ongoing CB-010 program.

The Regents of the University of California and the University of Vienna Intellectual Property

The UC/Vienna/Charpentier IP covers methods of use and compositions relating to engineered CRISPR/Cas9 systems for, among other things, cleaving or editing DNA and altering gene product expression in various organisms, including humans. The earliest claimed priority date for the patents in the UC/Vienna/Charpentier IP is May 25, 2012. As of December 31, 2023, this family includes over 50 issued patents in the U.S. and over 30 granted patents outside the U.S., including for example the U.K., Australia, China, Japan, Israel, Mexico and the approximately 40 countries that are members of the European Patent Convention. Applications continue to be prosecuted in the United States Patent and Trademark Office ("USPTO") and other patent agencies across the world. Patents issued from this family will expire in or after 2033, if successfully maintained.

In April 2013, Caribou entered into an exclusive, worldwide license in all fields, with the right to sublicense, for this patent family with UC/Vienna solely under UC/Vienna ownership rights. Caribou's license remains in effect for the life of the last-to-expire patent or last-to-be-abandoned patent application licensed, whichever is later. Through our license agreement with Caribou, we have an exclusive sublicense to UC/Vienna's interest in this foundational CRISPR/Cas9 patent family for use in human therapeutics, except for anti-fungal and anti-microbial uses as defined in the license agreement as our field of use. For therapeutic products covered by this license and their companion diagnostics, we will owe mid-single-digit royalties on net sales. We may also be subject to additional milestone payments in the future. Caribou has the right to terminate its agreement with UC/Vienna at any time or the agreement may be terminated by UC/Vienna due to an uncured material breach. We cannot guarantee that Caribou will maintain the UC/Vienna license for its full term. Should the license between Caribou and UC/Vienna be terminated for any reason, any compliant Caribou sublicenses as of the termination date will remain in effect and will be assigned to UC/Vienna in place of Caribou. Specifically, if we are in compliance with our obligations under our sublicense and Caribou and UC/Vienna terminate their agreement, UC/Vienna would replace Caribou as our licensor.

On June 25, 2019, the USPTO's Patent Trial and Appeal Board (the "PTAB") declared another interference between the UC/Vienna/Charpentier and certain patents issued to the Broad Institute, Massachusetts Institute of Technology, and the President and Fellows of Harvard College (collectively, the "Broad Institute patent family" or the "Broad"), which claim aspects of CRISPR/Cas9 systems and methods to edit genes in eukaryotic cells, including human cells. An interference is an adversarial proceeding conducted by the PTAB to determine who was the first to invent a particular invention claimed in U.S. patents and patent applications owned by different parties and in this situation, to determine which research group first invented the use of the CRISPR/Cas9 technology in eukaryotic cells and, therefore, is entitled to the patents covering the invention. On August 26, 2019, the PTAB redeclared the interference to include additional UC/Vienna/Charpentier patent applications covering the invention that had also been found allowable by the USPTO. As of December 31, 2023, the interference involved 14 allowable patent applications from the UC/Vienna/Charpentier eukaryotic patent family and 13 patents and one patent application from the Broad Institute

patent family. The PTAB held a hearing in this interference on February 4, 2022. On February 28, 2022, the PTAB issued a Decision of Priority and Judgment in the patent interference finding that the Broad patents and application have priority over the UC/Vienna/Charpentier involved applications with respect to the subject matter of the interference. On March 30, 2022, UC/Vienna/Charpentier filed a notice of appeal in the Broad Interference, and the Broad Institute has cross-appealed.

In addition, the PTAB has instituted and completed the motions phase in interferences between the same 14 allowable patent applications in the UC/Vienna/Charpentier portfolio, and certain patent rights owned by ToolGen, Inc. ("ToolGen"), and certain patent rights owned by Sigma-Aldrich Co. LLC, a Merck KGaA subsidiary ("Sigma-Aldrich"). In both interferences, ToolGen and Sigma-Aldrich, respectively, purport that their patent rights cover the use of CRISPR/Cas9 for gene editing in eukaryotic cells. Both interferences are stayed pending a decision from the Court of Appeals for the Federal Circuit in the Broad Interference. If either the Broad, ToolGen or Sigma-Aldrich were to succeed in their respective interference, the prevailing party or parties could seek to assert its issued patents against us based on our CRISPR/Cas9-based activities, including product commercialization. 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. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties, delay launch or redesign our infringing products, which may not be feasible or require substantial time and monetary expenditure. In that event, we may be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly.

Pioneer Hi-Bred International (DuPont Company) Intellectual Property

Pioneer, including the DuPont Company, have licensed to Caribou on a worldwide basis, various patent families relating to CRISPR/Cas systems, components and methods of use generally and CRISPR/Cas9 specifically in certain fields, which include Intellia's field of use under our license agreement with Caribou. In July 2015, we exercised our option under the license agreement with Caribou to sublicense these Pioneer patent families in our field of use. The license from Pioneer to Caribou will expire upon the expiration, abandonment or invalidation of the last patent or patent application licensed from Pioneer to Caribou.

The licensed Pioneer portfolio includes a family of applications filed by Vilnius University that discloses the components of a CRISPR/Cas9 system required for gene editing in non-bacterial organisms. The USPTO has issued patents to Vilnius University with claims covering the *in vitro* assembly and use of a recombinant CRISPR/Cas9 complex to modify DNA. Patents obtained from this patent family will expire in or after 2033, assuming payment of necessary maintenance fees. We cannot ensure that these additional applications in this family will lead to issued claims that cover our products or activities.

Invention Management Agreement

On December 15, 2016, we entered into a Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement (the "Invention Management Agreement"), with UC, Vienna, Dr. Charpentier, Caribou, CRISPR Therapeutics AG, ERS Genomics Ltd. and TRACR Hematology Ltd. Under the Invention Management Agreement, Dr. Charpentier retroactively consented to UC/Vienna's CRISPR/Cas9 license to Caribou as well as Caribou's sublicensing to Intellia certain of its rights to the UC/Vienna/Charpentier CRISPR/Cas9 IP, subject to the restrictions of our license from Caribou. Under the agreement, the parties commit to maintain and coordinate the prosecution, defense and enforcement of the CRISPR/Cas9 foundational patent portfolio worldwide, and each of the co-owners of the IP grants cross-consents to all existing and future licenses and sublicenses based on the rights of another co-owner. The Invention Management Agreement also includes retroactive approval by certain parties of certain prior assignments of interests in patent rights to other 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. Unless earlier terminated by the parties, the Invention Management Agreement will continue in effect until the later of the last expiration date of the UC/Vienna/Charpentier patents underlying the CRISPR/Cas9 technology, or the date on which the last underlying patent application is abandoned.

Manufacturing

We have entered into certain manufacturing and supply arrangements with third party suppliers to support production of our product candidates and their components. In addition, we have entered into a lease to build out a new manufacturing facility in Waltham, Massachusetts, which would support good manufacturing practice ("GMP") manufacturing for preclinical through commercial supply. We plan to continue to rely on qualified third party organizations and our own capabilities to produce or process bulk compounds, formulated compounds, viral vectors or engineered cells for IND-supporting activities and to supply materials for clinical trials. We expect that clinical and commercial quantities of any *in vivo* product or engineered cells that we may seek to develop will be manufactured in GMP compliant facilities and by processes that comply with FDA and other regulatory agency requirements. At the appropriate time in the product development process of each product candidate, we will determine whether to use our internal manufacturing capabilities and facilities or continue to rely on third parties to manufacture commercial quantities of such products that we may successfully develop.

Competition

The biotechnology and pharmaceutical industries are extremely competitive in the race to develop new products. While we believe we have significant competitive advantages with our industry-leading expertise in genome editing, clinical development expertise and dominant IP position, we currently face and will continue to face competition for our development programs from companies that use genome editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities such as small molecules and antibodies. The competition is likely to come from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions. Many of these competitors may have access to greater capital and resources than us. 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.

Specific to our NTLA-2001 program, we are aware of other companies that are currently commercializing or developing products and therapies used to treat ATTR amyloidosis, including Alnylam Pharmaceuticals, Inc., AstraZeneca Pharmaceuticals LP, BridgeBio Pharma Inc., Ionis Pharmaceuticals, Inc., Metagenomi Technologies, LLC, Novo Nordisk A/S and Pfizer, Inc.

Specific to our NTLA-2002 program, we are aware of other companies that are currently commercializing or developing products used to treat HAE including ADARx Therapeutics, Inc., Astria Therapeutics Inc., BioCryst Pharmaceuticals Inc., BioMarin Pharmaceutical Inc., CSL Limited, Ionis Pharmaceuticals, Inc., KalVista Pharmaceuticals, Inc., Pharming Group N.V., Pharvaris N.V. and Takeda Pharmaceutical Company Limited.

Competitors in our efforts to provide other genetic therapies to patients can be grouped into at least three sets based on their product discovery platforms:

Our platform and product foci are on the development of therapies using CRISPR-based technologies. Genome editing companies focused on CRISPR-based technologies include: Beam Therapeutics Inc., Caribou Biosciences, Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Metagenomi Technologies, LLC, Prime Medicine, Inc., ToolGen, Inc. and Verve Therapeutics Inc.

There are also companies developing therapies using additional gene-editing technologies, which include Allogene Therapeutics, Inc., bluebird bio, Inc., Cellectis S.A., Homology Medicines, Inc., Poseida Therapeutics, Inc., Precision Biosciences, Inc., Prime Medicine, Inc. and Sangamo Therapeutics, Inc.

We are also aware of companies developing therapies in various areas related to our specific research and development programs. For *ex vivo*, these companies include Allogene Therapeutics, Inc., Cellectis S.A., CRISPR Therapeutics AG and Precision BioSciences, Inc. For *in vivo*, these companies include CRISPR Therapeutics AG, Editas Medicine, Inc., Excision Biotherapeutics, Inc., Locus Biosciences, Inc., Metagenomi Technologies, LLC, Precision Biosciences, Inc. and Verve Therapeutics Inc.

Our competitors will also include companies that are or will be developing other genome editing methods as well as small molecules, biologics, *in vivo* gene therapies, engineered cell therapies and nucleic acid-based therapies for the same indications that we are targeting with our CRISPR/Cas9-based therapeutics.

Government Regulation and Product Approval

As a biopharmaceutical company, we are subject to extensive legal and regulatory requirements. For example, we need approval from regulatory agencies for our clinical studies, development, manufacturing, distribution, exportation and importation, commercialization, marketing and reimbursement relating to our products and product candidates. Relevant regulatory authorities include, but are not limited to, the FDA, the EMA, the EC, EU Member State agencies, such as Germany's Paul Ehrlich Institute ("PEI"), and other countries' similar agencies, such as the MHRA, as well as health technology assessment bodies and public authorities responsible for market access and pricing, such as the U.K. National Institute of Health and Care Excellence ("NICE").

We expect our future *in vivo* and *ex vivo* product candidates to be regulated as biologics. Biological products are subject to regulation under the Food, Drug and Cosmetic ("FD&C") Act and the Public Health Service Act ("PHS Act"), and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving drug and biological products. As is the case for all investigational products, before clinical testing of biological products in the U.S. may begin, we must submit an IND application to the FDA, which reviews the clinical protocol and other information, and the IND application must become effective before clinical trials may begin. Prior to initiating clinical trials in foreign countries, CTAs or other equivalent applications, similar to IND applications, must be approved.

Biologic products must be approved by the FDA before they may be legally marketed in the U.S. and by the appropriate foreign regulatory agencies before they may be legally marketed in foreign countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Within the FDA, the Center for Biologics Evaluation and Research ("CBER") regulates biological products, including gene and cell therapies. CBER's Office of Therapeutic Products ("OTP") is responsible for oversight of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee ("CTGTAC") advises CBER on its reviews. Human gene therapy products are defined as all products that mediate their effects by transcription or translation of transferred genetic material or by specifically altering host (human) genetic sequences. Some examples of gene therapy products include nucleic acids, genetically modified microorganisms (e.g., viruses, bacteria, fungi), engineered site-specific nucleases used for human genome editing, and *ex vivo* genetically modified human cells. FDA has published guidance documents related to, among other things, gene therapy products in general and their preclinical assessment, potency or other quality testing, and chemistry, manufacturing and control information in gene therapy IND applications, and long-term adverse event monitoring of clinical trial subjects; all of which are intended to facilitate industry's development of these products. More recently and as part of the implementation of the 21st Century Cures Act, FDA has issued a number of guidances pertaining to regenerative medicine advanced therapies, which include cell therapy, therapeutic tissue engineering products, human cell and tissue products and combination products using any such therapies or products. Additionally, gene therapies, including genetically modified cells, that lead to a durable modification of cells or tissues may meet the definition of a regenerative medicine therapy. A number of guidances have been revised to reflect the growing knowledge and incorporation of newer technology, including certain considerations for genome editing. A small, but growing number of gene therapy products, including gene editing therapies, have been approved by regulatory agencies.

U.S. Gene and Cell Therapy Products Development Process

The FDA approves biologics, including gene and cellular therapy products, through the Biologics License Application ("BLA") process before they may be legally marketed in the U.S. This process generally involves the following:

- completion of extensive nonclinical, sometimes referred to as preclinical laboratory tests, and preclinical animal studies and formulation studies in accordance with applicable regulations, including good laboratory practice ("GLP") and applicable requirements for the humane use of laboratory animals;

- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials, according to the FDA's regulations commonly referred to as good clinical practice ("GCP") and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed product for its intended use;
- submission to the FDA of a BLA for marketing approval that includes substantial evidence of safety, efficacy, and purity and potency, from nonclinical and *in vitro* testing and clinical trials;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the product is produced to assess compliance with current good manufacturing practice ("cGMP") 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 ("cGTP") requirements for the use of human cellular and tissue products;
- positive results from potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA;
- review of the proposed product by an FDA advisory committee, where appropriate and if applicable;
- payment of user fees for FDA review of the BLA (unless a fee waiver applies, such as for product candidates designated as orphan drugs); and
- FDA review and approval, or licensure, of the BLA.

Before testing any drug or biological product candidate, including gene and cellular therapy product candidates, in humans, the product candidate is evaluated through preclinical testing. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with applicable federal regulations and requirements, including GLP.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature, and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND application is submitted. The IND application automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the clinical trial sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to, among other reasons, safety concerns or non-compliance with regulatory requirements. If the FDA imposes a clinical hold, trials may not proceed without FDA authorization and then only under authorized terms. Accordingly, we cannot be sure that submission of an IND application will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that result in the suspension or termination of such trials.

Clinical trials involve the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and its amendments must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an independent institutional review board ("IRB") at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of study participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

In addition to the submission of an IND to the FDA before initiation of a clinical trial in the U.S., certain human clinical trials involving recombinant or synthetic nucleic acid molecules are subject to oversight of institutional biosafety committees, ("IBCs"), as set forth in the National Institutes for Health ("NIH") Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ("NIH Guidelines"). Under the 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.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The product candidate is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2. The product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency (for BLA products), and safety in an expanded patient population at dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product, including as compared to current standard treatments, and provide an adequate basis for product approval and labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional evidence about the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA typically advises that sponsors observe subjects for potential gene therapy-related delayed adverse events for up to a 15-year period after administration, including a minimum of five years of annual examinations followed by ten years of annual queries, either in person or by questionnaire.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the status of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events that are associated with the use of the product candidate, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research 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 product candidate has been associated with unexpected serious harm to patients.

There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products, including biologics such as gene and cellular therapy products, are required to register and disclose certain clinical trial information to NIH. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made publicly available as part of the registration at www.clinicaltrials.gov. Sponsors also are obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved, up to a maximum of two years.

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the physical characteristics of the product candidate, as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP, and in certain cases, cGTP, requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final product to support a BLA. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

FDA approval of a BLA must be obtained before commercial marketing of the product. The BLA must include results of product development, laboratory and animal trials, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA, for a product candidate with certain novel characteristics must contain data to assess the safety and effectiveness of the product candidate 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. The Food and Drug Administration Safety and Innovation Act of 2012 ("FDASIA") requires that a sponsor who is planning to submit a marketing application for a biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan ("PSP") within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA, unless exempt due to orphan drug designation. The initial PSP must include, among other things, an outline of the pediatric study or studies that the sponsor plans to conduct, including, to the extent practicable, study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information, along with any other information specified in FDA regulations. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, or other clinical development programs. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan drug designation has been granted. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act ("PDUFA"), as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews the BLA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission, including for failure to pay required fees, and may request additional information. In this event, the application must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the application to determine, among other things, whether the proposed product is safe and effective (or, in the case of biologics, to ensure safety, purity

and potency), and whether the product is being manufactured in accordance with cGMP, and in certain cases, cGTP, requirements to ensure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and 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. During the FDA review and approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy ("REMS") is necessary to assure the safe use of the biological product candidate. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the application without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP and, if applicable, cGTP requirements are adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP, cGTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the application identified by the FDA. Addressing the deficiencies identified may require significant development work, such as product reformulation or additional clinical trials. The complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the application, addressing all of the deficiencies identified in the letter, challenge the determination set forth in the letter by requesting a hearing or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases, dosages or patient subgroups or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, precautions or adverse events be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

One of the performance goals agreed to by the FDA under the PDUFA VII (Fiscal Years 2023-2027) is to review 90% of BLAs in 10 months from the 60-day filing date, and 90% of priority BLAs in six months from the 60-day filing date, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs, and its review goals are subject to change with PDUFA reauthorization. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission, also known as a Major Amendment, within the last three months before the PDUFA goal date.

Orphan Drug Designation

The FDA may grant orphan drug designation to biological products, including cellular and gene therapy products, intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., or, if it affects more than 200,000 individuals in the U.S., when there is no reasonable expectation that the cost of developing and marketing the product for this type of disease or condition will be recovered from sales in the U.S. Orphan drug designation must be requested before submission of BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same orphan indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan designated product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity, which may permit off-label use for the orphan indication. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA for the same orphan indication or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

Expedited Development and Review Programs

In the U.S. and the EU, as well as in other countries, there are a number of programs to expedite development, review and approval of products for serious or life-threatening disease or condition that address an unmet medical need in the relevant regulatory jurisdiction. In the U.S., these FDA programs include Fast Track Designation, priority review, accelerated approval, Breakthrough Therapy designation and Regenerative Medicine Advanced Therapies. Similar programs in the EU include accelerated assessment, conditional approval and the PRIME program.

The FDA's Fast Track program intends to expedite or facilitate the process for reviewing new drug and biological products that meet certain criteria. Specifically, new biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic, including gene and cellular therapy products, may request that the FDA designate the product as a Fast Track product at any time during the product's clinical development, but ideally not later than the pre-BLA meeting. The FDA may consider for review sections of the marketing application for a Fast Track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

In the U.S., any product is eligible for priority review if it treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness of the treatment, prevention, or diagnosis of that condition. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a product subject to accelerated approval perform adequate and well-controlled, post-marketing confirmatory clinical trials to confirm the effect on irreversible morbidity or mortality or other clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022 ("FDORA"), the FDA is now permitted to require, as appropriate, that post-approval confirmatory trials be underway prior to approval or within a specific time period after accelerated approval is granted. Failure to conduct required post-approval studies with due diligence, or to confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug from the market and, under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a product granted accelerated approval. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

FDA's Breakthrough Therapy designation program is intended to expedite the development and review of products that treat serious or life-threatening diseases or conditions. A breakthrough therapy is defined as a drug or biological product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug 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 designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance. The Breakthrough Therapy designation is a distinct status from both accelerated approval and priority review, but these can also be granted to the same product candidate if the relevant criteria are met. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. All requests for Breakthrough Therapy designation will be reviewed within 60 days of receipt, and FDA will either grant or deny the request.

Orphan designation, Fast Track designation, priority review, accelerated approval and Breakthrough Therapy designation do not change the standards for approval but may expedite the development or approval process.

Regenerative Medicine Advanced Therapies ("RMAT") Designation

As part of the 21st Century Cures Act, the FD&C Act was amended to facilitate an efficient development program for, and expedite review of regenerative advanced therapies, which include cell and gene therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. Gene therapies, including genetically modified cells, that lead to a durable modification of cells or tissues may meet the definition of a regenerative medicine therapy. This program is intended to facilitate efficient development and expedite review of regenerative medicine therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and qualify for RMAT designation. A drug sponsor may request that FDA designate a drug as a RMAT concurrently with or at any time after submission of an IND. FDA has 60 calendar days to determine whether the drug meets the criteria, including whether there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for a serious or life-threatening disease or condition. A BLA for a regenerative medicine therapy that has received RMAT designation may be eligible for priority review or accelerated approval through use of surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of RMAT designation also include early interactions with FDA and, for those granted accelerated approval, post-approval requirements may be fulfilled through the submission of clinical evidence from clinical studies, patient registries, or other sources of real-world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. Like the FDA's other expedited development programs, RMAT designation does not change the standards for approval but may expedite the development or approval process.

Post-Approval Requirements

Maintaining substantial compliance with applicable federal, state, and local statutes and regulations and, as applicable, their counterparts in other jurisdictions, requires the expenditure of substantial time and financial resources. Rigorous and extensive FDA regulation of biological products, including gene and cellular therapy products, continues after approval, particularly with respect to cGMP requirements. We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of certain components of products that we may commercialize. Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control, quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, 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 release by the FDA, the manufacturer submits samples of each lot of product to the FDA 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. The FDA also may perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products, including gene and cellular therapy products.

We also would have to comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet and social media platforms. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the labeling or marketing of a product, imposition of a REMS or post-market study requirement or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products, including gene and cellular therapy products, in the U.S. are required to register their establishments with the FDA and certain other federal and state agencies, and are subject to periodic unannounced inspections by the FDA and certain other federal and state agencies for compliance with cGMP, and in certain cases, cGTP, requirements and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market, as well as potential civil and criminal liability. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "Affordable Care Act" or "ACA"), signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product in the U.S. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, 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. Starting in 2015, the FDA commenced licensing biosimilars under the BPCIA, and there are currently numerous biosimilars approved in the U.S. and Europe. The FDA has issued a number of draft and final guidance documents outlining an approach to review and approval of biosimilars and interchangeable biological products.

The BPCIA also contains various provisions regarding exclusivity for reference and interchangeable products and procedures for sharing and litigating patents covering the reference product. A reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product is eligible for a period of exclusivity against other biologics submitted under the abbreviated approval pathway during which time the FDA may not determine that another product is interchangeable with the same reference product for any condition of use. The 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 for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologic's patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period. The BPCIA, however, is complex and only beginning to be interpreted and implemented

by the FDA. In addition, proposed legislation has sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and meaning of the BPCIA is subject to significant uncertainty.

A biological product can also obtain pediatric market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods for all formulations, dosage forms, and indications of the biologic. This six-month exclusivity, which runs from the end of other exclusivity protection, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining.

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 Conservancy and Recovery Act and the Toxic Substances Control Act, all affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our 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. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Other Healthcare and Privacy Laws

In addition to FDA restrictions on marketing of biological products, other U.S. federal and state healthcare regulatory laws restrict business practices in the pharmaceutical industry, which include, but are not limited to, state and federal anti-kickback, false claims, data privacy and security, and physician payment transparency laws. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement for or recommendation of the purchase, lease, order, arrangement for any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. 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. In addition, the ACA provides that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act ("FCA"). Violators are subject to civil and criminal fines and penalties, as well as imprisonment and exclusion from government healthcare programs;
- federal civil and criminal false claims laws, including, without limitation, the federal FCA, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims by, for example, promoting a product off-label. The FCA also permits a private individual acting as a "whistleblower" to bring civil whistleblower or *qui tam* actions against individuals (including biopharmaceutical manufacturers and sellers) on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. These laws impose criminal and civil penalties on violators;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), and its implementing regulations, which impose criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program 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. 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. HIPAA violations can lead to civil and criminal liability;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, which impose, among other things, requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state and non-U.S. laws govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating efforts to comply with their respective provisions;
- the U.S. federal physician payment transparency requirements, sometimes referred to as the "Physician Payments Sunshine Act," created under the ACA, and their implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually, to the Centers for Medicare and Medicaid Services ("CMS"), information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed healthcare practitioners, and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers, and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the Foreign Corrupt Practices Act ("FCPA") and other laws which prohibit improper payments or offers of payments to foreign governments and their officials and political parties by U.S. persons and issuers as defined by the statute for the purpose of obtaining or retaining business;
- the FD&C Act, which prohibits, among other things, the commercialization of adulterated or misbranded drugs and medical devices and the PHS Act, which prohibits, among other things, the commercialization of biological products unless a biologics license is in effect; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in

certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the limited 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.

In the event we decide to conduct clinical trials or enroll subjects in our future clinical trials, we may be subject to additional privacy restrictions. In the EU, the General Data Protection Regulation ("GDPR") regulates the collection, use, storage, disclosure, transfer or other processing of personal data, including personal health data. The GDPR covers any business, regardless of its location, that provides goods or services to residents in the EU and, thus, could incorporate our activities in EU Member States. The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for "sensitive information," which includes health and genetic information of individuals residing in the EU, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, ensuring certain accountability measures are in place and taking certain measures when engaging third party processors. The GDPR grants individuals the opportunity to object to the processing of their personal data, allows them to request deletion of personal data in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the EU to regions that have not been deemed to offer "adequate" privacy protections. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States, which may deviate slightly from the GDPR, may result in warning letters, mandatory audits and financial penalties, including fines of up to 4% of annual global revenues, or €20,000,000, whichever is greater. As a result of the GDPR, we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules, including as implemented by individual countries.

Further to the U.K.'s exit from the EU on January 31, 2020, the U.K. incorporated the GDPR (as it existed on December 31, 2020 but subject to certain U.K. specific amendments) into U.K. law, referred to as the U.K. GDPR. The U.K. GDPR and the U.K. Data Protection Act 2018 set out the U.K.'s data protection regime, which is independent from but currently still aligned to the EU's data protection regime. Non-compliance with the U.K. GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Although the U.K. is regarded as a third country under the EU's GDPR, the U.K. is recognized as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EU to the U.K. remain unrestricted. Likewise, the U.K. government has confirmed that personal data transfers from the U.K. to the European Economic Area ("EEA"), which consists of the EU Member States, plus Norway, Liechtenstein and Iceland remain free flowing.

In California, the California Consumer Privacy Act ("CCPA") requires covered businesses to comply with specific privacy and security obligations, such as providing disclosures to consumers in California about such companies' data collection, use and sharing practices, and providing consumers the ability to opt-out of certain sales or transfers of personal information, and providing consumers with a private right of action for certain data breaches. Further, the California Privacy Rights Act ("CPRA") substantially modifies the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information and by establishing a state agency vested with the authority to enforce the CCPA. The CPRA also creates additional obligations with respect to the processing of personal information, including regulating personal information collected about employees, applicants and retirees as well as that which is collected in a business-to-business capacity.

Several other U.S. states have either passed or enacted privacy legislation similar to the CCPA, which incorporate similar concepts of the CCPA, but contain key differences in the scope, application, and enforcement which may complicate compliance efforts.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs, individual imprisonment, and additional reporting obligations and oversight if we become subject to a corporate integrity

agreement or other agreement to resolve allegations of non-compliance with this law, any of which could adversely affect our ability to operate our business and our financial results.

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

Regulation in the European Union

Clinical Trial Approval

In April 2014, the EU adopted the new Clinical Trials Regulation, (EU) No 536/2014, which replaced the previous Clinical Trials Directive 2001/20/EC on 31 January 2022. The Clinical Trials Regulation is directly applicable in all EU Member States meaning no national implementing legislation in each EU Member State is required. The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the Regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System ("CTIS"); a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of CTAs. The role of the relevant ethics committees in the assessment procedure continues to be governed by the national law of the concerned EU Member State, however, overall related timelines are defined by the Clinical Trials Regulation. The Clinical Trials Regulation also provides for simplified reporting procedures for clinical trial sponsors.

Marketing Authorization

In the EU, medicinal products, including advanced therapy medicinal products ("ATMPs"), are subject to extensive pre- and post-market regulation by regulatory authorities at both the EU and national levels. ATMPs comprise gene therapy products, somatic cell therapy products and tissue engineered products. We anticipate that our gene therapy development products would be regulated as ATMPs in the EU.

To obtain regulatory approval of our medicinal products in the EU, we must submit a marketing authorization application ("MAA") to the EMA.

The centralized procedure provides for the grant of a single marketing authorization by the EC that is valid throughout the EU, and in the additional member states of the EEA (Iceland, Norway and Liechtenstein). 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, 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, autoimmune 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 diseases other than those listed above, or where the applicant can show that the product constitutes a significant therapeutic, scientific or technical innovation or for which the centralized procedure is in the interest of patients at an EU level.

Specifically, the grant of marketing authorization in the EU for ATMPs is governed by Regulation (EC) No. 1394/2007 on ATMPs, read in combination with Directive 2001/83/EC on medicinal products. 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 ATMPs must demonstrate the quality, safety, and efficacy of their products to the Committee for Advanced Therapies ("CAT"), at the EMA, which conducts a scientific assessment of the MAA and provides an opinion regarding the MAA for an ATMP.

The Committee for Medicinal Products for Human Use ("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 the 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 EC, who make 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.

Data and Market Exclusivity

The EU also provides opportunities for market exclusivity. For example, in the EU, upon receiving marketing authorization, innovative medicinal products generally receive eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator's pre-clinical and clinical trial 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 marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. The overall ten-year period will be extended to a maximum of 11 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 their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be an innovative medicinal product, and products may therefore 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 marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, pre-clinical tests and clinical trials.

Orphan Designation and Exclusivity

Products with an orphan designation in the EU will, upon the grant of a marketing authorization for such orphan product, receive ten years of market exclusivity, during which time no "similar medicinal product" for the same indication may be placed on the market. 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. An orphan product can also obtain an additional two years of market exclusivity in the EU where an agreed Pediatric Investigation Plan ("PIP") for pediatric studies has been complied with. No extension to any supplementary protection certificate ("SPC") can be granted on the basis of pediatric studies for orphan indications.

The criteria for designating an orphan medicinal product in the EU are similar in principle to those in the U.S. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as an orphan medicinal product if it is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made; or (b) it is unlikely that the product, without the 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 a method exists, the product will be of significant benefit to those affected by the condition, as defined in Regulation (EC) 847/2000. Orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to ten years of market exclusivity for the approved therapeutic indication. The application for orphan designation must be submitted before the application for marketing authorization. The applicant

will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the MAA is submitted. Orphan designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity may 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, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar medicinal product for the same therapeutic indication as an authorized orphan product at any time if:

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

Pediatric development

In the EU, companies developing a new medicinal product must agree upon a PIP with the EMA and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies, (e.g., because the relevant disease or condition occurs only in adults). This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The MAA for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a SPC provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires, even where the trial results are negative. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Post-approval controls

The holder of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports ("PSURs").

All new MAAs must include a risk management plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions.

The manufacturing of authorized medicinal 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 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.

All advertising and promotional activities for the product must be consistent with the approved Summary of Product Characteristics and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

The aforementioned EU rules are generally applicable in the EEA, which consists of the EU Member States, plus Norway, Liechtenstein and Iceland.

The EC 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). The EC has provided the legislative proposals to the European Parliament and the European Council for their review and approval. In October 2023, the European Parliament published draft reports proposing amendments to the legislative proposals, which will be debated by the European Parliament. Once the EC's legislative proposals are approved (with or without amendment), they will be adopted into EU law.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials must be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Brexit and the Regulatory Framework in the United Kingdom

The U.K. formally left the EU on January 31, 2020. The EU and the U.K. have concluded a trade and cooperation agreement ("TCA"), which was provisionally applicable since January 1, 2021 and 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 U.K. and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework currently continues to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently aligns with EU regulations in many ways, however it is possible that these regimes will diverge more significantly in the future now that Great Britain's regulatory system is independent from the EU.

The MHRA in the U.K. established a new medicines approval pathway following Brexit, known as the Innovative Licensing and Access Pathway ("ILAP"), which aims to accelerate the time to market and facilitate patient access to certain types of medicinal products in development which target a life-threatening or seriously debilitating condition, or where there is a significant patient or public health need. The first step in the ILAP is receipt of an Innovation Passport, which allows for enhanced engagement with the MHRA and its partner agencies. Once an Innovation Passport has been granted, the next step in the pathway is the preparation of a target development profile ("TDP") document by the MHRA and the U.K.'s health technology assessment agencies. The TDP sets out the regulatory and development milestones, identifies potential issues and creates a roadmap to achieving early patient access in the U.K. The TDP also gives access to a toolkit where a number of tools can be selected as needed for a particular medicine or stage of development. These tools include rolling review of an MAA, whereby data can be submitted for review on a rolling basis as it becomes available.

On January 1, 2024, a new international recognition framework was put in place by the MHRA, under which the MHRA may have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators.

On February 27, 2023, the U.K. government and the EC announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the U.K. In particular, the MHRA will be responsible for approving all medicinal products destined for the U.K. market (Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single U.K.-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the U.K., enabling products to be sold in a single pack and under a single authorization throughout the U.K. The Windsor Framework was approved by the EU-U.K. Joint

Committee on March 24, 2023, so the U.K. Government and the EU will enact legislative measures to enact it into law. On June 9, 2023, the MHRA announced that the medicines aspects of the Windsor Framework will apply from January 1, 2025.

Other Government Regulation

In addition to the healthcare laws and regulations in the U.S. and EU discussed above, we may be subject to a variety of regulations in these and other jurisdictions governing, among other things, animal research, clinical studies, manufacture, marketing approval, and any commercial sales and distribution of biological products. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries. These regulations may continue to change, and we may be required to change our operations and business conduct in response to these changes.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any biological product for which we obtain regulatory approval. In the U.S. 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 our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of any products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third party payors. Third party payors include government authorities, managed care providers, health maintenance organizations, private health insurers and other organizations. Coverage and reimbursement by a third party payor may depend upon a number of factors, including the third party payor's determination that use of a product is:

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

In the U.S., no uniform policy of coverage and reimbursement for biological products, including gene and cellular therapy products, exists among third party payors. As a result, obtaining coverage and reimbursement approval for such a product from a government or other third party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data regarding the products' clinical benefits and risks on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Additionally, third party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our gene-modifying products. Patients are unlikely to use, and health care providers may not prescribe, our product candidates unless coverage is provided, and reimbursement is adequate to cover a significant portion of the product's cost to the patient. Because our product candidates may have a higher cost of goods than conventional therapies, and may require long-term follow up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater. Moreover, increasing efforts by governmental and third party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for biological products and, as a result, they may not cover or provide adequate payment for our product candidates. In addition, we expect to experience pricing pressures in connection with the sale of any of our product candidates upon their approval due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes. For these reasons, there is significant uncertainty related to coverage and reimbursement of our future products. It is difficult to predict at this time what third party payors will decide with respect to the coverage and reimbursement for our product candidates.

Third-party and government payors consistently seek to reduce reimbursements for medical products and services. Additionally, the containment of healthcare costs is a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our products or a decision by a third-party payor to not cover our products could reduce physician usage of the products and have a material adverse effect on our sales, results of operations and financial condition.

Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

It is likely that our product candidates, once approved, will have to be administered by a health care provider. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare Part B. As a condition of receiving Medicare Part B reimbursement, the manufacturer of the therapy is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program, both of which require the manufacturer to provide rebated pricing under certain conditions. For example, the Medicaid Drug Rebate Program requires pharmaceutical manufacturers to have a national rebate agreement with the federal government as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to program eligible entities, which generally are federally funded clinics and hospitals that serve large numbers of low-income and uninsured patients.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A Member State may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. 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. Historically, products launched in the EU do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Healthcare Reform

In the U.S. and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare, and containing or lowering the cost of healthcare.

For example, in 2010, the ACA was enacted in the U.S. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA of greatest importance to the pharmaceutical industry are that the ACA:

- subjects biological products to potential competition by biosimilars;
- increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program;
- created a Medicare Part D coverage gap discount program, in which manufacturers must agree to provide a 70% point-of-sale discount off the negotiated price of applicable branded drugs to eligible beneficiaries

during their coverage gap period, as a condition for a manufacturer's outpatient drugs being covered under Medicare Part D;

- extended a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expanded the entities eligible for discounts under the 340B Drug Discount Program;
- imposed an annual, nondeductible fee and tax on any entity that manufactures or imports certain branded prescription drugs, apportioned among these entities according to their market share in certain government healthcare programs; and
- established mechanisms to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes relevant to the healthcare system have been adopted in the U.S. since the ACA was enacted.

- In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress that include aggregate reductions of Medicare payments to providers of 2% per fiscal year, which remain in effect through 2031.
- In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers, cancer centers and other treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.
- On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.
- In May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option to use step therapy, a type of prior authorization, for Part B drugs. This final rule codified CMS's policy change that was effective January 1, 2019.
- On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. 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.

Additionally, there have been a number of proposed regulatory actions and legislative recommendations aimed at lowering prescription drug prices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs.

- In August 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. The IRA includes several provisions that will impact our business to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries, impose new manufacturer financial liability on all drugs in Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D

pricing for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for drug prices that increase faster than inflation, and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effect of the IRA on our business and the healthcare industry in general is not yet known.

- In addition, President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. In February 2023, the Department of Health and Human Services also issued a proposal in response to an October 2022 executive order from President Biden that includes a proposed prescription drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through FDA's accelerated approval pathway. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates and may affect our overall financial condition and ability to develop product candidates.

Human Capital

We believe the success of Intellia's mission largely depends on our ability to attract and retain highly skilled employees. We believe programs that foster company engagement, diversity, equity and inclusion, growth and development while providing competitive compensation and benefits will attract a diverse population of employees who will bring innovative ideas and creative solutions that will enable the achievement of our goals.

Company Communications and Engagement. Many of our employees actively participate in our Cultural Ambassador program, fostering a grassroots approach to engagement with support and guidance from our executive leadership team. Our Cultural Ambassador programs focus on the following: diversity, equity and inclusion, continuous learning, wellness and sustainability, social events, community outreach, and Intellia values and engagement.

Diversity, Equity and Inclusion. As we continue to grow as an organization, we remain dedicated to championing a culture that celebrates diversity and fosters collaboration inside the organization and in our community. Through our partnerships, we can build key relationships in our community and help pave the way for those wanting to pursue a career in the biotechnology industry. We are committed to increasing representation of underrepresented minorities at Intellia, particularly in leadership roles. Our recruiting team underwent bias awareness training, and we have sponsored career fairs and conferences at organizations focused on underrepresented communities to ensure we continue to attract the best talent and increase representation. In addition, current employees are participating in unconscious bias training throughout the year. We continue to expand our DEI efforts with the launch of Employee Resource Groups ("ERGs") which are voluntary, employee-led groups focused on fostering a diverse, inclusive workplace aligned with ONE Intellia. They are led and participated in by employees who share a characteristic, whether by identity or interest. The groups exist to provide support and help in personal or career development and to create a safe space where employees can bring their whole selves to the table. Coworkers are also invited to join the ERG to support their colleagues. Our team of Senior and Executive Vice Presidents is 54% female and 31% are ethnically diverse. Overall, as of February 16, 2024, our employee population consists of 54% women and 46% men.

Compensation and Benefits, Health and Wellness. We are committed to equitable pay, irrespective of gender, race, ethnicity, or sexual orientation, and conduct comprehensive pay-equity analyses on a semi-annual basis. We offer competitive benefits, including competitive salaries, excellent health insurance, and a 401(k) match. We are committed to pay equity, regardless of race, color, religion, gender, national origin, age, sexual orientation, marital or veteran status, disability, or any other legally protected status.

Growth and Development. Investing in our employees' personal and career growth is an important priority at Intellia. We aim to provide a wide range of on-the-job development opportunities, as well as in-person, virtual and off-site training seminars, and tools. Our goal is to ensure our employees have the skills they may need in the future. Of particular importance is fostering leadership with our quarterly "Development Day" series, which serves as a reminder for employees to check-in with themselves and their manager on their development goals. Additionally, we offer seminars and tools to our employees focused on career development within the organization. As part of these initiatives, we conduct an annual development program for our employees to work with their managers to set professional development goals and an action plan. We also have an internal mentorship program for our research and development employees, who can work with more senior employees to learn new skills.

Conduct and Ethics. We believe it is imperative that the board of directors and senior management strongly support a no-tolerance stance for workplace harassment, biases and unethical behavior. All employees, including senior management, are required to abide by, review and confirm compliance to the company's Code of Business Conduct and Ethics Policy and other internal policies that outline our high expectations.

Employees

As of February 16, 2024, we had 526 full-time employees, 414 of whom were primarily engaged in research and development activities and 160 of whom have an M.D. or Ph.D. degree.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in May 2014 under the name AZRN, Inc. and amended our certificate of incorporation in July 2014 to change our name from AZRN, Inc. to Intellia Therapeutics, Inc. Our principal executive offices are located at 40 Erie Street, Suite 130, Cambridge, Massachusetts 02139. Our telephone number is (857) 285-6200, and our website is located at www.intelliatx.com. References to our website are inactive textual references only and the content of our website should not be deemed incorporated by reference into this Annual Report on Form 10-K.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any exhibits and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, are available free of charge on our website located at www.intelliatx.com as soon as reasonably practicable after they are filed with or furnished to the Securities and Exchange Commission (the "SEC").

The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding us and other issuers that file electronically with the SEC. The SEC's Internet website address is http://www.sec.gov.

A copy of our Corporate Governance Guidelines, Code of Conduct and Business Ethics and the charters of the Audit Committee, Compensation and Talent Development Committee and Nominating and Corporate Governance Committee are posted on our website, www.intelliatx.com, under "Investors & Media".

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. In evaluating us and our business, careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K for the year ended December 31, 2023 and in other documents that we file with the SEC. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing us. New risk factors can emerge from time to time, and we cannot predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

Risks Related to Our Business

Risks Related to Preclinical and Clinical Development

CRISPR/Cas9 genome editing technology has only recently been clinically validated for human therapeutic use. The approaches we are taking to discover and develop novel therapeutics using CRISPR/Cas9 systems are unproven and may never lead to marketable products. If we are unable to develop viable product candidates, achieve regulatory approval for any such product candidate or market and sell any product candidates, we may never achieve profitability.

We are focused on developing curative medicines utilizing CRISPR/Cas9 genome editing technology, including *in vivo* therapies and *ex vivo* engineered cell therapies. Although there have been significant advances in recent years in the fields of gene therapy and genome editing, *in vivo* CRISPR-based genome editing technologies are relatively new and their therapeutic utility is largely unproven. Our approach to developing therapies centers on using CRISPR/Cas9 technology to alter, introduce or remove genetic information *in vivo* to treat various disorders, or to engineer human cells *ex vivo* to create therapeutic cells that can be introduced into the human body to address the underlying disease.

Successful development of products by us will require solving a number of issues, including developing or obtaining technologies to safely deliver a therapeutic agent into target cells within the human body or engineer human cells while outside of the body such that the modified cells can have a therapeutic effect when delivered to the patient, optimizing the efficacy and specificity of such products, and ensuring and demonstrating the therapeutic selectivity, efficacy, potency, purity and safety of such products. There can be no assurance we will be successful in solving any or all of these issues. With regards to CRISPR/Cas9-based therapies specifically, we are in clinical-stage development for NTLA-2001 and NTLA-2002 and advancing towards clinical testing for our other *in vivo* and *ex vivo* product candidates. Although one CRISPR/Cas9-edited *ex vivo* therapy has been recently approved in the United States ("U.S.") and European Union ("EU"), no genome editing *in vivo* therapy has been approved in the U.S., EU countries or other key jurisdictions, and the potential to successfully obtain approval for any of our CRISPR/Cas9 product candidates remains unproven.

Our future success also is highly dependent on the successful development of CRISPR-based genome editing technologies, cellular delivery methods and therapeutic applications for the indications on which we have focused our ongoing research and development efforts. We may decide to alter or abandon these programs as new data become available and we gain experience in developing CRISPR/Cas9-based therapeutics. We cannot be sure that our CRISPR/Cas9 efforts and technologies will yield satisfactory products that are safe and effective, sufficiently pure or potent, manufacturable, scalable or profitable in our selected indications or any other indication we pursue. We cannot guarantee that progress or success in developing any particular CRISPR/Cas9-based therapeutic product will translate to other CRISPR/Cas9-based products.

Public perception and related media coverage of potential therapy-related efficacy or safety issues, including adoption of new therapeutics or novel approaches to treatment, as well as ethical concerns related specifically to genome editing and CRISPR/Cas9, may adversely influence the willingness of subjects to participate in clinical trials, or if any therapeutic is approved, of physicians and patients to accept these novel and personalized treatments. Physicians, healthcare providers and third party payors often are slow to adopt new products, technologies and treatment practices, particularly those that may also require additional upfront costs and training. Physicians may not be willing to undergo training to adopt these novel and potentially personalized therapies, may decide the particular therapy is too complex or potentially risky to adopt without appropriate training, and may choose not to administer the therapy. Further, due to health conditions, genetic profile or other reasons, certain patients may not be candidates for the therapies. In addition, responses by federal and state agencies, congressional committees and foreign governments to negative public perception, ethical concerns or financial considerations may result in new legislation, regulations, or medical standards that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. New government requirements may be established that could delay or prevent regulatory approval of our product candidates under development. It is impossible to predict whether legislative changes will be enacted, regulations, policies or guidance changed, or interpretations by agencies or courts changed, or what the impact of such changes, if any, may be. Based on these and other factors, healthcare providers and payors may decide that the benefits of these new therapies do not or will not outweigh their costs.

Clinical development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.

All of our programs are still in the discovery, preclinical or clinical stage. Our current and future product candidates will require preclinical and clinical activities and studies, regulatory review and approval in each jurisdiction in which we intend to market the products, substantial investment, establishing manufacturing capabilities, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. Before obtaining marketing approval from regulatory authorities for the sale of a product candidate, we must conduct extensive clinical trials to demonstrate the safety, purity, potency and efficacy of the product in humans. It is impossible to predict when or if any of our programs will prove effective and safe in humans or will receive regulatory approval. Preclinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We may be unable to establish clinical endpoints that regulatory authorities consider clinically meaningful, and a clinical trial can fail at any stage. The outcome of preclinical testing and clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain approval of their products.

Successful completion of clinical trials is a prerequisite to submitting a Biologics License Application ("BLA") to the U.S. Food and Drug Administration ("FDA"), and similar applications to comparable foreign regulatory authorities, for each product candidate and, consequently, the ultimate approval and commercial marketing of any product candidates. We do not know whether any of our clinical trials will begin or be completed on schedule, if at all. In addition, the regulatory requirements for later phase clinical trials, such as pivotal trials, are generally more stringent than earlier phase clinical trials, such as Phase 1 trials. We may not meet the requirements of regulatory authorities, such as the FDA, for initiating later phase clinical trials for our product candidates, which could delay the development of our product candidates, including the submission of a BLA or comparable marketing application.

Because these are new therapeutic approaches, discovering, developing, manufacturing and commercializing our product candidates may subject us to a number of challenges or delays in completing our preclinical studies and initiating or completing clinical trials. We also may experience numerous unforeseen events during, or as a result of, any current or future clinical trials that we conduct, which could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- challenges in obtaining regulatory authorization or approval to conduct clinical trials in the U.S. from the FDA through an investigational new drug ("IND") application or from other regulatory agencies outside the U.S., such as the United Kingdom ("U.K.") Medicines and Healthcare products Regulatory Agency ("MHRA") or the European Medicines Agency ("EMA"), through corresponding applications, such as a clinical trial application, a Clinical Trial Notification or a Clinical Trial Exemption, because these agencies have very limited or no experience with the clinical development of CRISPR/Cas9-based therapeutics, particularly *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;
- successfully developing processes for the safe administration of these product candidates, including long-term follow-up for patients who receive treatment with any of our product candidates;
- regulators, institutional review boards ("IRBs") or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial;
- inability to reach, or delays in reaching, agreement on acceptable terms with trial sites and contract research organizations ("CROs");
- clinical trials of any product candidates may fail to show safety or efficacy, or could produce negative or inconclusive results, which could result in having to conduct additional preclinical studies or clinical trials or terminating the product development programs;
- we may not be able to initiate or complete clinical trials of a product candidate if the required number of subjects is larger than we anticipated, the number of subjects willing to enroll is smaller than required, the

pace of enrollment is slower than anticipated, or subjects drop out or fail to return for post-treatment follow-up at a higher rate than we anticipated;

- we may need to educate medical personnel, including clinical investigators, and patients regarding the potential benefits and side effect profile of each of our product candidates;
- regulatory agencies may require us to amend our INDs or equivalent regulatory filings, modify the design of our clinical trials or perform more extensive or lengthier preclinical or clinical testing compared to existing therapeutic modalities, any of which may delay the initiation or progression of any of our clinical trials;
- animal models may not exist, or available animal models may be inadequate, for some of the human diseases we choose to pursue in our programs, or the preclinical studies we perform as part of our programs;
- our third party contractors may fail to comply with regulatory requirements or meet their performance obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of preclinical studies and clinical trials of any product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct preclinical studies and clinical trials of our product candidates may be insufficient or inadequate, or not available in a reasonable timeframe, and any transfer of manufacturing activities may require unforeseen manufacturing or formulation changes;
- we may face challenges in sourcing preclinical, clinical and, if approved, commercial supplies for the materials used to manufacture and process our product candidates, which may include importing or exporting materials between different jurisdictions;
- our product candidates may have undesirable side effects or other unexpected characteristics, such as effects or characteristics resulting from their biodistribution or mechanism of action, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other gene therapies or genome editing-based therapies that raise safety or efficacy concerns about our product candidates;
- the FDA or other regulatory authorities may require us to submit additional data, such as long-term toxicology studies, or impose other requirements, including submitting preclinical data earlier in clinical development compared to existing therapeutic modalities or requiring amendments to our regulatory filings, before permitting us to initiate or rely on a clinical trial;
- we may face challenges in establishing sales and marketing capabilities in anticipation of, and after obtaining, any regulatory approval to gain market authorization;
- the FDA or other regulatory authorities may revise the requirements for authorizing our clinical trials or approving our product candidates, or their interpretation of the authorization or approval requirements may not be what we anticipate or require us to adopt a Risk Evaluation and Mitigation Strategy ("REMS") or similar requirements as a condition of approval; and
- we may not ultimately obtain regulatory approval for a BLA, or corresponding applications outside the U.S., such as a marketing authorization application in the U.K. and other similar regulatory authorities, such as the EMA, which may have very limited or no experience with the clinical development of CRISPR/Cas9-based therapeutics, particularly *in vivo* therapeutics.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, the relevant ethics committee or the FDA or other relevant regulatory authorities, or

if the Data Monitoring Committee ("DMC") for such trial recommends such suspension or termination. Such authorities may impose or recommend such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities, resulting in the imposition of a clinical hold, manufacturing or quality control issues, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also lead to a delay in submitting a BLA or comparable marketing application or ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

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

- regulatory guidance regarding the requirements governing gene and genome editing therapy products have changed and may continue to change in the future, including, e.g., the finalized 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 *in vivo* gene transfer have been approved globally;
- improper modulation of a gene sequence, including unintended editing events, insertion of a sequence into certain locations in a patient's chromosome or other effects related to the biodistribution of our product candidates, could lead to cancer, 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
- regulatory agencies may require extended follow-up observation periods of patients who receive treatment using genome editing products including, for example, the FDA's recommended 15-year follow-up observation period for these patients, and we will need to adopt such observation periods for our product candidates if required by the relevant regulatory agency, which could vary by country or region.

Further, because our *ex vivo* product candidates involve editing human cells and then delivering modified cells to patients, we are subject to many of the challenges and risks that engineered cell therapies face. For example, patients treated with engineered cell-based gene therapies may experience an allogeneic response leading to allograft rejection and potential local and systemic toxicities, which could be severe or life-threatening.

To date, most human clinical trials utilizing either *in vivo* or *ex vivo* CRISPR-based therapeutics, including our clinical trials for NTLA-2001 for transthyretin ("ATTR") amyloidosis and NTLA-2002 for hereditary angioedema ("HAE"), are still at a clinical stage, with only one *ex vivo* CRISPR-based therapeutic product approved in December 2023 in the U.S. and EU. We have ongoing clinical trials in various countries for NTLA-2001 and NTLA-2002 for patients with ATTR amyloidosis and HAE, respectively. There is no certainty that the FDA or other similar agencies will continue to apply to all our CRISPR/Cas9 product candidates the same regulatory pathway and requirements it is applying to other *in vivo* therapies or *ex vivo* engineered therapeutics.

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 bodies, 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 the FDA cleared the INDs that we have submitted, it is possible that the FDA may impose requirements that result in a delay of any of our programs, including our submission of a BLA or comparable marketing application, or their regulatory approval. For example, following the March 2023 IND clearance for NTLA-2002, the FDA requested supplemental preclinical data related to the inclusion of female patients of child-bearing potential. We expect to submit these data in advance of the planned Phase 3 trial, which will complement the clinical data collected from female patients of child-bearing potential dosed in the ongoing Phase 1/2 study. We cannot guarantee the timing or outcome of these preclinical studies or whether the FDA may require that additional preclinical studies be conducted before commencement of our Phase 3 trial for NTLA-2002. If we are unable to complete the required studies satisfactorily, the FDA or other regulatory bodies 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 *in vivo* or *ex 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 bodies 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 may experience manufacturing delays or other issues that prevent us from executing the clinical trials for NTLA-2001, NTLA-2002, NTLA-3001 or our other product candidates on the timeline we expect. Moreover, we cannot guarantee that the FDA, MHRA, the New Zealand Medicines and Medical Devices Safety Authority, or other regulatory authorities will not change their requirements in the future or approve amendments to our INDs or equivalent regulatory filings, including for NTLA-2001, NTLA-2002, NTLA-3001 or our other product candidates on the timeline we expect.

Results, including data from our preclinical and clinical studies, are not necessarily predictive of our other ongoing and future preclinical and clinical studies, and they do not guarantee or indicate the likelihood of approval of any potential product candidate by the FDA or any other regulatory agency. If we cannot replicate positive results from any of our preclinical or clinical activities and studies, we may be unable to successfully develop, obtain regulatory approval for and commercialize any potential product candidate.

From time to time, we may disclose interim data from our clinical trials, such as the interim results of our ongoing Phase 1 study of NTLA-2001 or Phase 1/2 study of NTLA-2002 or planned Phase 1 study of NTLA-3001. Interim data from clinical trials that have not been completed are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Consequently, interim data should be viewed with caution until we make the final data and analysis available.

In addition, there is a high failure rate, as well as potential substantial and unanticipated delays, for product candidates progressing through preclinical and clinical studies. Even if we are able to successfully complete our ongoing and future preclinical and clinical activities and studies for any potential product candidate, we may not be able to replicate, or may have to engage in significant efforts and resource and time investments to replicate, any positive results from these or any other studies in any of our future preclinical and clinical trials, and they do not guarantee approval of any potential product candidate by the FDA or any other necessary regulatory authorities in a timely manner or at all. For more information regarding these risks, see also the remainder of this risk factor section.

Negative public opinion and increased regulatory scrutiny of CRISPR/Cas9 use, genome editing or gene therapy generally may damage public perception of the safety of any product candidates that we develop and adversely affect our ability to conduct our business or obtain regulatory approvals for such product candidates.

Gene therapy in general, and genome editing in particular, remain novel technologies, with only a limited number of gene therapy products approved to date in the U.S. and EU. Public perception may be influenced by claims that gene therapy or genome editing, including the use of CRISPR/Cas9, is unsafe or unethical, or carries an undue risk of side

effects, such as improper modification of a gene sequence in a patient's chromosome that could lead to cancer, and gene therapy or genome editing may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of diseases targeted by our product candidates prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are more familiar and for which greater clinical data may be available. In addition, responses by the U.S., state or foreign governments to negative public perception or ethical concerns may result in new legislation or regulations that could limit our ability to develop or commercialize any product candidates, obtain or maintain regulatory approval or otherwise achieve profitability. More restrictive statutory regimes, government regulations or negative public opinion could have an adverse effect on our business, financial condition and results of operations and prospects, and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, certain gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death. Serious adverse events, such as these, in our clinical trials, or other clinical trials involving gene therapy or genome editing products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity could result in increased government regulation, unfavorable public perception, 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 candidate. In addition, the use of the technology by third parties in areas that are not being pursued by us, such as for targeting and editing of embryonic cells, could adversely impact public and governmental perceptions regarding the ethics and risks of the CRISPR/Cas9 technology and lead to social or legal changes that could limit our ability to apply the technology to develop human therapies addressing disease. For example, reports of the use of CRISPR/Cas9 in China and Russia to edit embryos *in utero* have generated, and may continue to generate, negative public perception about the use of the technology in humans. Negative public and governmental perception of the technology, or additional governmental regulation of our technologies, could also adversely affect our stock price or our ability to enter into revenue generating collaborations or obtain additional funding from the public markets.

Risks Related to the Industry

Inconclusive results, lack of efficacy, adverse events or additional safety concerns in clinical trials that we or others conduct may impede the regulatory approval process or overall market acceptance of our product candidates.

Therapeutic applications of genome editing technologies, and CRISPR/Cas9 in particular, for both *in vivo* products and *ex vivo* products, are unproven and must undergo rigorous clinical trials and regulatory review before receiving marketing authorization. If the results of our clinical studies or those of any other third parties, including with respect to genome editing technology or engineered cell therapies, are inconclusive or fail to show efficacy or if such clinical trials give rise to safety concerns or adverse events, we may:

- be prevented from, or delayed in, obtaining marketing approval for our product candidates;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to the addition of labeling statements, such as warnings or contraindications, or other types of regulatory restrictions or scrutiny;
- be subject to changes in the way the product is administered;
- be required to perform additional clinical studies to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities modify or withdraw their legal requirements or written guidance, if any, regarding the applicable regulatory approval pathway or any approval of the product in question, or impose restrictions on its distribution in the form of a modified REMS or similar strategy;
- be sued; or
- experience damage to our reputation.

Additionally, our product candidates could potentially cause other adverse events that have not yet been predicted and the potentially permanent nature of genome editing effects, including CRISPR/Cas9's effects, on genes or novel cell therapies in the organs of the human body may make these adverse events irreversible. The inclusion of critically ill patients in our clinical studies or those of our competitors may result in deaths or other adverse medical events, including those due to other therapies or medications that such patients may be using. Any of these events could prevent us from achieving or maintaining regulatory approval or market acceptance of our product candidates and impair our ability to achieve profitability.

Research and development of biopharmaceutical products is inherently risky. We may not be successful in our efforts to use and enhance our genome editing technology to create a pipeline of product candidates, establish the necessary manufacturing capabilities, obtain regulatory approval and develop commercially successful products, or we may expend our limited resources on programs that do not yield a successful product candidate and fail to capitalize on potential product candidates or diseases that may be more profitable or for which there is a greater likelihood of success. If we fail to develop product candidates, our commercial opportunity, if any, will be limited.

We are at a clinical stage of development and our technology and approach has not yet led, and may never lead, to the approval or commercialization of any of our product candidates, including NTLA-2001 for ATTR amyloidosis or NTLA-2002 for HAE, or for other product candidates, including NTLA-3001 for alpha-1 antitrypsin deficiency, being deemed appropriate for clinical development and ultimately approval by a regulatory agency. Even if we are successful in building our pipeline of product candidates, completing clinical development, establishing the necessary manufacturing processes and capabilities, obtaining regulatory approvals and commercializing product candidates will require substantial additional funding and are subject to the risks of failure inherent in therapeutic product development. Investment in biopharmaceutical product development involves significant risk that any potential product candidate will fail to demonstrate acceptable safety and efficacy profiles, gain regulatory approval, or become commercially viable.

We cannot provide any assurance that we will be able to successfully advance any of our product candidates, including NTLA-2001, NTLA-2002, NTLA-3001 or product candidates developed through our collaborations, through the entire research and development process. Any of our other programs may show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons. For more information regarding these risks, see the above risk factor section entitled "Risks Related to Preclinical and Clinical Development."

Even if we obtain regulatory approval of any product candidates, such candidates may not gain market acceptance among physicians, patients, hospitals, third party payors and others in the medical community.

The use of the CRISPR/Cas9 system to create genome editing-based therapies is a recent development and may not become broadly accepted by patients, healthcare providers, third party payors and other stakeholders. A variety of factors will influence whether our product candidates are accepted in the market, including, for example:

- the clinical indications for which our product candidates are approved;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the incidence and severity of any side effects, including any unintended deoxyribonucleic acid ("DNA") changes;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the timing of market introduction of our product candidates;
- availability or existence of competitive products;
- the cost of treatment in relation to alternative treatments;
- the amount of upfront costs or training required for healthcare providers to administer our product candidates;
- the availability of adequate coverage, reimbursement and pricing by government authorities and other third party payors;

- patients' ability to access healthcare providers capable of delivering our product candidates;
- patients' willingness and ability to pay out-of-pocket in the absence of coverage and reimbursement by government authorities and other third party payors;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies;
- any restrictions on the use of our product candidates together with other medications;
- interactions of our product candidates with other medicines patients are taking;
- potential adverse events for any products developed, or negative interactions with regulatory agencies, by us or others in the gene therapy and genome editing fields; and
- the effectiveness of our sales and marketing efforts and distribution support.

Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete. In addition, adverse publicity due to the ethical and social controversies surrounding the therapeutic *in vivo* use of CRISPR/Cas9, genome edited modified cells, or other therapeutics mediums, such as viral vectors that we may use in our clinical trials may limit market acceptance of our product candidates. If our product candidates are approved but fail to achieve market acceptance among physicians, patients, hospitals, third party payors or others in the medical community, we will not be able to generate significant revenue. Our efforts to educate the healthcare providers, patients and third party payors about our products may require significant resources and may never be successful.

Risks Related to Intellectual Property

Risks Related to Third Party and Licensed 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.

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 product candidates and 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. Our development candidates are complex and may include multiple components such as Cas9 protein or messenger ribonucleic acid encoding Cas9 protein, guide ribonucleic acids ("gRNAs"), targeting molecules, or formulation components such as lipids. We cannot guarantee that any of these components of our technology, processes, future product candidates or the use of such product candidates do not infringe third party patents. It is also possible that we have failed to identify relevant third party patents or applications. 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 may assert that we infringe their patents or that we are otherwise employing their proprietary technology without authorization, and may sue us. There may be third party patents with claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover product candidates we discover and develop. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies or the manufacture, use or sale of our product candidates or products that we develop infringes these patents. If a court of competent jurisdiction were to hold that we infringed such patents,

the holders of any such patents may be able to block our ability to commercialize the applicable product candidate or products unless we obtain a license under the applicable patents, or until such patents expire or are finally determined to be held invalid or unenforceable. Such a license may not be available on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing, manufacturing or importing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing one or more of our product candidates or products that we develop, force us to redesign our infringing products or force us to cease some or all of our business operations, any of which 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. If we are unable to obtain a necessary license to a third party patent on commercially reasonable terms, our ability to commercialize our product candidates or products that we develop may be impaired or delayed, which could in turn significantly harm our business. In addition, we may be obligated to defend and/or indemnify our existing or potential collaborators, clinical investigators, contract manufacturing organizations ("CMOs"), CROs, consultants or vendors if a third party asserts similar infringement claims against them based on use of our technologies or the manufacture, use or sale of our product candidates or products that we develop, including product candidates or products developed with our collaborators. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Even if we are not found liable for infringing or misappropriating the intellectual property of a third party, such claims could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

Third parties may seek to claim intellectual property rights that encompass or overlap with intellectual property that we own or license from them or others. 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 or products that we develop, including product candidates or products developed with our collaborators. For example, through a license agreement between Caribou Biosciences, Inc. and us (the "Caribou License"), we sublicense the rights of the Regents of the University of California and the University of Vienna (collectively, "UC/Vienna") to a worldwide patent portfolio that covers methods of use and compositions relating to engineered CRISPR/Cas9 systems for, among other things, cleaving or editing DNA and altering gene product expression in various organisms, including eukaryotic cells. We sublicense the UC/Vienna rights to this portfolio for human therapeutic, prophylactic and palliative uses, including companion diagnostics, except for anti-fungal and anti-microbial uses. This patent portfolio to-date includes, for example, multiple granted, allowed, and/or allowable patent applications in the U.S., as well as granted patents from the European Patent Office, the United Kingdom's Intellectual Property Office, the German Patent and Trade Mark Office, Australia's Intellectual Property agency and China's Intellectual Property Office, among others. Because UC/Vienna co-own this portfolio with Dr. Emmanuelle Charpentier (who has separately licensed her rights to other parties), we refer to this co-owned worldwide patent portfolio as the "UC/Vienna/Charpentier patent family."

Third parties could assert that our licensors, such as UC/Vienna/Charpentier, do not have rights to the licensed technology (such as the CRISPR/Cas9 technology in the case of the Caribou License), including inventorship and ownership rights to currently issued or allowable patents, or that any rights owned by our licensors, such as UC/Vienna/Charpentier, are limited. If such third parties were found to have rights to the licensed technology (such as CRISPR/Cas9 technology), we could be required to obtain rights from such parties or cease our development and commercialization efforts. For example, under our Caribou License, we have rights to patent applications owned by UC/Vienna/Charpentier covering certain aspects of CRISPR/Cas9 systems to edit genes in eukaryotic cells, including human cells (collectively, the "UC/Vienna/Charpentier eukaryotic patent family"). The Broad Institute, Massachusetts Institute of Technology, the President and Fellows of Harvard College and the Rockefeller University (collectively, the "Broad Institute") co-own patents and patent applications that also claim CRISPR/Cas9 systems to edit genes in eukaryotic cells (collectively, the "Broad Institute patent family"). Because the respective owners of various UC/Vienna/Charpentier patent applications and the Broad Institute patent family both allege owning intellectual property claiming overlapping aspects of CRISPR/Cas9 systems and methods to edit genes 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. On June 25, 2019, the Patent Trial and Appeal Board ("PTAB") of the U.S. Patent and Trademark Office ("USPTO") declared an interference between the UC/Vienna/Charpentier eukaryotic patent family and the Broad Institute patent

family to determine which research group first invented the use of the CRISPR/Cas9 technology in eukaryotic cells and, therefore, is entitled to the U.S. patents covering that invention. The interference involved 14 allowable patent applications from the UC/Vienna/Charpentier eukaryotic patent family and 13 patents and one patent application from the Broad Institute patent family. On February 28, 2022, the PTAB issued a Decision of Priority and Judgment in the interference finding that the Broad Institute patent family has priority over the UC/Vienna/Charpentier patent family with respect to the subject matter of the interference. An appeal and cross-appeal from the interference are pending at the United States Court of Appeals for the Federal Circuit as Case Nos. 22-1594 and 22-1653.

On December 14, 2020, the PTAB declared an additional interference between the same 14 allowable patent applications in the UC/Vienna/Charpentier patent family, and one patent application owned by ToolGen, Inc. And, on June 21, 2021, the PTAB declared another interference between the same 14 allowable patent applications in the UC/Vienna/Charpentier patent family and one patent application owned by Sigma-Aldrich Co. LLC (a subsidiary of Merck KGaA). Because the patent applications involved in these interferences also purport to cover the use of CRISPR/Cas9 for gene editing in eukaryotic cells, the PTAB seeks to determine between the various groups which one invented first and is entitled to the resulting U.S. patents. A decision on motions issued in the ToolGen interference on September 28, 2022, and the priority phase of that interference was suspended until a mandate concludes the Federal Circuit appeal and cross-appeal in the UC/Vienna/Charpentier interference with the Broad Institute. The Sigma-Aldrich interference is in its motions phase, and an order scheduling oral argument issued on October 24, 2022. If either the Broad Institute, ToolGen or Sigma-Aldrich were to succeed in any of their respective interferences, the prevailing party or parties could seek to assert its issued patents against us based on our CRISPR/Cas9-based activities, including commercialization. In addition, the prevailing party may assert similar infringement claims against our existing or potential collaborators, clinical investigators, CMOs, CROs, consultants or vendors, and we may be obligated to defend and/or indemnify those parties against such infringement claims.

In addition, other third parties, such as Vilnius University and Harvard University, filed patent applications claiming CRISPR/Cas9-related inventions around or within a year after the first patent application filed in the UC/Vienna/Charpentier patent family and allege (or may allege) that they invented one or more of the inventions claimed by UC/Vienna/Charpentier before UC/Vienna/Charpentier. If the USPTO deems the scope of any of such third party's claims sufficiently overlap with the allowable claims from the applicable patent applications in the UC/Vienna/Charpentier patent family, the USPTO could declare other interference proceedings to determine the actual inventor of such claims. If these third parties were to prevail in their inventorship claims or obtain patent claims that cover our product candidates or related activities through these various legal proceedings, then we could be prevented from utilizing the intellectual property we have licensed from Caribou, as well as from developing and commercializing all or some of our products candidates unless we can obtain rights to the third parties' intellectual property or avoid or invalidate it.

Further, many third parties, including the third parties described above, have also filed patent applications and obtained patents covering aspects of the CRISPR/Cas9 technology in other key jurisdictions, including the EU members, the U.K., China and Japan. If these patents are deemed valid and cover our product candidates or related activities, we could be prevented from developing and commercializing all or some of our product candidates unless we license the relevant intellectual property or avoid it.

Defense of any potential infringement 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. In the event of a successful claim of infringement against us, or a third party that we are obliged to defend and indemnify, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In that event, we could be unable to further develop and commercialize our product candidates, which could harm our business significantly.

We depend on intellectual property licensed from third parties and termination or modification of any of these licenses could result in the loss of significant rights, which would harm our business.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others, including Caribou. Any termination of these licenses, loss by our licensors of the rights they receive from others, diminution of our rights or those of our licensors, or a finding that such intellectual property lacks legal effect, could result in the

loss of significant rights and could harm our ability to commercialize any product candidates. For example, UC/Vienna could challenge Caribou's rights under their agreement, including Caribou's right to sublicense its rights to others, such as Intellia, and on what terms such a sublicense would be granted, each of which could adversely impact our rights under our agreement with Caribou. Similarly, Caribou or other licensors, or other third parties from which we derive rights, could challenge the scope of our licensed rights or fields under our license agreement, which could adversely impact our exclusive rights to use CRISPR/Cas9 technology in our human therapeutics field. For example, in connection with the arbitration regarding the scope of the Caribou License, we executed a leaseback agreement with Caribou granting it a sublicense to develop and commercialize CB-010, which is a chimeric antigen receptor T ("CAR-T") cell therapy directed at CD19. The leaseback agreement could adversely affect our business or that of our collaborators developing similar human therapeutics.

Disputes have and may arise between us and our licensors, our licensors and their licensors, or us and third parties that co-own intellectual property with our licensors or their licensors, regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights, if any, granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology, products and processes infringe on, or derive from, intellectual property of the licensor that is not subject to the license agreement;
- whether our licensor or its licensor had the right to grant the license agreement, or whether they are compliant with their contractual obligations to their respective licensor(s);
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property without their authorization;
- our right to sublicense patent and other rights to third parties, including those under collaborative development relationships;
- whether we are complying with our obligations with respect to the use of the licensed technology in relation to our development and commercialization of product candidates;
- our involvement in the prosecution, defense and enforcement of the licensed patents and our licensors' overall patent strategy;
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners; and
- the amounts of royalties, milestones or other payments due under the license agreement.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, or are insufficient to provide us the necessary rights to use the intellectual property, we may be unable to successfully develop and commercialize the affected product candidates. If we or any such licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

We depend, in part, on our licensors to file, prosecute, maintain, defend and enforce patents and patent applications that are material to our business.

Patents relating to our product candidates are controlled by certain of our licensors or their respective licensors. Each of our licensors or their licensors generally has rights to file, prosecute, maintain and defend the patents we have licensed from such licensor. If these licensors or any future licensees and in some cases, co-owners from which we do not yet have licenses, having rights to file, prosecute, maintain, and defend our patent rights fail to adequately conduct these activities for patents or patent applications covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using or selling competing products. We cannot be certain that such activities by our licensors or their respective licensors have been or will be conducted in compliance with applicable laws and regulations or in our best interests, or will result in valid and enforceable patents or other intellectual property rights. Pursuant to the terms of the license agreements with our licensors, the licensors may have the right to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents and, even if we are permitted to pursue such

enforcement or defense, we cannot ensure the cooperation of our licensors or, in some cases, other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license. We cannot be certain that our licensors or their licensors, and in some cases, their respective co-owners, will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. For example, with respect to our sublicensed rights from Caribou to UC/Vienna/Charpentier intellectual property, UC retained the right to control the prosecution, enforcement and defense of this intellectual property in its license agreement with Caribou and, pursuant to an Invention Management Agreement, shares these responsibilities with CRISPR Therapeutics AG and, under certain circumstances, ERS Genomics, Ltd., as the designated managers of the intellectual property. For these reasons, UC may be unable or unwilling to prosecute certain patent claims that would be best for our product candidates, or enforce its patent rights against infringers of the UC/Vienna/Charpentier patent family.

Even if we are not a party to legal actions or other disputes involving our licensed intellectual property, an adverse outcome could harm our business because it might prevent us from continuing to license intellectual property that we may need to operate our business. In addition, even when we have the right to control patent prosecution of licensed patents and patent applications, enforcement of licensed patents, or defense of claims asserting the invalidity of those patents, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to or after our assuming control.

We may not be successful in obtaining or maintaining necessary rights to product components and processes or other technology for our product development pipeline.

The growth of our business will likely depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates, delivery systems or technologies that may require the use of additional proprietary rights held by third parties, including competitors. Our ultimate product candidates may also require specific modifications or formulations to work effectively and efficiently. These modifications or formulations may be covered by intellectual property rights held by others, including competitors. We may be unable to acquire or in-license any relevant third party intellectual property rights that we identify as necessary or important to our business operations.

Additionally, we sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

The licensing and acquisition of third party intellectual property rights is a competitive practice and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. 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 that we may seek to acquire.

If we are unable to successfully obtain rights to valid third party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

We may be required to pay certain milestones and royalties under our license agreements with third party licensors.

Under our current and future license agreements and other technology agreements, we may be required to pay milestones and royalties based on our revenues, including sales revenues of our products, utilizing the technologies acquired, licensed or sublicensed from third parties, including Caribou and Rewrite Therapeutics, Inc. ("Rewrite"), 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. 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. Further, our counterparties, including our licensors (or their licensors) or licensees, 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 counterparties, including licensors or their licensors, or in a claim of breach of the applicable agreement, our ability to research, develop and obtain approval of product candidates, or to commercialize products, could be significantly impaired.

In addition, these agreements contain diligence milestones and we may not be successful in meeting all of the milestones in the future on a timely basis or at all. 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 the continuation of these agreements with their counterparties, including our licensors or their licensors.

Risks Related to Patents and Trademarks

We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies.

We anticipate that we will file additional patent applications both in the U.S. and in other countries, as appropriate. However, we cannot predict:

- if and when any patents will issue;
- the scope, degree and range of protection any issued patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- whether others will apply for or obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether certain governments will appropriate our intellectual property rights and allow competitors to use them; or
- whether we will need to initiate litigation or administrative proceedings to assert or defend our patent rights, which may be costly whether we win or lose.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. We cannot be certain, however, that any claims in our pending or future patent applications covering the composition of matter of our product candidates will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any of our ultimately issued patents will be considered valid and enforceable by courts in the U.S. or foreign countries. Method of use patents protect the use of a product for the specified method, for example a method of treating a certain indication using a product. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label” for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field can be uncertain, and evaluating the scope of such patents involves complex legal and scientific analyses. The patent applications that we own or in-license may fail to result in issued patents with claims that cover any product candidates or uses thereof in the U.S. or in other foreign countries.

Further, the patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third

parties. We may also require the cooperation of our licensors or other necessary parties, such as the co-owners of the intellectual property from which we have not yet obtained a license, in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. and we may fail to seek or obtain patent protection in all major markets. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we will be unable to know with certainty whether we were the first to make any inventions claimed in any patents or patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. There is a substantial amount of litigation as well as administrative proceedings for challenging patents, including interference, derivation, reexamination, and other post-grant proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, and we expect this to be true for the CRISPR/Cas9 space as well. Indeed, a number of third parties have filed oppositions challenging the validity, and seeking the revocation, of several CRISPR/Cas9 genome editing patents granted to UC/Vienna/Charpentier by the European Patent Office ("EPO"). To date, UC/Vienna/Charpentier have successfully defended before the EPO's opposition division the validity of their first European patent, which covers compositions comprising Cas9 and single gRNA molecules, as well as methods of editing DNA *in vitro* or *ex vivo* using Cas9 and single gRNAs. The opponents to this patent have appealed the decision of the EPO's opposition division. If UC/Vienna/Charpentier fail in defending the validity of its first European patent, we may lose valuable intellectual property rights, such as the right to exclude others from using such intellectual property. Such an outcome could have a material adverse effect on our business in Europe. Similarly, third parties are opposing the other patents issued by the EPO to UC/Vienna/Charpentier, including their second European patent that was recently revoked by the EPO's opposition division, a decision that UC/Vienna/Charpentier have appealed. Although the claims of these other patents are more limited in scope compared to the first European patent, the inability to defend their respective validity could result in loss of valuable rights. In addition, since the passage of the America Invents Act in 2013, U.S. law also provides for other procedures to challenge patents, including *inter partes* reviews and post-grant reviews, that add uncertainty to the possibility of challenge to our developed or licensed patents and patent applications in the future. Furthermore, for U.S. applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. See the above risk factor titled "*Third party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery and development efforts*."

Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, 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. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing their products to avoid being covered by our claims. If the breadth or strength of protection provided by the 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. Further, if we encounter delays in our clinical trials, the period of time during which we could market product candidates under patent protection would be reduced. Because patent applications in the U.S. and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates.

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. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Litigation or other administrative proceedings challenging our intellectual property, including interferences, derivation, reexamination, *inter partes* reviews and post-grant reviews, 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. Furthermore, there could be public announcement of the results of hearings, motions or other interim proceedings or developments in any proceeding challenging the issuance, scope, validity and enforceability of our developed or licensed intellectual property. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Any of these potential negative developments could impact the scope, validity, enforceability or commercial value of our patent rights and, as a result, have material adverse effect on our business, financial condition, results of operations or prospects.

We may be subject to claims challenging the inventorship of our patents and other intellectual property.

We may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor or other claims challenging the inventorship of our patents or ownership of our intellectual property (including patents and intellectual property that we in-license). For example, the UC/Vienna/Charpentier patent family that is covered by our license agreement with Caribou is co-owned by UC/Vienna and Dr. Charpentier, and our sublicense rights are derived from the first two co-owners and not from Dr. Charpentier. Therefore, our rights to these patents are not exclusive and third parties, including competitors, may have access to intellectual property that is important to our business. In addition, we may have inventorship disputes arise from conflicting obligations of collaborators, consultants or others who are involved in developing our technology and product candidates. Litigation or other legal proceedings may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

We have limited intellectual property rights outside the U.S. Filing, prosecuting, maintaining and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can have a different scope and strength than do those in the U.S. In addition, the laws of some foreign countries, such as China, Brazil, Russia, India and South Africa, do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or adequate to prevent them from competing. In addition, in jurisdictions outside the U.S., a license may not be enforceable unless all the owners of the intellectual property agree or consent to the license. Further, patients may choose to travel to countries in which we do not have intellectual property rights or which do not enforce these rights to obtain the products or treatment from competitors in such countries.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, such as China, Brazil, Russia, India and South Africa, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to biopharmaceutical products, which could make it difficult in those jurisdictions for us to stop the infringement or

misappropriation of our patents or other intellectual property rights, or the marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, such proceedings could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims of infringement or misappropriation against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We may be involved in lawsuits to protect or enforce our patents, the patents of our licensors or our licenses, which could be expensive, time-consuming, and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To cease such infringement or unauthorized use, we may be required to file patent infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding or a declaratory judgment action against us, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

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.

Further, if a party to our licenses, either a licensee or licensor, were to breach or challenge our rights under the relevant license agreement (or if one of our licensor's own licensors were to challenge our licensor's rights), we may have to initiate or participate in a legal proceeding to enforce our rights. Any such legal proceeding could be expensive and time-consuming. In addition, if a court or other tribunal were to rule against us, we could lose key intellectual property and financial rights. Pursuing or defending against these legal claims, regardless of merits, would involve substantial legal expense and would be a substantial diversion of employee resources from our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or contractual litigation there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or proceeding. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court or before the USPTO or comparable foreign authority.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the U.S., 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 U.S. or other jurisdictions, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post-grant review and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity, unpatentability and/or unenforceability, we would lose at least part, and perhaps all, of the

patent protection on our product candidates. For example, as highlighted in the above risk factor entitled "*We could be unsuccessful in obtaining or maintaining adequate patent protection for one or more of our products or product candidates, or asserting and defending our intellectual property rights that protect our products and technologies*", various third parties have filed challenges to the validity of UC/Vienna/Charpentier's European patents, which cover compositions comprising Cas9 and gRNA molecules, as well as methods of editing DNA *in vitro* or *ex vivo* using Cas9 and gRNAs. If UC/Vienna/Charpentier fail in defending the validity of these patents, we may lose valuable intellectual property rights, such as the exclusive right to use such intellectual property. Such an outcome could have a material adverse effect on our business in Europe.

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 our trademarks and trade names 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 and trade names 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 or trade names 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 and trade names, which we need to build name recognition among potential partners or future, potential customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, 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 Potential Disclosure of Confidential Information

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect our proprietary and confidential information. We also utilize proprietary processes for which it would be difficult to enforce patents. In addition, other elements of our product discovery and development processes involve proprietary know-how, information, or technology that is not covered by patents. Trade secrets, however, may be difficult to protect. We seek to protect our proprietary processes, in part, by entering into confidentiality agreements with our employees, consultants, outside scientific advisors, contractors, and collaborators, and we also rely on federal and state laws requiring our directors, employees, contractors and collaborators to protect our proprietary information. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, outside scientific advisors, contractors, and collaborators might intentionally or inadvertently disclose our trade secret information to competitors. In addition, competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, 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 U.S. As a result, we may encounter significant

problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, or misappropriation of our intellectual property by third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results, and financial condition. Our trade secrets and other confidential information of ours may also be exposed through cybersecurity attacks, ransomware attacks, and other hacking attempts directed at our information technology systems and those of our employees, consultants, outside scientific advisors, contractors, vendors and collaborators. For more information, see the risk factor section entitled "Risks Related to Data and Privacy."

We may be subject to claims that our employees, directors, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies as well as academic research institutions. We may be subject to claims that we or our employees, directors, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against these claims, which could result in money damages or a judicial order prohibiting the use of certain intellectual property. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to Our Financial Position and Need for Additional Capital

Risks Related to Past Financial Condition

We have never generated any revenue from product sales and our ability to generate revenue from product sales and become profitable depends significantly on our success in a number of areas.

We have no products approved for commercial sale, have not generated any revenue from product sales, and do not anticipate generating any revenue from product sales until we have received regulatory approval for the commercial sale of one of our product candidates. Our ability to generate revenue, and achieve and retain profitability, depends significantly on our success in many areas, including:

- obtaining regulatory approvals and marketing authorizations for our lead programs;
- obtaining market acceptance of our product candidates as viable treatment options;
- launching and commercializing product candidates for which we obtain regulatory approvals and marketing authorizations, either directly or with a collaborator or distributor;
- accurately assessing the size and addressability of potential patient populations;
- addressing any competing technological and market developments;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding infringement of or obtaining licenses to any valid intellectual property owned or controlled by third parties;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter or which may be necessary for us to develop, manufacture or commercialize our product candidates;
- maintaining good relationships with our collaborators and licensors;
- attracting, hiring and retaining qualified personnel;
- developing a sustainable and scalable manufacturing process for product candidates, including establishing and maintaining commercially viable supply relationships with third parties, such as CMOs, and potentially establishing our own manufacturing capabilities and infrastructure;
- successfully completing research, preclinical and clinical development of product candidates;

- investing resources in developing commercial manufacturing and operational infrastructure prior to clinical evidence of safety and efficacy for a given product candidate; and
- selecting commercially viable product candidates and effective delivery methods.

Even if one or more product candidates that we discover and develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate and the timing of such costs may be out of our control. If we are not able to generate revenue from the sale of any approved products, we may never become profitable.

Our operating history may make difficult the evaluation of our business's success to date and assessment of our future viability.

We are a clinical-stage company. We were founded and commenced operations in mid-2014. All of our product candidates are still in the preclinical development or clinical stage. We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture clinical and commercial scale therapeutics, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Our ability to generate product revenue or profits, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We may never be able to develop or commercialize a marketable product.

Each of our programs may require additional discovery research and then preclinical and clinical development, regulatory approval in multiple jurisdictions, obtaining manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before we generate any revenue from product sales. In addition, our product candidates must be approved for marketing by the FDA, or certain other foreign regulatory agencies, before we may commercialize any product.

Our operating history, particularly in light of the rapidly evolving genome editing field, may make it difficult to evaluate our current business and predict our future performance. Our relatively short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by clinical-stage companies in rapidly evolving fields. If we do not address these risks successfully, our business will suffer.

We have incurred net losses in each period since our inception, anticipate that we will continue to incur net losses in the future and may never achieve profitability.

We are not profitable and have incurred losses in each period since our inception. Our net loss was $481.2 million for the year ended December 31, 2023. As of December 31, 2023, we had an accumulated deficit of $1,658.4 million. We expect these losses to increase as we continue to incur significant research and development and other expenses related to our ongoing operations, seek regulatory approvals for our future product candidates, scale-up manufacturing capabilities, maintain, expand and protect our intellectual property portfolio and hire additional personnel to support the development of our product candidates and to enhance our operational, financial and information management systems. We expect to finance our operations through a combination of collaboration revenue, equity or debt financings or other sources, which may include collaborations with third parties.

A critical aspect of our strategy is to invest significantly in our technology to improve the efficacy and safety of potential product candidates that we discover. Even if we succeed in discovering, developing and ultimately commercializing one or more of these product candidates, we will continue to incur losses for the foreseeable future relating to our substantial research and development expenditures to develop our technologies. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Further, the net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

Risks Related to Future Financial Condition

We may need to raise substantial additional funding to fund our operations. If we fail to obtain additional financing, we may be unable to complete the development and commercialization of any product candidates.

Our operations have required substantial amounts of cash since inception, and we expect to spend substantial amounts of our financial resources on our discovery programs going forward and future development efforts. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development, manufacture (or have manufactured) product candidates and components, and then conduct extensive clinical trials to demonstrate the safety and efficacy of any of our future product candidates in humans. Because preclinical and clinical testing is expensive and can take many years to complete, we may require additional funding to complete these undertakings. Further, if we are able to identify product candidates that are eventually approved, we will require significant additional amounts in order to launch and commercialize our product candidates. For the foreseeable future, we expect to continue to rely on additional financing to achieve our business objectives. 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 drug discovery, preclinical development, laboratory testing and clinical trials for our current or future product candidates, including additional expenses attributable to adjusting our development plans (including any supply related matters).

We will require additional capital for the further development and commercialization of any product candidates and may need to raise additional funds sooner if we choose to expand more rapidly than we presently anticipate or due to other unanticipated factors. Disruptions in the financial markets in general have made equity and debt financing more difficult to obtain, and may have a material adverse effect on our ability to meet our fundraising needs.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development, manufacture or commercialization of our product candidates or other research and development initiatives. Our collaboration and license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements. We could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Raising additional capital may cause dilution to our stockholders and restrict our operations.

We will need additional capital in the future to continue our planned operations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. In addition, the valuation of public companies may require selling equity at lower prices to ensure appropriate capitalization. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Unfavorable national or global economic conditions or political developments could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the national or global economy and financial markets. For example, governmental statements, actions or policies, political unrest and global financial crises can cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, political unrest or additional global financial crises, could result in a variety of risks to our business, including weakened demand for our products, if approved, or our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate, further political developments and financial market conditions could adversely impact our business.

Inadequate funding for, or change of priorities or disruptions at, the FDA and other government agencies in or outside the U.S. could hinder their ability to hire, retain, or deploy key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA and other similar regulatory agencies 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 authorization to accept the payment of user fees, reallocation of resources to address unique or new healthcare issues (or other future public health concerns), and statutory, regulatory, and policy changes. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. 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 Securities and Exchange Commission (the "SEC"), have had to furlough critical FDA, SEC and other government employees and stop critical activities.

If a prolonged government shutdown occurs in the U.S. or other jurisdictions where we plan to conduct our clinical trials, manufacturing, or other operations, it could significantly impact the ability of the relevant agency, such as the FDA, to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Manufacturing and Supply

In vivo ***genome editing products and*** **ex vivo** ***engineered cell therapies based on CRISPR/Cas9 genome editing technology are novel and may be complex and difficult to manufacture. We could experience manufacturing problems 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 CRISPR/Cas9-based *in vivo* and engineered cell therapy product candidates may be complex, as they are novel and have not been validated for late phase clinical and commercial production and may require components that are difficult to obtain or manufacture at the necessary quantities and in accordance with regulatory requirements. Several factors could cause production interruptions, including equipment malfunctions; facility unavailability or contamination; raw material cost, shortages or contamination; natural disasters, such as pandemics or other outbreaks or similar public health crises; disruption in utility services; human error; insufficient personnel; inability to meet legal or regulatory requirements; or disruptions in the operations of our suppliers.

Because our product candidates are regulated as biologics, their processing steps will be more complex than those of most small molecule drugs. Moreover, unlike small molecules, the physical and chemical properties of a complex product such as ours generally cannot be fully characterized. As a result, assays of the finished product or relevant components may not be sufficient to ensure that the product will perform in the intended manner. For this reason, we will employ multiple steps to control the manufacturing process to ensure that the process results in product candidates that meet their specifications, but complications at any one step could adversely impact our manufacturing of products. Further, we may encounter problems achieving adequate quantities and quality of clinical grade materials that meet the FDA or other relevant regulatory agency's applicable standards or our specifications with consistent and acceptable production yields and costs. Manufacturing process irregularities, even minor deviations from the normal process, could result in product defects or manufacturing issues that cause lot failures, product recalls, product liability claims and litigation, insufficient inventory or production interruption. In addition, product manufacturing and supply could be delayed if the FDA and other regulatory authorities require us to submit lot samples, testing results and protocols, or if they require that we not distribute a lot until they authorize the product's release.

Further, certain of our product candidates may require components that are unavailable or difficult to acquire or manufacture at the necessary scale and in compliance with regulatory requirements to support our clinical trials or, if approved, commercial efforts. We expect to continue to rely on third party CMOs to manufacture these components and the final product candidates for the foreseeable future. We may not have full control of these CMOs and they may prioritize other customers or be unable to provide us with enough manufacturing capacity to meet our objectives.

Further, we may rely on CMOs outside the U.S. 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.

We also may encounter problems developing our own manufacturing capabilities, including hiring and retaining the experienced scientific, engineering, quality and manufacturing personnel needed to operate or supervise the necessary manufacturing processes. These issues could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any of these manufacturing and supply issues or delays could restrict our ability to meet clinical or market demand for our products, and be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Further, any problems in manufacturing processes or facilities 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.

Risks Related to Government Regulation

Risks Related to Obtaining Regulatory Approval

While the regulatory framework for approval of gene therapy including genome editing products exists, the limited precedent for genome-edited products makes the regulatory approval process potentially more unpredictable and we may experience significant delays in the clinical development and regulatory approval, if any, of our product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products, including genome editing therapeutics and engineered cell therapies, are subject to extensive regulation by the FDA in the U.S. and other regulatory authorities in other jurisdictions. For example, we are not permitted to market any drug or biological product, including *in vivo* products or engineered cell therapies, until we receive regulatory approval from the relevant regulatory agency, such as the FDA in the U.S. or EMA in the EU. We expect the novel nature of our product candidates to create challenges or raise questions from regulatory agencies in obtaining regulatory approval. For example, in the U.S., the FDA has not approved any *in vivo* gene editing-based therapeutic and has only approved one *ex vivo* CRISPR/Cas9 genome editing therapy for human therapeutic use. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The Advisory Committee's opinion, although not binding, may significantly impact our ability to obtain approval of our product candidates. Moreover, while we are not aware of any specific genetic or biomarker tests for which regulatory approval would be necessary to advance any of our product candidates to clinical trials or commercialization, regulatory agencies could require the development and approval of such tests. Accordingly, the regulatory approval pathway for such product candidates may be uncertain, complex, expensive and lengthy, as well as different in each jurisdiction, and approval may not be obtained in any, some or all jurisdictions.

Other non-regulatory entities may impact the regulatory agencies' and ethics committees' evaluation and approval decision regarding our product candidates. For example, in December 2018, the World Health Organization ("WHO") established the Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing. While the standards are expected to focus primarily on germline modifications, the guidelines could impact somatic cell editing research programs, such as ours. In March 2019, the WHO Expert Advisory Committee recommended initiating the first phase of a new global registry (the "Registry") to track research on human genome editing. Accepting this recommendation, the WHO announced plans in August 2019 for an initial phase of the registry using the International Clinical Trials Registry Platform. This phase will include worldwide registries for both somatic cell editing and germline editing clinical trials. Although registration of these clinical trials in the WHO's Registry currently is voluntary, failure to register could impact the evaluation by the regulators and ethics committees. In July 2021, the WHO Expert Advisory Committee issued recommendations and a governance framework for human genome editing research intended for the international, regional, national and institutional level. For example, the WHO recommended that: clinical trials using somatic human genome editing technologies be reviewed and approved by the appropriate research ethics committee before inclusion in its Registry; basic and preclinical gene editing research also be included in a registry; somatic or germline human genome editing research should only take place in jurisdictions with domestic policy and oversight mechanisms; and relevant patent holders help ensure equitable access to human genome editing interventions. We cannot predict the impact of the WHO's current and future

recommendations, or any policies or actions that ethics committees or regulatory agencies may take in response to such recommendations, on our research, clinical and business plans and results.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including willingness of physicians to use an experimental therapy, the availability of existing treatments, the trial's geographic locations and the number of patients in each geographic location. In addition, our ability to enroll and dose patients may be delayed by the relevant regulatory authority, as well as the IRB or another ethics committee (whether local or national). For example, as set forth in the National Institutes of Health ("NIH") Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ("NIH Guidelines"), gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. Before a clinical trial can begin at any institution, that institution's IRB and its IBC assesses the safety of the research and identifies any potential risk to public health or the environment. 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. Further, a clinical trial may be suspended or terminated by us, the relevant IRBs or ethics committees of the trial, or the FDA or other regulatory authorities, or upon a recommendation of the trial's DMC, due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience termination of, or delays in the completion of, any clinical trial of product candidates, the commercial prospects for such product candidates will be harmed, and our ability to generate product revenue will be impaired. In addition, any delays in completing any clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenue.

We are currently conducting and may in the future conduct other clinical trials for our product candidates outside the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are currently conducting our Phase 3 clinical trial of NTLA-2001, and may in the future conduct clinical trials for our other product candidates, some of which are outside the U.S. The acceptance of data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. The FDA will generally not consider the data from a foreign clinical trial not conducted under an IND unless (i) the trial was well-designed and well-conducted in accordance with good clinical practice ("GCP") requirements, including requirements for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials in a way that provides assurance that the data and reported results are credible and accurate and that the rights, safety, and well-being of trial subjects are protected, and (ii) the FDA is able to validate the data from the trial through an onsite inspection, if necessary. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

We have received orphan drug designation for NTLA-2001 and NTLA-2002 and may in the future seek orphan drug designation for some of our other product candidates, but we may be unable to obtain such designations or to maintain the benefits associated with orphan drug status, including market exclusivity, which may cause our revenue, if any, to be reduced.

Regulatory authorities in some jurisdictions, including the U.S. and Europe, may in response to a request from the sponsor designate products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a product intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the U.S., or a patient population of 200,000 or more in the U.S. when there is no reasonable expectation that the cost of developing and making available the product in the U.S. will be recovered from sales in the U.S. for that product. Orphan drug designation must be requested before submitting a BLA. In the U.S., orphan drug designation entitles a party to financial incentives such as opportunities

for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the product and its potential orphan use are disclosed publicly by the FDA. In the EU, a medicinal product may be designated as orphan if (1) it 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 in 10,000 persons in the EU when the application is made, or (b) it is unlikely that the product, without the 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 a method exists, the product will be of significant benefit to those affected by the condition. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the approval of another marketing application for the same drug for the same indication for that time period. The applicable period is seven years in the U.S. and ten years in the EU (which can be extended to 12 years if the sponsor complies with an agreed-upon pediatric investigation plan). Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In addition, the FDA can subsequently approve a marketing application for the same drug, or a product with the same active moiety, for treatment of the same disease or condition if it concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Similarly, the EMA may grant a marketing authorization to a similar medicinal product for the same indication as an authorized orphan product at any time if it is established that the second product, although similar, is safer, more effective or otherwise clinically superior to the authorized product. The FDA and EMA also can approve a different drug for the same orphan indication, or the same drug for a different indication, during the orphan exclusivity period.

We have received orphan drug designation from the FDA for NTLA-2001 for the treatment of ATTR amyloidosis and from the FDA and European Commission ("EC") for NTLA-2002 for the treatment of HAE. We may seek orphan drug designation for some of our other product candidates in orphan indications in which there is a medically plausible basis for the use of these product candidates. Even where we obtain orphan drug designation, exclusive marketing rights in the U.S. may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we intend to seek orphan drug designation for other product candidates, we may never receive such designations.

The FDA may reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. In addition, the EC introduced a legislative proposal in April 2023 that, if implemented, could reduce the current 10-year marketing exclusivity period in the EU for certain orphan medicines. Depending on what changes the FDA and the EC may make to their orphan drug regulations and policies, our business could be adversely impacted.

We have received regenerative medicine advanced therapy ("RMAT") designation by the FDA for NTLA-2002 for the treatment of HAE, and may in the future seek such designation for some of our product candidates, but such designation may not actually lead to a faster development or regulatory review or approval process and we may be unable to obtain or maintain the benefits associated with such designation.

We have received the RMAT designation from the FDA for NTLA-2002 for the treatment of HAE. A product candidate is eligible for RMAT designation if: (1) it is a cell therapy, therapeutic tissue engineering product, human cell or tissue product, or a combination product using any such therapies or products; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) there is preliminary clinical evidence that indicates that the product candidate has the potential to address unmet medical needs for such disease or condition. This program is intended to facilitate efficient development and expedite review of RMATs. A BLA for a product candidate with RMAT designation may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained

from a meaningful number of sites. Benefits of such designation also include early interactions with the FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A product candidate that has RMAT designation and is subsequently granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence, such as electronic health records, the collection of larger confirmatory data sets, or post-approval monitoring of all patients treated with such therapy prior to its approval. RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for RMAT designation, the FDA may disagree and instead determine not to grant such designation. In any event, the receipt of RMAT designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualifies for RMAT designation, the FDA may later decide that the product candidate no longer meets the conditions for qualification.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA approves a product candidate, comparable regulatory authorities in foreign jurisdictions must also authorize the marketing and sale of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and review periods different from those in the U.S., including additional preclinical studies or clinical trials, as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U.S., a product candidate must be approved for reimbursement before it can be sold in that jurisdiction. In some cases, the price that we are allowed to charge for our products is also subject to approval or to other legal restrictions.

Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the relevant regulatory requirements or to receive applicable marketing approvals, our target markets will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Risks Related to Ongoing Regulatory Obligations

Even if we receive regulatory approval of any product candidates or therapies, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product candidates.

If any of our product candidates are approved, they may be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, distribution, storage, advertising, promotion, sampling, record-keeping, and submission of safety and efficacy data, and other post-market information and potential obligations (such as post-marketing studies), including both federal and state requirements in the U.S. and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with current good manufacturing practice ("cGMP") and GCP, and in certain cases, current good tissue practice ("cGTP"), requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, as applicable, including ensuring that quality control and manufacturing procedures conform to cGMP and, in certain cases, cGTP requirements, and applicable product tracking and tracing requirements. As such, we and our CMOs will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA, other marketing applications, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. For example, the FDA or other regulatory agencies may also require a REMS or similar program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with their respective legal or regulatory requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA or other regulatory agencies may seek to impose consent decrees, withdraw approval or prohibit the export or import of a product if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with our product candidates, including adverse events of unanticipated severity or frequency, or with our third party manufacturers or 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 studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from clinical trials or the market, or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions until issues identified by regulatory inspections are remediated;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA or the relevant regulatory agency to approve pending applications or supplements to approved applications filed by us or suspension or revocation of license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the U.S. market, and the relevant foreign regulatory agencies do the same in their respective jurisdictions. 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.

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.

Our employees, independent contractors, clinical investigators, CMOs, CROs, consultants, collaborators, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of non-compliance, fraud, misconduct or other illegal activity by our employees, independent contractors, clinical investigators, CMOs, CROs, consultants, collaborators, commercial partners and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails to: comply with federal and state laws and those of other applicable jurisdictions; provide true, complete and accurate information to the FDA and other regulatory bodies in the U.S. or outside the U.S.; comply with manufacturing standards; comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and similar foreign privacy or fraudulent misconduct laws; or report financial information or data accurately; or disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the U.S., our potential exposure under such laws will increase significantly, and our costs associated

with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with clinical investigators and research patients, as well as proposed and future sales, marketing and education programs. In particular, the promotion, sales and marketing of healthcare products and services, as well as certain 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 may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, including promotion and marketing of off-label uses of our products, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 governmental 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 or government 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, including the imposition of significant fines or other sanctions.

The exit of the United Kingdom from the EU may result in an increased regulatory burden of conducting business in Europe.

The U.K.'s withdrawal from the EU, or Brexit, became effective on January 31, 2020. On December 24, 2020, the U.K. and EU signed an EU-U.K. Trade and Cooperation Agreement ("TCA"), which became provisionally applicable on January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of cGMP, inspections of manufacturing facilities for medicinal products and cGMP documents issued, but does not provide for wholesale mutual recognition of U.K. and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework currently continues to apply in Northern Ireland). The regulatory regime in Great Britain therefore currently aligns for the most part with EU regulations; however, it is possible that these regimes will diverge more significantly in the future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of U.K. and EU pharmaceutical legislation.

For instance, the new Clinical Trials Regulation which became effective in the EU on January 31, 2022 and provides for a streamlined clinical trial application and assessment procedure covering multiple EU Member States has not been implemented into U.K. law, and a separate application must be submitted for clinical trial authorization in the U.K. In addition, Great Britain is no longer covered by the centralized procedure for obtaining European Economic Area ("EEA")-wide marketing authorizations from the EMA for medicinal products and a separate process for authorization of drug products is required in Great Britain. On January 1, 2024, a new international recognition framework was put in place in the U.K. (known as the International Recognition Procedure, or IRP), whereby the MHRA will have regard to decisions made by certain foreign regulators, including the EMA and the competent authorities of the EU Member States. Under this procedure, the MHRA will take into account the decision-making of such foreign regulators and will conduct a targeted assessment of the applications submitted through the IRP, but will retain the authority to reject applications if the evidence provided is considered insufficiently robust. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would delay or prevent us from commercializing our current or future product candidates in the U.K. and could restrict our ability to generate revenue from that market.

Failure to comply with health and data protection laws and regulations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business.

We and many of our existing or potential collaborators, clinical investigators, CMOs, CROs, consultants or vendors are subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the U.S., numerous federal and state laws and regulations, including federal health information privacy laws, state data breach notification laws, state health information privacy laws, and federal and

state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information could apply to our operations or the operations of our collaborators. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), or by comparable laws in other jurisdictions. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a covered entity in a manner that is not authorized or permitted by laws or regulations.

Compliance with U.S., both state and federal, and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with these laws and regulations could result in government enforcement actions (which could include civil, criminal and administrative penalties), private litigation, and/or adverse publicity and could negatively affect our operating results and business. Moreover, clinical trial subjects, employees and other individuals about whom we or our existing or potential collaborators obtain personal information, as well as the providers who share this information with us, may limit our ability to collect, use and disclose the information. 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.

If we, or our collaborators, clinical investigators, CMOs, CROs, consultants or vendors, fail to comply with environmental, health and safety, and laboratory animal welfare laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We and many of our existing or potential collaborators, clinical investigators, CMOs, CROs, consultants or vendors are subject to numerous federal, state and local environmental, health and safety, and laboratory animal welfare laws and regulations. These legal requirements include those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes, as well as those which regulate the care and use of animals in research. Our operations, and those of our collaborators, clinical investigators, CMOs, CROs, consultants or vendors, acting on our behalf, may involve research using research animals and the use of hazardous and flammable materials, including chemicals and biological materials. Our operations, and those of our collaborators, clinical investigators, CMOs, CROs, consultants or vendors, acting on our behalf, also may produce hazardous waste products. We generally anticipate contracting with third parties for the disposal of these materials and waste. 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.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety, and laboratory animal welfare 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.

Failure to comply with labor and employment laws and regulations could subject us to legal liability and costs, including fines or penalties, as well as reputational damage that could harm our business.

We are subject to numerous federal, state and local laws and regulations relating to the recruiting, hiring, compensation and treatment of employees and contractors. These laws and regulations cover financial compensation (including wage and hour standards), benefits (including insurance and 401(k) plans), discrimination, workplace safety and health, and workers' compensation.

The Commonwealth of Massachusetts, where most of our employees are based, also has laws that expand on federal laws or create additional rights for employees or obligations for employers. For example, on July 1, 2018, the Massachusetts Equal Pay Act went into effect, which added protections employers must comply with regarding pay equity for "comparable work". There is currently uncertainty regarding the exact scope of these new legal limits and such uncertainty may remain for the foreseeable future. We may face increased employment and legal costs to ensure we are complying with this law. In addition, on October 1, 2018, a new Massachusetts non-compete law went into effect, placing additional restrictions on employers seeking to enter into non-competition agreements with employees. Further, other jurisdictions in which our employees may work limit enforcement of non-competition agreements. For example, in California non-competition agreements with employees are generally unenforceable after termination of employment and Illinois contains strict laws affecting the enforcement of non-competition agreements. These non-compete laws may negatively impact our ability to prevent employees from working with direct or indirect competitors in the future and may affect our ability to retain key talent in a competitive market.

Our failure to comply with these and other related laws could expose us to civil and, in some cases, criminal liability, including fines and penalties. Further, government or employee claims that we have violated any of these laws, even if ultimately disproven, could result in increased expense and management distraction, as well as have an adverse reputational impact on us.

Risks Related to Our Reliance on Third Parties

Risks Related to Our Reliance on Collaboration Partners

Our technological advancements and any potential for revenue may be derived in part from our collaborations, including, for example, with Regeneron, and if the collaboration or co-development agreements related to a material collaboration were to be terminated or materially altered in an adverse manner, our business, financial condition, results of operations and prospects would be harmed.

We rely on strategic collaborations to advance our technology and co-develop products that we plan to co-commercialize. If our collaboration partner in a material collaboration fails to develop, obtain regulatory approval for or ultimately commercialize any product candidate from the development programs governed by the respective collaboration agreements, including, e.g., a co-development or co-commercialization agreement, or breaches or terminates our collaboration with it, our business, financial condition, results of operations and prospects could be harmed. In addition, any material alteration, in an adverse manner, of any material collaboration agreement, or dispute or litigation proceedings we may have related to a material collaboration in the future could delay development programs, create uncertainty as to ownership of or access to intellectual property rights, distract management from other business activities and generate substantial expense.

As described within Note 9 "Collaborations and Other Arrangements" of this Annual Report on Form 10-K, we have entered into co-development and co-promotion arrangements with Regeneron. Regeneron may change its strategic focus or pursue alternative technologies in a manner that results in reduced, delayed or no revenue to us under these arrangements. For example, Regeneron has a variety of marketed products and product candidates either by itself or with other companies, including some of our competitors. In addition, the corporate objectives of our collaborators, such as Regeneron, may not be consistent with our best interests. Regeneron may change its position regarding its participation and funding of our joint activities, which may impact our ability to successfully pursue those programs.

Our existing and future collaborations will be important to our business. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.

We have limited capabilities for product development and do not yet have any capability for sales, marketing or distribution. Accordingly, we have entered, and plan to enter, into collaborations with other companies, including our therapeutic-focused collaboration agreements with Regeneron, which we believe can provide such capabilities. For example, in October 2023, we announced an expanded research collaboration with Regeneron to develop therapies for the treatment of neurological and muscular diseases. These current and future therapeutic-focused collaborations could provide us with important technologies and/or funding for our programs and technology. Our existing and future therapeutic collaborations may have a number of risks, including that collaborators:

- have significant discretion in determining the efforts and resources that they will apply;

- may not perform their obligations as expected;
- may dispute the amounts of payments owed;
- may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs or license arrangements based on clinical trial results, changes in their strategic focus or available funding, or external factors, such as a strategic transaction that may divert resources or create competing priorities;
- may delay, insufficiently fund, stop, initiate new or repeat clinical trials, reformulate a product candidate for clinical testing, or abandon a product candidate;
- could develop independently, or with third parties, products that compete directly or indirectly with our products and product candidates;
- may view product candidates discovered in our collaborations as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the development or commercialization of our product candidates;
- may dispute ownership or rights in jointly developed technologies or intellectual property;
- may fail to comply with applicable legal and regulatory requirements regarding the development, manufacture, sale, distribution or marketing of a product candidate or product;
- with sales, marketing, manufacturing and distribution rights to our product candidates may not commit sufficient resources to the product's sale, marketing, manufacturing and distribution;
- may disagree with us about material issues, including proprietary rights, contract interpretation, payment obligations or the preferred course of discovery, development, sales or marketing, which might cause delays or terminations of the research, development or commercialization of product candidates, lead to additional and burdensome responsibilities for us with respect to product candidates, or result in litigation or arbitration, any of which would be time-consuming and expensive;
- may not properly maintain or defend their or our relevant intellectual property rights or may use our proprietary information or sublicensed intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation and liability;
- may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- could become involved in a business combination or cessation that could cause them to deemphasize or terminate the development or commercialization of any product candidate licensed to it by us; and
- may terminate our collaborations, which could require us to raise additional capital to develop or commercialize the applicable product candidates, or lose access to the collaborator's intellectual property.

If our therapeutic collaborations do not result in the successful discovery, development and commercialization of products or if a collaborator terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. All of the risks relating to product discovery, development, regulatory approval and commercialization summarized and described in this report also apply to the activities of our therapeutic collaborators.

Additionally, if one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

As part of our business strategy, we may pursue acquisitions or licenses of assets or acquisitions of businesses, or disposition of assets or technologies. For example, in February 2022, we announced the acquisition of Rewrite in order to add additional capabilities to our growing platform, which acquisition included an exclusive license from the Regents of the University of California under certain patents related to DNA writing technology. We also may pursue strategic alliances and joint ventures that leverage our core technology and industry experience. If we decide to

collaborate with other companies to discover, develop and commercialize therapeutic products, we face significant competition in seeking appropriate collaborators because, for example, third parties have comparable rights to the CRISPR/Cas9 system or similar genome editing technologies. In addition, we have limited experience with acquiring, disposing of or licensing assets or forming strategic alliances and joint ventures. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail, delay or abandon discovery efforts or development programs, and the development, manufacture or commercialization of a product candidate, or increase our expenditures and undertake these activities at our own expense. If we elect to fund and undertake discovery, development, manufacturing or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary discovery, development, manufacturing and commercialization activities, we may not be able to further develop our product candidates, manufacture the product candidates, bring them to market or continue to develop our technology and our business may be materially and adversely affected. Furthermore, we may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the anticipated benefits of any acquisition, license, strategic alliance or joint venture.

Risks Related to AvenCell

We launched a new company, AvenCell, alongside Cellex Cell Professionals GmbH and Blackstone Life Sciences Advisors L.L.C. We are exposed to risks associated with the launch of the new company and may not realize the advantages we expect from it.

In July 2021, we launched AvenCell Therapeutics, Inc. ("AvenCell") alongside Cellex Cell Professionals GmbH ("Cellex") and Blackstone Life Sciences Advisors L.L.C. ("BXLS"). AvenCell acquired GEMoaB GmbH ("GEMoaB"), a wholly owned subsidiary of Cellex. AvenCell combines GEMoaB's clinical-stage universal CAR-T program and platforms with our allogeneic universal cell engineering platform, which we licensed to AvenCell pursuant to a license and collaboration agreement with AvenCell (the "AvenCell License"). Under the AvenCell License, we will collaborate with AvenCell to develop at least seven allogeneic universal CAR-T cell therapies. AvenCell may not be successful in the timeframe we expect, or at all. We, BXLS, and Cellex (together with certain related entities) each have equal ownership of AvenCell and, therefore, share control over portions of the operations of AvenCell. Other than our ownership interest in AvenCell and the potential to co-develop with AvenCell an allogeneic universal CAR-T cell therapy, we do not receive any financial benefit from AvenCell. Because of our minority ownership in AvenCell, we have a lesser degree of control over its business operations than our own, thereby potentially increasing the financial, legal, operational and compliance risks Intellia may face in the future. In addition, we may be dependent on controlling shareholders or management of AvenCell who may have business interests, strategies or goals that are inconsistent with ours. These risks include the possibility that AvenCell, BXLS or Cellex has economic or business interests or goals that are or become inconsistent with our economic or business interests or goals; is in a position to take action contrary to our instructions, requests, policies or objectives; subjects us to unexpected liabilities or risks; takes actions that reduce our return on investment, including reducing or eliminating the value of our ownership in AvenCell and related financial benefits; acts in a manner that compromises our key licensed rights, or important IP or other rights that we own or license; or takes actions that harm our reputation or restrict our ability to run our business. Furthermore, as a result of our ownership in AvenCell, we are required to include AvenCell's financial information in our consolidated financial results. This could subject us to increased risk in accurately representing and incorporating AvenCell's financial statements into our own, which could result in delayed filings with the SEC and the finding of a material or significant weakness, among others. This could result in harmful consequences to our business, including an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

Risks Related to Our Reliance on Other Third Parties

We currently rely, and expect to continue to rely in part 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, if approved. Our business could be harmed if the third parties fail to provide us with sufficient quantities of product inputs or fail to do so at acceptable quality levels or prices or fail to meet legal and regulatory requirements.

We are in the early stages of establishing our own manufacturing facility to provide preclinical, clinical and commercial supply of our product candidates and must rely on outside vendors, such as CMOs, to manufacture supplies and process our product candidates. We have only recently begun to manufacture and process product candidate components on a clinical scale and may not be able to successfully complete or continue to do so. We will make changes to optimize the manufacturing process, and cannot be sure that even minor changes in the process will result in therapies that are safe, pure and potent. We are also unable to predict how changing global economic conditions or ongoing geopolitical conflicts and related global economic sanctions, or potential global health concerns will affect our third party suppliers and manufacturers. Any negative impact of such matters on our third party suppliers and manufacturers may also have an adverse impact on our results of operations or financial condition.

Any facility that we may have in the future and the facilities used by our CMOs to manufacture our product candidates must be inspected and approved by, as applicable, the FDA or other foreign regulatory agencies after we apply for approval or marketing authorization. For the foreseeable future, we will be dependent on our CMO partners to properly manufacture adequate supply of our product candidates and components in a timely manner and in accordance with our specification. We also will depend on these entities for compliance with relevant legal and regulatory requirements for manufacture of our product candidates, including cGMP, and in certain cases, cGTP requirements. If we or our CMOs cannot successfully manufacture material that conforms to our specifications and the strict relevant regulatory requirements, we and our CMOs will not be able to secure or maintain regulatory approval for our respective manufacturing facilities. In addition, we have no control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel, particularly as we increase the scale of our manufactured material. If the FDA or relevant foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval, 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 any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we may not be able to do on reasonable terms, if at all. In such scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our product candidates may be unique to the original CMO and we may have difficulty transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

We currently rely, and expect to continue to rely on, third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with legal and regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any potential product candidates.

We currently depend, and expect to continue to depend, upon third parties, including independent investigators, to conduct our clinical trials under agreements with universities, medical institutions, CROs, strategic partners and others. We expect to have to negotiate budgets and contracts with CROs, trial sites and other service and goods providers, which may result in delays to our development timelines and increased costs. For example, in February

2023, the U.S. Department of Justice investigated the research practices of a significant CRO with respect to their non-human primate imports. Issues of that nature may affect our ability to conduct preclinical studies that are required to advance our product candidates.

We currently rely, and expect to continue to rely heavily, on third parties over the course of our preclinical studies and clinical trials, and, as a result, will have limited control over the clinical investigators and other service providers, and limited visibility into their day-to-day activities, including with respect to their compliance with the approved clinical protocol and other legal, regulatory and scientific standards. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our legal responsibilities. We and these third parties are required to comply with GCP, which are regulations and guidelines enforced by the FDA, EMA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the relevant regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP, and in certain cases, cGTP, requirements and may require a large number of test articles for studies involving a large number of test patients.

Our or these third parties' failure to comply with these requirements or to recruit a sufficient number of patients may require us to delay, suspend, repeat or terminate clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates applicable federal, state or local, as well as foreign, laws and regulations, such as the fraud and abuse or false claims laws and regulations or privacy and security laws. In jurisdictions such as the U.K. and EU, penalties for violations of privacy laws and other regulations can be financially significant. Further, if any of our CROs, clinical investigators or others involved in our clinical trials fail to comply with such laws and regulations, we could be held responsible for its actions or omissions and be negatively impacted. In the event of non-compliance with the U.K.'s Data Protection Act 2018 and the U.K. General Data Protection Regulation ("U.K. GDPR") (such laws collectively being described as "European Data Protection Law"), we could be subject to substantial fines and other penalties, including fines of up to 10,000,000 Euros or up to 2% of our total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to 4% of our total worldwide annual turnover for more serious offenses.

Any third parties conducting our current or future clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether they devote sufficient time and resources to our ongoing preclinical, clinical, and nonclinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties fail to meet their contractual obligations, legal requirements or expected deadlines, need to be replaced, or generate inaccurate or substandard clinical data by failing to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

A resurgence of the COVID-19 pandemic (or other future public health concern) and measures taken in response by U.S. or other governments may have a significant impact on our CROs, clinical sites and other service and goods providers, which may affect our ability to initiate and complete preclinical studies and clinical trials.

If any of our relationships with these third party CROs, clinical sites or other third parties terminate, we may not be able to enter into arrangements with alternative CROs, clinical sites or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs, clinical sites or other providers involves additional cost and requires management time and focus. In addition, the transition to a new CRO may result in delays, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with these parties, there can be no assurance that we will not encounter similar challenges or delays in

the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Risks Related to Data and 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 operations and development efforts.

We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business. In the ordinary course of business, we collect, store, and transmit large amounts of confidential information (including but not limited to intellectual property, such as trade secrets, proprietary business information, and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have also outsourced elements of our operations to third parties, and as a result we manage a number of third party vendors who may or could have access to our confidential information. Our third party collaborators, vendors and service providers (including our CMOs and CROs) also have access to large amounts of confidential information relating to our operations, including our research and development efforts. The size and complexity of our information technology systems, and those of third party vendors, service providers and collaborators, and the large amounts of confidential information stored on those systems, make such systems potentially vulnerable to service interruptions or systems failures, or to security breaches from inadvertent or intentional actions by our employees, third party vendors, service providers, collaborators, and/or business partners, or from cyber-attacks by malicious third parties.

In addition to such risks, the adoption of new technologies may also increase our exposure to cybersecurity breaches and failures. Further, having a significant portion of our workforce working from home for extended periods of time puts us at greater risk of cybersecurity attacks. Cyber-attacks are increasing in their frequency, sophistication, and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, denial-of-service attacks, attacks enhanced or facilitated by artificial intelligence ("AI"), social engineering, "phishing" scams, ransomware, network security breaches, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information. Certain of our service providers have been subject to such attacks in the past, and while no such attacks have resulted in a material impact to our business, our company or our service providers may be materially impacted by such attacks in the future. Significant disruptions to our information technology systems could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including but not limited to trade secrets or other intellectual property, proprietary business information, and personal information), and could result in financial, legal, business, and reputational harm to us and would adversely affect our operations, including our discovery and research and development programs. Any security breaches that lead to unauthorized access, use, or disclosure of personal information, including personal information regarding our employees or current or future clinical trial participants, could harm our reputation, require us to comply with onerous legal requirements under laws and regulations that protect the privacy and security of personal information, and subject us to significant liability including fines, litigation, and loss of current and future business.

Also, the loss of preclinical or clinical trial data from completed or future preclinical or clinical trials, respectively, 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. Security breaches, insider threats and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the types summarized and described above. While we have implemented security measures to protect our information technology systems and infrastructure, there is no assurance that such measures will prevent service interruptions or security breaches or incidents that could adversely affect our business.

Interruptions in the availability of server systems or communications with internet or cloud-based services, or failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems, could harm our business.

We rely upon a variety of internet service providers, third party web hosting facilities, cloud computing platform providers and software as a service ("SaaS") vendors to support our business. Failure to maintain the security, confidentiality, accessibility or integrity of data stored on such systems could result in interruptions in our operations, damage our reputation in the market, increase our service costs, cause us to incur substantial costs, subject us to liability for damages and/or fines, and divert our resources from other tasks, any one of which could materially adversely affect our business, financial condition, results of operations and prospects. If our security measures or those of our third party data center hosting facilities, cloud computing platform providers, SaaS vendors or third party service partners, are breached, and unauthorized access is obtained to our data or our information technology systems, we may incur significant legal and financial exposure and liabilities.

We also do not have control over the operations of the facilities of our cloud service providers, SaaS vendors or our third party web hosting providers, and they also may be vulnerable to damage or interruption from natural disasters, hardware or software outages, cybersecurity attacks, terrorist attacks and similar events or acts of misconduct. In addition, any changes in these providers' service levels may adversely affect our ability to meet our requirements and operate our business.

Social media platforms and artificial intelligence-based platforms present new risks and challenges to our business.

As social media continues to expand, it also presents us with new risks and challenges. Social media is increasingly being used to communicate information about us, our programs and the diseases our therapeutics are being developed to treat. Social media practices in the pharmaceutical and biotechnology industries are evolving, which creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media platforms to comment on the effectiveness of, or adverse experiences with, a product or a product candidate, which could result in reporting obligations or other consequences. Further, the accidental or intentional disclosure of non-public information by our workforce or others through media channels could lead to information loss. In addition, there is a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us, our products, or our product candidates on any social media platform. The nature of social media prevents us from having real-time control over postings about us on social media. We may not be able to reverse damage to our reputation from negative publicity or adverse information posted on social media platforms or similar mediums. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business including quick and irreversible damage to our reputation, brand image and goodwill. While we have undertaken measures to restrict the use of public AI platforms, their use by people, including our vendors, suppliers and contractors, with access to our proprietary and confidential information, including trade secrets, may continue to increase and may lead to the release of such information, which may impact our ability to realize the benefit of our intellectual property.

Risks Related to Competition

We face significant competition in an environment of rapid technological change. The possibility that our competitors may achieve regulatory approval before we do or develop therapies that are more advanced or effective than ours may harm our business and financial condition or our ability to successfully market or commercialize our product candidates.

The biotechnology and pharmaceutical industries are extremely competitive in the race to develop new products. While we believe we have significant competitive advantages with our industry-leading expertise in genome editing, clinical development expertise and dominant IP position, we currently face and will continue to face competition for our development programs from companies that use genome editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities such as small molecules and antibodies. The competition is likely to come from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions. Many of these competitors may have access to greater capital and resources than us. 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.

Specific to our NTLA-2001 program, we are aware of other companies that are currently commercializing or developing products and therapies used to treat ATTR amyloidosis, including Alnylam Pharmaceuticals, Inc., AstraZeneca Pharmaceuticals LP, BridgeBio Pharma Inc., Ionis Pharmaceuticals, Inc., Metagenomi Technologies, LLC, Novo Nordisk A/S and Pfizer, Inc.

Specific to our NTLA-2002 program, we are aware of other companies that are currently commercializing or developing products used to treat HAE, including ADARx Therapeutics, Inc., Astria Therapeutics Inc., BioCryst Pharmaceuticals Inc., BioMarin Pharmaceuticals Inc., CSL Limited, Ionis Pharmaceuticals, Inc., KalVista Pharmaceuticals, Inc., Pharming Group N.V., Pharvaris N.V. and Takeda Pharmaceutical Company Limited.

Competitors in our efforts to provide other genetic therapies to patients can be grouped into at least three sets based on their product discovery platforms:

Our platform and product foci are on the development of therapies using CRISPR-based technologies. Genome editing companies focused on CRISPR-based technologies include: Beam Therapeutics Inc., Caribou Biosciences, Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Metagenomi Technologies, LLC, Prime Medicine, Inc., ToolGen, Inc. and Verve Therapeutics Inc.

There are also companies developing therapies using additional genome editing technologies, which include Allogene Therapeutics, Inc., bluebird bio, Inc., Cellectis S.A., Homology Medicines, Inc., Poseida Therapeutics, Inc., Precision Biosciences, Inc., Prime Medicine, Inc. and Sangamo Therapeutics, Inc.

We are also aware of companies developing therapies in various areas related to our specific research and development programs. For *ex vivo*, these companies include Allogene Therapeutics, Inc., Cellectis S.A., CRISPR Therapeutics AG and Precision BioSciences, Inc. For *in vivo*, these companies include CRISPR Therapeutics AG, Editas Medicine, Inc., Excision Biotherapeutics, Inc., Locus Biosciences, Inc. Metagenomi Technologies, LLC, Precision Biosciences, Inc. and Verve Therapeutics Inc.

Our competitors will also include companies that are or will be developing other genome editing methods as well as small molecules, biologics, *in vivo* gene therapies, engineered cell therapies and nucleic acid-based therapies for the same indications that we are targeting with our CRISPR/Cas9-based therapeutics.

Any advances in gene therapy, engineered cell therapies or genome editing technology made by a competitor may be used to develop therapies that could compete against any of our product candidates.

Many of these competitors have substantially greater research and development capabilities and financial, scientific, technical, intellectual property, manufacturing, marketing, distribution and other resources than we do, and we may not be able to successfully compete with them.

Even if we are successful in selecting and developing any product candidates, in order to compete successfully we may need to be first-to-market or demonstrate that our CRISPR/Cas9-based products are superior to therapies based on the same or different treatment methods. If we are not first-to-market or are unable to demonstrate such superiority, any products for which we are able to obtain approval may not be commercially successful. Furthermore, in certain jurisdictions, if a competitor has orphan drug status for a product and if our product candidate is determined to be contained within the scope of a competitor's orphan drug exclusivity, then approval of our product for that indication or disease could potentially be blocked, for example, for up to seven years in the U.S. and 10 years in the EU.

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. 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.

Risks Related to Commercialization

If, in the future, we are unable to establish sales, marketing and distribution capabilities or enter into agreements with third parties to sell, market and distribute products based on our technologies, we may not be successful in commercializing our products if and when any product candidates or therapies are approved and we may not be able to generate any revenue.

We do not currently have a sales, marketing or distribution 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. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services.

Factors that may inhibit our efforts to commercialize our product candidates 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 candidates 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;
- the location of patients in need of our product candidates and the treating physicians who may prescribe the products; and
- unforeseen costs and expenses, as well as legal and regulatory requirements, associated with creating and operating a sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, we would likely have lower product revenue or profitability than if we ourselves were to market and sell our product candidates. In addition, we may be unable to enter into sales and marketing arrangements with third parties, or into arrangements with 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, marketing and distribution capabilities successfully, either on our own or through third parties, we may not be successful in commercializing our product candidates, and our business, results of operations, financial condition and prospects will be materially adversely affected.

Risks Related to Employee Matters and Managing Our Workforce

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, manufacturing, commercialization, legal, financial and business development expertise of John M. Leonard, M.D., our President and Chief Executive Officer, James Basta, our Executive Vice President, General Counsel and Corporate Secretary, Eliana Clark, our Executive Vice President and Chief Technical Officer, Glenn Goddard, our Executive Vice President, Chief Financial Officer and Treasurer, Derek Hicks, our Executive Vice President and Chief Business Officer, David Lebwohl, our Executive Vice President and Chief Medical Officer, and Laura Sepp-Lorenzino, our Executive Vice President and Chief Scientific Officer, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment arrangements 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.

Execution of our business plans and strategies requires capable personnel with specialized skills and expertise in the research, development, manufacturing and commercialization of biopharmaceutical products, and, as a result, we may encounter difficulties in hiring or retaining capable personnel in key positions.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be important for our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives, and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products using our technology. Competition to hire from this limited pool is intense, and 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, universities and research institutions for similar personnel. The market for qualified personnel in the biotechnology space generally, and genome editing and gene therapy fields in particular, in and around the Cambridge, Massachusetts area is especially competitive. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategies. 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. Further, some of the qualified personnel that we hire and recruit are not U.S. citizens, and there is uncertainty with regard to their future employment status due to the current U.S. administration's announced intention of modifying the legal framework for non-U.S. citizens to be employed in the U.S. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks Related to Healthcare

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, if approved, which could make it difficult for us to sell any product candidates or therapies profitably.

The success of our product candidates, if approved, depends on the availability of adequate coverage and reimbursement from third party payors, including government agencies, private health insurers and health maintenance organizations. There is significant uncertainty related to the insurance coverage and reimbursement of any newly approved product, but in particular novel genome editing and engineered cell products. All the therapeutic indications approved by the relevant authorities may not be covered or reimbursed. In addition, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates because they are novel treatments for diseases using a new technology and delivery approaches. For more information on coverage and reimbursement see the section entitled **"Business – Government Regulation and Product Approval –** ***Coverage and Reimbursement.***"

In the U.S. and some other jurisdictions, patients generally rely on third party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the U.S., and commercial payors are critical to new product acceptance.

Government authorities and other third party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. In the U.S., the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services ("CMS"), an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare, and private payors often follow CMS's coverage decisions. Other jurisdictions have agencies, such as the National Institute for Health and Care Excellence in the U.K., that evaluate the use and cost-effectiveness of therapies, which impact the utilization and price of the medicine in such jurisdiction.

In the U.S., no uniform policy of coverage and reimbursement for products exists among third party payors. As a result, obtaining coverage and reimbursement approval of a product from a third party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each potential payor, with no assurance that coverage and adequate reimbursement will be obtained from all or any of them. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might be insufficient or may require co-payments that patients find unacceptably high, which may prevent us from

achieving or sustaining profitability. Additionally, third party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our genome editing products.

In addition, each country in which we seek approval to market our product candidates has unique laws and market practices regulating coverage and reimbursement for human therapeutics. Market acceptance and sales of our products in each country will depend on our ability to meet each of these jurisdiction's requirements for coverage and reimbursement. Further, changes to the country's existing requirements may also affect our ability to commercialize our products in the future, or achieve profitability from their sale.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payment transparency laws, health information privacy and security laws and anti-corruption laws. If we are unable to comply, or have not fully complied, with such laws or their relevant foreign counterparts, we could face substantial penalties.

The sale, distribution and marketing of human therapeutics and our relationship with healthcare providers are strictly regulated by laws in the U.S. and most other jurisdictions in which we intend to seek approval for our product candidates. In addition, the collection and use of personal information, including Protected Health Information ("PHI"), is regulated by federal, state and foreign privacy, data security and data protection laws. Failure to comply with these laws could impair our ability to properly sell our product candidates in particular jurisdictions and subject us to liability from private and governmental entities. Addressing these diverse and sometimes contradictory requirements in myriad jurisdictions may necessitate that we expend significant resources on compliance efforts. Any failure to comply with these requirements may leave us exposed to possible enforcement actions and potential liability. For more information on these laws and regulations see the section titled "**Business – Government Regulation and Product Approval –** ***Other Healthcare and Privacy Laws****."*

The scope and enforcement of each of these laws is not always certain and is subject to legislative, judicial or prosecutorial changes. Further, because of the breadth of these laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Indeed, U.S. federal and state enforcement bodies have increasingly scrutinized healthcare companies and providers interactions, which has led to a number of investigations, prosecutions, convictions and settlements in the industry. Ensuring business arrangements comply with applicable laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert the attention of our staff and resources from performing the duties required for the general operation of our business.

The increasingly global nature of our business operations, including clinical development efforts, subjects us to domestic and foreign anti-bribery and anti-corruption laws and regulations, such as the Foreign Corrupt Practices Act ("FCPA") and the U.K. Bribery Act. These activities create the risk of unauthorized payments or offers of payments that are prohibited under the FCPA, the U.K. Bribery Act or similar laws. It is our policy to implement safeguards to discourage these practices by our employees and agents. However, these safeguards may ultimately prove ineffective, and our employees, consultants, and agents may engage in conduct for which we might be held responsible. Violations of the FCPA may result in severe criminal or civil sanctions, and we may be subject to other liabilities, which could negatively affect our business, operating results and financial condition.

Further, the U.S. federal and state governments, as well as other jurisdictions, have myriad laws regulating the collection, storage, distribution, safeguarding and use of personal information of employees, patients, agents, and others. These different laws governing the privacy and security of health and other personal information often differ from each other in significant ways and may not have the same effective requirements, thus complicating efforts to comply with their respective provisions. For example:

- in the U.S., HIPAA, as amended by HITECH, imposes requirements relating to the privacy, security and transmission of PHI on certain covered healthcare providers, health plans, and healthcare clearinghouses, and their respective business associates that perform services for them that involve the use or disclosure of such information. These laws impose civil and criminal monetary penalties, and give state attorneys general the authority to file civil actions for damages or injunctions, and attorney's fees, in federal courts to enforce the laws;

- the California Consumer Privacy Act ("CCPA") requires covered companies to provide disclosures to California consumers and afford such consumers rights with respect to their personal information, including the rights to: request deletion of their information, receive the information on record for them, know what categories of information are being maintained about them, and opt-out of certain sales of their information. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches that result in the loss of personal information, which may increase the likelihood of, and risks associated with, data breach litigation. The CCPA was amended by the California Privacy Rights Act ("CPRA"), which became effective on January 1, 2023. The CPRA substantially modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information, by establishing a state agency vested with the authority to enforce the CCPA and by creating additional obligations with respect to the processing of personal information, including regulating personal information collected about employees, applicants and retirees as well as that which is collected in a business to business capacity. We anticipate additional costs associated with CCPA and other U.S. state privacy law compliance and we cannot yet fully determine the impact that such laws, regulations and standards may have on our business;

- broad consumer privacy and data protection laws have been or are predicted to be passed in a number of additional states. Many state privacy and data protection laws differ from each other in significant ways, and it is not yet fully clear how these laws will be enforced and interpreted. In addition, other states have passed laws regulating specific aspects of privacy. For example, the State of Washington recently passed a law that regulates health and medical information that is not subject to HIPAA and a small number of states have enacted laws that specifically target the collection and use of biometric information. Furthermore, other U.S. states have enacted stringent data security laws; and

- around the world, many countries have enacted laws that regulate data protection. In the EU and EEA the collection and use of personal data is regulated by the General Data Protection Regulation and the member states' related data protection and privacy laws, and in the U.K. by the U.K. GDPR. Because the European Data Protection Law applies not only to businesses that are established within the EEA or the U.K. but also to any business that offers goods or services to individuals in those territories, it could apply to us. European Data Protection Law imposes strict requirements, including special protections for "sensitive" personal data which includes health and genetic information of individuals in the EEA or the U.K.; expanded disclosures about the personal data use; information retention limitations; mandatory data breach notification requirements; and additional oversight obligations relating to third parties retained to process the personal data. European Data Protection Law grants or enhances the rights of individuals with respect to their personal data, including the rights to object to the processing of the data and request deletion of the same. In addition, European Data Protection Laws include strict requirements on, and prohibit, the transfer of personal data subject to European Data Protection Law to jurisdictions that have not been deemed by competent authorities to offer "adequate" privacy protections ("third countries"), unless a derogation exists or a valid European Data Protection Law transfer mechanism (for example, the EC approved Standard Contractual Clauses, certification to the EU-U.S. Data Privacy Framework (which allows for transfers for relevant U.S.-based organizations who self-certify compliance and participate in the framework) and the U.K. International Data Transfer Agreement/Addendum) has been put in place and a transfer impact assessment has been carried out. Our compliance with international data transfer obligations under European Data Protection Law, where applicable, may require significant effort and cost, and may limit our ability to transfer such personal data to other jurisdictions or to work with certain service providers that process personal data, and may require us to make strategic considerations around where such personal data is stored. Further, although the EC has acknowledged that the U.K. currently has adequate protections for international data transfers, there may be post-Brexit developments in the future that result in additional costs and operational challenges in complying with the U.K. GDPR and any other developments regulating the transfer of personal data between the U.K. and EU. For example, the U.K. government has now introduced a Data Protection and Digital Information Bill (the "U.K. Bill") into the U.K. legislative process. The aim of the U.K. Bill is to reform the U.K.'s data protection regime following Brexit. If passed, the final version of the U.K. Bill may have the effect of further altering the similarities between the U.K. and EEA data protection regime and threaten the U.K. adequacy decision from the EC. Failure to comply with the requirements of the European Data Protection Law may result in warning letters, mandatory audits, orders to cease/change the use of data, and financial penalties, including fines of up to 4% of global revenues, or 20.0 million Euros (£17.5 million in the U.K.), whichever is

greater. Moreover, data subjects can seek damages for violations, and non-profit organizations can bring claims on behalf of data subjects.

The costs associated with ensuring compliance with these laws, including in particular European Data Protection Law, may be onerous and may adversely affect our business, financial condition, results of operations and prospects. We may also need to rely on multiple third parties, such as partners and service providers, to meet these legal requirements, which could result in additional liability for us if they do not comply.

Efforts to ensure that we comply with all applicable healthcare and data privacy laws and regulations, as well as other domestic and foreign legal requirements, will involve substantial costs. It is possible that governmental and enforcement authorities in the U.S. or outside the U.S. will conclude that our business practices do not comply with current or future legal requirements. If any noncompliance actions are instituted against us, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, individual imprisonment, exclusion from participation in federal healthcare programs (such as Medicare and Medicaid), contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and affect the results of our operations. Any action alleging a violation of these laws, even if successfully defended, could result in significant legal expenses and divert management's attention from the operation of the business. Prohibitions or restrictions on sales (including importation or exportation) or withdrawal of future marketed products could materially affect business in an adverse way.

Healthcare cost control initiatives, including healthcare legislative and regulatory reform measures, may have a material adverse effect on our business and results of operations.

The U.S. and many other jurisdictions have enacted or proposed legal changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates, affect our ability to profitably sell our product candidates once approved, and restrict or regulate post-approval activities. Changes in the legal requirements, or their interpretation, could impact our business by compelling, for example, modification to: our manufacturing arrangements; product labeling; pricing and reimbursement arrangements; private or governmental insurance coverage; the sale practices for, or availability of, our products; or record-keeping activities. If any such changes were to be imposed, they could adversely affect the operation of our business. For more information on these laws and regulations see the section entitled "**Business – Government Regulation and Product Approval – *Healthcare Reform*.**"

Third party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In the U.S. and certain other jurisdictions, there have been, and are expected to continue to be, a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In the U.S., however, significant uncertainty exists regarding the provision and financing of healthcare because the newly elected administration and federal legislators have publicly declared their intention to review and potentially significantly modify the current legal and regulatory framework for the healthcare system.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Current legislation at the U.S. federal and state levels seeks to reduce healthcare costs and improve the quality of healthcare. For example, the U.S. Affordable Care Act ("ACA"), enacted in March 2010, subjected biologic products to potential competition by lower-cost biosimilars; introduced a new methodology to calculate manufacturers' rebates under the Medicaid Drug Rebate Program for certain drugs, including infused or injected drugs; increased manufacturers' minimum Medicaid rebates under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate Program to pharmaceutical prescriptions of individuals enrolled in Medicaid managed care organizations; imposed new annual fees and taxes for certain branded prescription drugs and biologic agents; created the Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts as of January 1, 2019, off negotiated prices on certain brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research. Congress also could consider additional legislation to repeal, replace, or further modify elements of the ACA. Thus, the full impact of the ACA, or any law replacing elements of it, and the political uncertainty regarding any repeal and replacement on the ACA, on our business remains unclear.

Risks Related to Our Common Stock

Risks Related to Investment in Securities

An active trading market for our common stock may not be sustained.

If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at or above the prices at which they acquired their shares or sell their shares at the time they would like to sell. Any inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our common stock historically has been volatile, which may affect the price at which you could sell any shares of our common stock.

The market price for our common stock historically has been highly volatile and could continue to be subject to wide fluctuations in response to various factors. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including:

- the success of our products or technologies or competing products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- developments or disputes concerning issued patents, patent applications or other intellectual property rights;
- regulatory or legal developments in the U.S. and other countries;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, manufacture, acquire or in-license our current and additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares;
- changes in the structure of healthcare payment systems;

- market conditions in the pharmaceutical and biotechnology sectors;
- public perception of the safety of genome editing based therapeutics;
- general economic, industry and market conditions; and
- the other factors summarized and described in this *Risk Factors* section.

Companies trading in the stock market in general, and in The Nasdaq Global Market in particular, have also experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may not publish an adequate amount of research on us, which may negatively impact the trading price for our stock. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. Further, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

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

Risk Related to Ownership Generally

Our principal stockholders and management own a significant percentage of our stock and, if they choose to act together, will be able to control or exercise significant influence over matters subject to stockholder approval.

As of December 31, 2023, our executive officers, directors, 5% or greater stockholders and their affiliates beneficially owned approximately 38.4% of our outstanding voting stock. These stockholders may have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have broad discretion over the use of our cash, cash equivalents and marketable securities, and may not use them effectively, including that we may be exposed to liquidity issues and other systemic financial risks at the financial institutions holding our cash and cash equivalents.

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

A portion of our cash may be held by financial institutions that may have been, or could in the future become, exposed to liquidity issues, bank failures or other systemic financial risks. Our uninsured cash deposits with such financial institutions may be at risk in the event they experience liquidity problems or other financial losses. For example, in May 2023, the Federal Deposit Insurance Corporation ("FDIC") took control of First Republic Bank and JP Morgan Chase & Co. has since acquired a substantial amount of assets and certain liabilities of First Republic. Although the U.S. Department of Treasury, FDIC and Federal Reserve Board have announced a program to provide up to $25.0 billion of loans to financial institutions secured by certain government securities held by financial institutions to mitigate the risk of potential losses on the sale of such instruments, there is no guarantee that such loans will fully mitigate the risk of potential losses or that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to uninsured funds in the future in the event of the closure of other banks or financial institutions, or that they would do so in a timely fashion. We assess our banking relationships as we believe necessary or appropriate, but uncertainty remains over liquidity concerns in the broader financial services industry, and our business, our business partners, or industry as a whole may be adversely impacted in ways that we cannot predict at this time, including our ability to access cash in amounts adequate to finance or capitalize our current and/or projected business operations could be significantly impaired by factors that affect the financial institutions with which we have banking relationships, and in turn, us. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements (including cash management arrangements), disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. In addition, our vendors, such as our CMOs, CROs or business partners, may be susceptible to the foregoing liquidity or other financial risks and factors, which could, in turn, have a material adverse effect on our current and/or projected business operations and results of operations and financial condition.

We 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, and particularly since we are no longer an "emerging growth company" under applicable SEC regulations, we incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, 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 to these compliance initiatives.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 ("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. We conduct a process each year to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

Risks Related to Future Financial Condition

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

We will need additional capital in the future to continue our planned operations in addition to the proceeds we received from our initial public offering ("IPO") in May 2016 and follow-on public offerings since then. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more

than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

In March 2022, we entered into an Open Market Sale Agreement (the "2022 Sale Agreement") with Jefferies LLC (the "Sales Agent"), to provide for the offering, issuance and sale of up to an aggregate amount of $400.0 million of our common stock from time to time in "at-the-market" offerings. We will pay to the Sales Agent cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement. Through December 31, 2023, we issued 7,518,163 shares of our common stock at an average price of $42.70 per share in accordance with the 2022 Sale Agreement for aggregate net proceeds of $310.9 million, after payment of cash commissions to the Sales Agent and approximately $0.5 million related to legal, accounting and other fees in connection with the sales. In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock.

Given the volatility in the capital markets, we may not be willing or able to continue to raise equity capital through "at-the-market" offerings. We may, therefore, need to turn to other sources of funding that may have terms that are not favorable to us, or reduce our business operations given capital constraints. In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. We cannot predict the effect that future sales of common stock or other equity-related securities would have on the market price of our common stock. Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to the Sales Agent at any time throughout the term of the Sale Agreement. The number of shares that are sold by the Sales Agent after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with the Sales Agent in any instruction to sell shares, and the demand for our common stock during the sales period. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares or the gross proceeds to be raised in connection with those sales, if any, that will be ultimately issued.

Risks Related to our Charter and Bylaws

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us difficult, limit attempts by our stockholders to replace or remove our current management and adversely affect our stock price.

Provisions of our certificate of incorporation and by-laws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our stock. Among other things, the certificate of incorporation and by-laws:

- permit the board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide the board of directors into three classes;
- provide that a director may only be removed from the board of directors by the stockholders for cause;

- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders, and may not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and meet specific requirements as to the form and content of a stockholder's notice;
- prevent cumulative voting rights (therefore allowing the holders of a plurality of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- require that, to the fullest extent permitted by law, a stockholder reimburse us for all fees, costs and expenses incurred by us in connection with a proceeding initiated by such stockholder in which such stockholder does not obtain a judgment on the merits that substantially achieves the full remedy sought;
- provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer (or president, in the absence of a chief executive officer) or by the board of directors; and
- provide that stockholders will be permitted to amend the bylaws only upon receiving at least two-thirds of the total votes entitled to be cast by holders of all outstanding shares then entitled to vote generally in the election of directors, voting together as a single class.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any "interested" stockholder for a period of three years following the date on which the stockholder became an "interested" stockholder.

Our certificate of incorporation and by-laws designate certain courts as the sole and exclusive forums for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation and by-laws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for any state law claims for any derivative action or proceeding brought on our behalf alleging state law claims, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our by-laws, any action to interpret, apply, enforce, or determine the validity of our certificate of incorporation or bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine (the "Delaware Forum Provision"). The Delaware Forum Provision does not apply to claims arising under the Exchange Act or the Securities Act. Our by-laws further provide that the U.S. District Court for the District of Massachusetts will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (the "Federal Forum Provision"). We have chosen the U.S. District Court for the District of Massachusetts as the exclusive forum for such Securities Act causes of action because our principal executive offices are located in Cambridge, Massachusetts. Our by-laws provide that any person or entity purchasing or otherwise acquiring any interest in any shares of our common stock is deemed to have notice of and consented to the foregoing Delaware Forum Provision and the Federal Forum Provision.

The Delaware Forum Provision and the Federal Forum Provision may impose additional litigation costs on stockholders in pursuing the claims identified above, particularly if the stockholders do not reside in or near the State of Delaware or the Commonwealth of Massachusetts. Additionally, the Delaware Forum Provision and the Federal Forum Provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the Delaware Forum Provision and the Federal Forum Provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. The Court of Chancery of the State of Delaware or the U.S. District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Risks Related to Tax Matters

Changes in tax law may adversely affect our business and financial condition.

The laws and rules dealing with U.S. federal, state and local income taxation are routinely being reviewed and modified by governmental bodies, officials and regulatory agencies, including the Internal Revenue Service and the U.S. Treasury Department. Since we were founded in 2014, many such changes have been made and changes are likely to continue to occur in the future. We cannot predict whether, when, in what form, or with what effective dates, tax laws, regulations and rulings may be enacted, promulgated or issued, that could result in an increase in our or our stockholders' tax liability.

Our ability to use our net operating loss ("NOL") carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2023, we had federal and state NOLs of $954.0 million and $922.8 million, respectively, some of which begin to expire in 2034. Federal and certain state NOLs generated in taxable years ending after December 31, 2017 are not subject to expiration. As of December 31, 2023, we had federal and state research and development and other credit carryforwards of approximately $100.7 million and $64.1 million, which begin to expire in 2034 and 2029, respectively. Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change NOLs, and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. During 2022, we completed an assessment of the available net operating loss carryforwards and other tax attributes under Section 382 that covered the period from inception through December 31, 2022. This analysis did not result in a material limitation to our other tax attributes. We have not completed an analysis through December 31, 2023. To the extent there was a change in control during 2023, our tax attributes could be subject to limitation. We may experience ownership changes in the future. As a result, if we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credits to offset such taxable income and income tax, respectively, could be subject to limitations. Similar provisions of state tax law may also apply. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Risk management and strategy:

We face a number of cybersecurity risks in connection with our business and recognize the growing threat within the general marketplace and our industry. To help the Company address these risks, we have implemented a cybersecurity risk management program that is informed by recognized industry standards and frameworks and incorporates elements of the same, including elements of the National Institute of Standards and Technology Cybersecurity Framework.

Our cybersecurity risk management program includes a number of components, including but not limited to a Cybersecurity Incident Response Plan ("CSIRP"), annual cybersecurity awareness training for our employees, vendor risk management, regular system maintenance including application of security patches as appropriate, regular penetration test and security assessments and implementation of enhancements to security measures used to protect our systems and data.

We maintain a CSIRP that is designed to guide our incident response process for cybersecurity incidents that could affect our systems, network, or data. The CSIRP identifies the individuals responsible for developing, maintaining, and following appropriate procedures to identified cybersecurity incidents. We periodically test our CSIRP using tabletop exercises with the goal of improving our processes and preparedness.

Risks from cybersecurity threats have not to date materially affected us, including our business strategy, results of operations or financial condition. For more information about the cybersecurity risks we face, see the risk factor entitled "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 operations and development efforts" in Item 1A-Risk Factors.

Governance:

The Board of Directors, as a whole and through its committees, has responsibility for the oversight of risk management, which includes ensuring that the risk management process implemented within our organization is appropriate and functioning as designed. The Audit Committee of our Board of Directors oversees cybersecurity risks pursuant to its charter, and our governance framework includes oversight by the Audit Committee. The Audit Committee, with assistance from our management, including our Head of IT, periodically reports to the full Board of Directors to inform them of potential cyber risks and threats, the status of projects to further develop our information security systems, and the emerging cybersecurity threat landscape.

Our Head of IT is responsible for strategic leadership of our cybersecurity risk management program. The Head of IT role is currently held by an individual who has approximately eighteen years of professional IT management experience. Our Head of IT also provides regular updates on our cybersecurity risk to our executive leadership team and other management committees responsible for IT and cybersecurity risk management.

Item 2. Properties

Our headquarters are located at 40 Erie Street in Cambridge, Massachusetts, where we occupy approximately 65,000 square feet of office and laboratory space. We have a ten-year lease agreement expiring in September 2026, with an option to extend the term of the lease for an additional three years. In addition, we lease approximately 15,200 square feet of office and laboratory space at 130 Brookline Street in Cambridge, Massachusetts, which expires in 2031. In March 2020, we entered into an agreement to lease approximately 39,000 square feet of office and laboratory space at 281 Albany Street in Cambridge, Massachusetts with an initial term of ten years and an option to extend the lease for two successive five-year terms. In July 2021, we entered into an agreement to lease approximately 14,000 square feet of office space at 17 Tudor Street in Cambridge, Massachusetts with an initial term of five years and an option to extend the lease for one three-year term. In January 2022, we entered into an agreement to lease approximately 38,000 square feet of office and laboratory space at 730 Main Street, Cambridge, Massachusetts with an initial term of ten years and an option to extend the lease for one five-year term. We have subleased approximately 13,000 square feet of this property for office and laboratory use through March 2026. In February 2022, we entered into an agreement to lease approximately 140,000 square feet of office, general laboratory and manufacturing space at 840 Winter Street, Waltham Massachusetts, which will provide us with the ability to manufacture products in a good manufacturing practice ("GMP") compliant facility in the future. This lease is expected to commence in the second half of 2024 with an initial term of twelve years and an option to extend the lease for two five-year terms. In June 2022, we entered into an agreement to lease approximately 62,000 square feet of office and laboratory space at 640 Memorial Drive, Cambridge, Massachusetts with a term of five years, ending in August 2027.

Item 3. Legal Proceedings

In the ordinary course of business, we are from time to time involved in lawsuits, claims, investigations, proceedings, and threats of litigation related to intellectual property ("IP"), commercial arrangements and other matters. The outcome of any such legal proceedings, regardless of the merits, 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 legal 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 the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is traded on the Nasdaq Global Market under the symbol "NTLA".

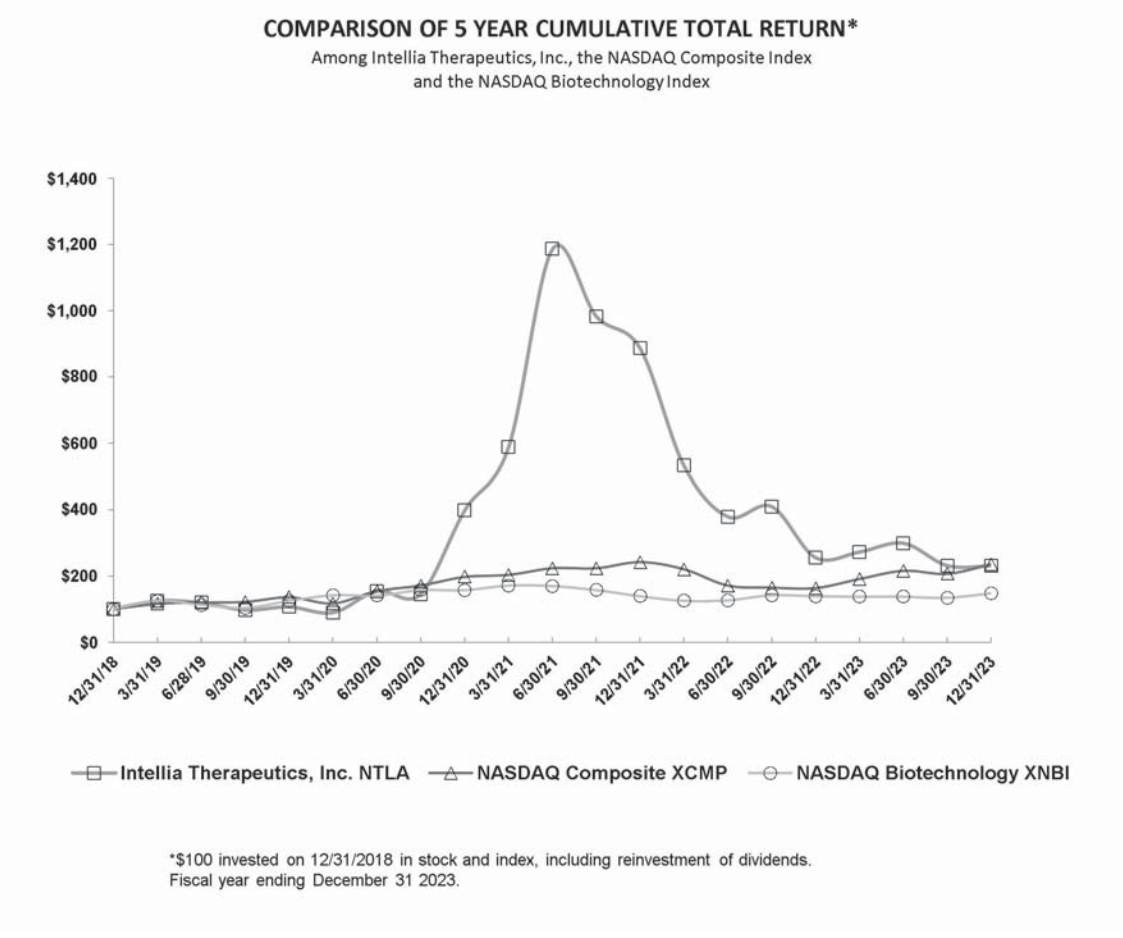
As of February 16, 2024, the number of holders of record of our common stock was 14. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. The number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

Stock Performance Graph

The following graph shows a comparison from December 31, 2018 through December 31, 2023, of the cumulative total return on an assumed investment of $100.00 in cash in our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. Such returns are based on historical results and are not intended to suggest future performance. Data for the Nasdaq Composite Index and the Nasdaq Biotechnology Index assume reinvestment of dividends.



The performance graph in this Item 5 is not deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section, and shall not be deemed incorporated by reference into any of our filings under the Securities Act of 1933 or the Securities Exchange Act of 1934, except to the extent we specifically incorporate it by reference into such a filing.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 6. [Reserved].

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

Our management's discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements included in this Annual Report on Form 10-K, which have been prepared by us in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") and with Regulation S-X, promulgated under the Securities Exchange Act of 1934, as amended. This discussion and analysis should be read in conjunction with these consolidated financial statements and the notes thereto included 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, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in Part I, Item 1A. *Risk Factors* 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.

Information pertaining to fiscal year 2021 was included in our Annual Report on Form 10-K for the year ended December 31, 2022 under Part II, Item 7, "Management's Discussion and Analysis of Financial Position and Results of Operations," which was filed with the Securities and Exchange Commission (the "SEC") on February 23, 2023.

Management Overview

Intellia Therapeutics, Inc. ("we," "us," "our," "Intellia," or the "Company") is a leading clinical-stage gene editing company, focused on developing potentially curative therapeutics using CRISPR/Cas9-based technologies. CRISPR/Cas9, an acronym for Clustered, Regularly Interspaced Short Palindromic Repeats ("CRISPR")/CRISPR associated 9 ("Cas9"), is a technology for genome editing, the process of altering selected sequences of genomic deoxyribonucleic acid ("DNA"). To fully realize the transformative potential of CRISPR/Cas9-based technologies, we are building a full-spectrum gene editing company, by leveraging our modular platform, to advance *in vivo* and *ex vivo* therapies for diseases with high unmet need by pursuing two primary approaches. For *in vivo* applications to address genetic diseases, we deploy CRISPR/Cas9 as the therapy. Our *in vivo* programs use CRISPR to enable precise editing of disease-causing genes directly inside the human body. In addition, we are advancing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where we use CRISPR/Cas9 as the tool to create the engineered cell therapy. For our *ex vivo* programs, CRISPR/Cas9 is used to engineer human cells outside the body. Our deep scientific, technical and clinical development experience, along with our robust intellectual property ("IP") portfolio, have enabled us to unlock broad therapeutic applications of CRISPR/Cas9 and related technologies to create new classes of genetic medicine. For more information regarding our business, mission and pipeline, see above sections in Part I entitled "**Overview**", "**Strategy**" and "**Our Pipeline**".

Financial Overview

Collaboration Revenue

Our revenue consists of collaboration revenue, including amounts recognized related to upfront technology access payments for licenses, technology access fees, research materials shipped, research funding and milestone payments earned under our collaboration and license agreements.

Research and Development

Research and development costs consist of expenses incurred in performing research and development activities, such as compensation and benefits, which includes stock-based compensation, for full-time research and development employees, allocated facility-related expenses, overhead expenses, license and milestone fees, contract research, development and manufacturing services, clinical trial costs and other related costs.

General and Administrative

General and administrative expenses consist primarily of compensation and benefits, including stock-based compensation, for our executive, finance, legal, human resources, business development and support functions. Also included in general and administrative expenses are allocated facility-related costs not otherwise included in research and development expenses, travel expenses and professional fees for auditing, tax and legal services, including IP-related legal services, and other consulting fees and expenses.

Other Income (Expense), Net

Other income (expense) consists of interest income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities, loss from equity method investment and change in fair value of contingent consideration.

Results of Operations

The following discussion of the financial condition and results of operations should be read in conjunction with the accompanying consolidated financial statements and the related footnotes thereto.

Comparison of Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations for the years ended December 31, 2023 and 2022 (in thousands):

	Year Ended December 31,		Period-to-Period Change
	2023	2022	
Collaboration revenue	$ 36,275	$ 52,121	$ (15,846)
Operating expenses:			
Research and development	435,069	419,979	15,090
General and administrative	116,497	90,306	26,191
Total operating expenses	551,566	510,285	41,281
Operating loss	(515,291)	(458,164)	(57,127)
Other income (expense), net:			
Interest income	49,832	8,542	41,290
Loss from equity method investment	(15,633)	(11,079)	(4,554)
Change in fair value of contingent consideration	(100)	(13,485)	13,385
Total other income (expense), net	34,099	(16,022)	50,121
Net loss	$ (481,192)	$ (474,186)	$ (7,006)

Collaboration Revenue

Collaboration revenue decreased by $15.8 million to $36.3 million during the year ended December 31, 2023, as compared to $52.1 million during the year ended December 31, 2022. This decrease was primarily driven by a $10.3 million cumulative adjustment related to a contract modification resulting from Regeneron exercising a one-time option to extend the term of our technology collaboration for an additional two years. Refer to Note 9 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for further details.

Research and Development

Research and development expenses increased by $15.1 million to $435.1 million during the year ended December 31, 2023, as compared to $420.0 million during the year ended December 31, 2022.

The following table summarizes our research and development expenses for the years ended December 31, 2023 and 2022, together with the changes in those items in dollars (in thousands) and the respective percentages of change.

	Year Ended December 31,		Period-to-Period Change	Percent Change
	2023	2022		
External development expenses by program:				
NTLA-2001	$ 54,454	$ 37,849	$ 16,605	44%
NTLA-2002	24,560	11,611	12,949	112%
NTLA-3001	17,312	11,506	5,806	50%
NTLA-5001	-	17,827	(17,827)	-100%
Unallocated research and development expenses:				
Employee-related expenses	136,628	112,931	23,697	21%
Research materials and contracted services	60,726	74,834	(14,108)	-19%
In-process research and development	-	55,990	(55,990)	-100%
Research milestone	874	-	874	-
Facility-related expenses	53,141	37,618	15,523	41%
Stock-based compensation	82,211	56,279	25,932	46%
Other	5,163	3,534	1,629	46%
Total research and development expenses	$ 435,069	$ 419,979	$ 15,090	4%

The increase in research and development expenses for the year ended December 31, 2023 compared to the year ended December 31, 2022 was primarily attributable to:

- a $16.6 million increase in external costs related to the development of NTLA-2001, our lead product candidate, primarily due to an increase in spend on drug components and contracted services;
- a $12.9 million increase in external costs related to the development of NTLA-2002, primarily due to an increase in spend on drug components, contracted services and consulting services;
- a $5.8 million increase in external costs related to NTLA-3001, primarily related to an increase in spend on drug components and consulting and professional services, offset in part by a decrease in spend on contracted services;
- a $17.8 million decrease in external costs related to the development of NTLA-5001, as we discontinued this program as part of our pivot to an allogeneic pipeline;
- a $23.7 million increase in employee-related expenses, primarily driven by the increase in personnel growth to support our lead programs;
- a $14.1 million decrease in research materials and contracted services primarily driven by a decrease in drug component expenses and contracted services related to early stage programs;
- a $56.0 million decrease in in-process research and development expense related to the acquisition of Rewrite Therapeutics, Inc. in the first half of 2022;
- a $15.5 million increase in facility-related expenses primarily related to rent, depreciation, maintenance and services, and technology expense allocated to research and development; and
- a $25.9 million increase in stock-based compensation driven by increases in employee headcount in 2023 compared to 2022.

During 2024, we expect research and development expenses to increase as we advance our global pivotal trials for NTLA-2001 and NTLA-2002, progress our NTLA-3001 program and nominate new development candidates.

General and Administrative

General and administrative expenses increased by $26.2 million to $116.5 million during the year ended December 31, 2023, compared to $90.3 million during the year ended December 31, 2022. This increase was primarily related to an increase in employee-related expenses, including stock-based compensation of $16.7 million.

Other Income (Expense), Net

The increase in other income (expense), net of $50.1 million is primarily related to a $41.3 million increase in interest income, driven by an increase in market rates, and a $13.4 million decrease in other expense related to the change in fair value of contingent consideration, offset in part by a $4.6 million increase in the loss from our equity method investment.

Liquidity and Capital Resources

Since our inception through December 31, 2023, we have raised an aggregate of $2,534.1 million to fund our operations through our collaboration agreements, our initial public offering and concurrent private placements, follow-on public offerings, at-the-market offerings and the sale of convertible preferred stock.

As of December 31, 2023, we had $1,012.1 million in cash, cash equivalents and marketable securities.

At-the-Market Offering Programs

2019 Sale Agreement

In August 2019, we entered into an Open Market Sale Agreement (the "2019 Sale Agreement") with Jefferies LLC ("Jefferies"), under which Jefferies was able to offer and sell, from time to time in "at-the-market" offerings, shares of our common stock having aggregate gross proceeds of up to $150.0 million. We agreed to pay cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2019 Sale Agreement. Under the 2019 Sale Agreement, we issued 3,778,889 shares of our common stock.

During the first quarter of 2022, we issued 579,788 shares of our common stock in a series of sales at an average price of $69.43 per share in accordance with the 2019 Sale Agreement, for aggregate net proceeds of $38.9 million after payment of cash commissions and legal, accounting and other fees in connection with the sales. The 2019 Sale Agreement expired in the third quarter of 2022.

2022 Sale Agreement

In March 2022, we entered into an Open Market Sale Agreement (the "2022 Sale Agreement") with Jefferies, under which Jefferies is able to offer and sell, from time to time in "at-the-market" offerings, shares of our common stock having aggregate gross proceeds of up to $400.0 million. We agreed to pay cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement. Through December 31, 2023 we have issued 7,518,163 shares of our common stock under the 2022 Sale Agreement.

During the year ended December 31, 2023, we issued 4,122,824 shares of our common stock, in a series of sales, at an average price of $30.57 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of $121.9 million, after payment of cash commissions and legal, accounting and other fees in connection with the sales. As of December 31, 2023, $2.1 million of these proceeds are included in "Prepaid expenses and other current assets" on our consolidated balance sheet, representing offerings with trade dates in December 2023 that were settled in January 2024.

During the year ended December 31, 2022, we issued 3,395,339 shares of our common stock, in a series of sales, at an average price of $57.43 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of $189.0 million, after payment of cash commissions and legal, accounting and other fees in connection with the sales.

Follow-on Offering

In December 2022, we closed an underwritten public offering of 7,532,751 shares of common stock, including the exercise in full of the underwriters' option to purchase an additional 982,532 shares of common stock, at the public offering price of $45.80 per share, for aggregate net proceeds of $337.9 million, after deducting the underwriting discount, commissions and legal, accounting and other fees in connection with the sales.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, research and development research materials and contracted services, clinical trial costs, compensation and related expenses, laboratory and office facilities, research supplies, legal and regulatory expenses, patent prosecution filing and maintenance costs for our licensed IP, milestone and royalty payments and general overhead costs. During 2024, we expect our expenses to increase compared to prior periods in connection with our ongoing activities as we continue to develop our clinical programs and advance additional programs into clinical development.

We are eligible to earn a significant amount of milestone payments and royalties, in each case, on a per-product basis under our collaborations with SparingVision SAS ("SparingVision") and ONK Therapeutics, Ltd. ("ONK"), on a per-target basis under our collaboration with Regeneron Pharmaceuticals, Inc. ("Regeneron") and upon achievement of certain events under our collaboration with Kyverna Therapeutics, Inc. ("Kyverna"). Our ability to earn these milestone payments and the timing of achieving these milestones is dependent upon the outcome of our research and development activities and is uncertain at this time. Our rights to payments under our collaboration agreements are our only committed external source of funds.

Because our lead programs are in the clinical stage and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of any future product candidates or whether, or when, we may achieve profitability. Until such time as we can generate substantial product revenues, if ever, we expect to fund our ongoing cash needs through equity financings and collaboration arrangements. We receive cost reimbursements from Regeneron related to our collaboration agreements with them. Additionally, we are eligible to earn milestone payments and royalties, in each case, on a per-product basis under our collaborations with SparingVision and ONK, on a per-target basis under our collaboration with Regeneron, and upon achievement of certain events with Kyverna, subject to the provisions of our agreements with each of them. Except for these sources of funding, we will not have any committed external source of liquidity. To the extent that we raise additional capital through the future sale of equity, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. If we raise additional funds through 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 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 expectations related to the progress of our programs, we expect that our cash, cash equivalents and marketable securities as of December 31, 2023, as well as research and cost reimbursement funding from our collaboration agreements will enable us to fund our ongoing operating expenses and capital expenditure requirements into mid-2026, excluding any potential milestone payments or extension fees that could be earned and distributed under our collaboration agreements or any strategic use of capital not currently in the base case planning assumptions. We have based this estimate on current assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. In January 2024, following an internal strategic review, we announced an effort to streamline company-wide operations to further focus resources on key strategic priorities and programs. These changes resulted in a pause of select exploratory research-stage programs and a workforce reduction of approximately 15%.

Our ability to generate revenue and achieve profitability depends significantly on our success in many areas, including: developing our delivery technologies and our CRISPR/Cas9 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; 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, protecting, and expanding our portfolio of IP rights, including patents, trade secrets, and know-how; and attracting, hiring, and retaining qualified personnel.

Cash Flows

The following is a summary of cash flows for the years ended December 31, 2023 and 2022:

	Year Ended December 31,	
	2023	2022
	(In thousands)	
Net cash used in operating activities	$ (394,086)	$ (333,287)
Net cash (used in) provided by investing activities	(31,347)	160,309
Net cash provided by financing activities	130,323	582,955

Net cash used in operating activities

Net cash used in operating activities of $394.1 million during the year ended December 31, 2023 primarily consists of a net loss of $481.2 million, further reduced by changes in operating assets and liabilities of $52.5 million, including the receipt of $18.7 million in payments from our collaboration partners during that period and offset in part by non-cash charges of stock-based compensation of $134.1 million, loss on equity method investment of $22.3 million and depreciation of $9.0 million.

Net cash used in operating activities of $333.3 million during the year ended December 31, 2022 primarily consists of a net loss of $474.2 million, further reduced by changes in operating assets and liabilities of $53.9 million, including the receipt of $10.7 million in payments from our collaboration partners during that period and offset in part by non-cash charges of stock-based compensation of $91.4 million, in-process research and development expense of $56.0 million, losses on equity method investment of $22.5 million and depreciation of $7.6 million.

Net cash (used in) provided by investing activities

During the year ended December 31, 2023, our investing activities used cash of $31.3 million primarily due to $904.5 million of marketable securities purchased and $14.0 million in cash for the purchase of property and equipment, offset in part by $887.1 million in marketable securities maturing.

During the year ended December 31, 2022, our investing activities provided net cash of $160.3 million primarily due to $647.6 million in marketable securities maturing, offset in part by $429.0 million of marketable securities purchased, $44.8 million in net cash for the acquisition of Rewrite, and $13.6 million in cash for the purchase of property and equipment.

Net cash provided by financing activities

Net cash provided by financing activities of $130.3 million during the year ended December 31, 2023 is primarily due to the receipt of $119.8 million in net proceeds from at-the-market offerings, $6.6 million in cash received from the exercise of stock options and $3.9 million in cash received from the issuance of shares through our employee stock purchase plan.

Net cash provided by financing activities of $583.0 million during the year ended December 31, 2022 is primarily due to the receipt of $337.9 million in net proceeds from a follow-on offering of our common stock, $227.9 million in net proceeds from at-the-market offerings, $14.5 million in cash received from the exercise of stock options and $2.6 million in cash received from the issuance of shares through our employee stock purchase plan.

Contractual and Other Obligations

We have entered into arrangements that contractually obligate us to make payments that will affect our liquidity and cash flows in future periods.

Property Leases - Commenced

As of December 31, 2023, our contractual commitments for leases were $146.5 million, which will be paid over the term of such leases. For additional information on our leases and timing of future payments refer to Note 12 of the consolidated financial statements included in this Annual Report on Form 10-K.

Property Leases – Not Yet Commenced

In February 2022, we entered into a lease agreement for office, general laboratory and planned good manufacturing practice ("GMP") manufacturing space at 840 Winter Street in Waltham, Massachusetts, which is described in further detail in Note 12 of the consolidated financial statements included in this Annual Report on Form 10-K. In connection therewith, we have committed to making at least $146.0 million in rental payments over a lease term of 144 months estimated to begin in the second half of 2024.

Other Obligations

We enter into contracts in the normal course of business with various third parties for clinical trials, preclinical research studies, supply manufacturing and other services and products for operating purposes. These contracts are generally cancelable at any time by us upon prior written notice.

We do not include any potential future pass-through milestone payments or royalty payments we may be required to make under our existing license agreements or the merger agreement related to our acquisition of Rewrite due to the uncertainty of the occurrence of the events requiring payment under those agreements. These payments are not reflected in the disclosures above. In January 2023, a research milestone related to Rewrite was achieved and settled (see Note 11 of the consolidated financial statements included in this Annual Report on Form 10-K).

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S. The preparation of these consolidated financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities as of the date of the balance sheets and the reported amounts of collaboration revenue and expenses during the reporting periods. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances at the time such estimates are made. Actual results and outcomes may differ materially from our estimates, judgments and assumptions. We periodically review our estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates are reflected in the consolidated financial statements prospectively from the date of the change in estimate. Refer to Note 2 to our consolidated financial statements of this Annual Report on Form 10-K for our significant accounting policies related to our critical accounting estimates.

We define our critical accounting policies as those accounting principles generally accepted in the U.S. that require the most significant judgments and estimates about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles. We believe the critical accounting policies used in the preparation of our consolidated financial statements which require significant estimates and judgments are as follows:

Revenue Recognition

We recognize revenue in accordance with Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers (Topic 606)* and its related amendments (collectively known as Accounting Standard Codification ("ASC") 606 ("ASC 606").

At inception, we determine whether contracts are within the scope of ASC 606 or other topics. For contracts that are determined to be within the scope of ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which we expect to be entitled to receive in exchange for these goods and services. To achieve this core principle, we apply the following five steps: (i) identify the contract with the customer; (ii) identify the performance obligations in the contract; (iii) determine the

transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when or as we satisfy a performance obligation. We only apply the five-step model to contracts when 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.

As of December 31, 2023, our revenue recognized is solely related to collaboration agreements with third parties which are either within the scope of ASC 606, under which we license certain rights to our product candidates to third parties, or within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808") if it involves a joint operating activity pursuant to which we are an active participant and are exposed to significant risks and rewards with respect to the arrangement. As discussed in further detail in Note 9 to our consolidated financial statements of this Annual Report on Form 10-K, we enter into out-licensing agreements which are within the scope of ASC 606, under which we license certain rights to our product candidates to third parties and may provide services related to the research and development of the product candidates. The terms of these arrangements typically include consideration payable to us of one or more of the following: nonrefundable, upfront fees; development, regulatory, and commercial milestone payments; research and development funding payments; and royalties on the net sales of licensed products. Additionally, the terms of certain arrangements may include an equity interest in the other company. Consideration received from each of these payments results in collaboration revenues, except for revenues from royalties on the net sales of licensed products, which are classified as royalty revenues. For arrangements within the scope of ASC 808, the terms of these arrangements typically include payments received or made under the cost sharing provisions which are recognized as a component of collaboration revenues in the consolidated statements of operations and comprehensive loss.

In determining the accounting for each contract, the significant areas of management judgment or estimation include the determination of accounting for contract changes as modifications and whether those are separate and distinct or part of a partially satisfied performance obligation, determining the transaction price, identifying the distinct performance obligations within a contract, determining the standalone selling prices for distinct performance obligations when more than one distinct performance obligation is identified within a contract and determining the revenue recognition pattern for each performance obligation that best reflects the timing of when we transfer control of goods and services to the customer. If the consideration received in exchange for entering into a contract is in the form of noncash consideration, we are required to estimate the fair value of the noncash consideration received. If our estimates of the noncash consideration received are not appropriate it could impact the total amount of revenue recognized for the contract. Furthermore, many of our performance obligations, whether distinct or combined, do not have readily available standalone selling prices and therefore we are required to make judgments and estimates regarding the standalone selling prices when relevant. To the extent the estimates are not appropriate in the circumstances, it could impact the timing of our revenue recognition. We evaluate the measure of progress each reporting period and if estimates related to the measure of progress change, related revenue recognition is adjusted accordingly.

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 vendors in connection with clinical research organizations ("CROs") 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 preclinical 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 expense.

Stock-Based Compensation

We measure employee stock-based compensation based on the grant date fair value of the equity awards using the Black-Scholes option pricing model. Stock-based compensation expense is recognized on a straight-line basis over the requisite service period of the awards and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur. For equity awards that have a performance or market condition, we recognize stock-based compensation expense using the accelerated attribution method. Estimates of stock-based compensation expense for an award with a performance condition are based on our assessment of the probability that the performance condition will be achieved. Our stock price is a key input that will drive the grant date fair value of the equity awards.

Significant judgments made with respect to stock-based compensation relate to certain assumptions made when selecting model inputs used in the Black-Scholes option pricing model, in particular the volatility and expected life assumptions. Volatility assumptions are calculated based on historical volatility of the Company's stock. We estimate the expected term of options using the simplified method. In addition, an expected dividend yield of zero is used in the option valuation model because we do not pay cash dividends and do not expect to pay any cash dividends in the foreseeable future. The fair value of market-based restricted stock units is determined using a Monte Carlo simulation model, which uses multiple input variables to determine the probability of satisfying the market condition requirements.

Stock-based compensation expense for an award with performance conditions also include significant judgment with respect to the probability that the performance condition will be achieved, as the amount of expense recorded is based on the probable outcome of the performance conditions.

We classify stock-based compensation expense in our consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

Recent Accounting Pronouncements

Refer to Note 2 to our consolidated financial statements included in Part IV, Item 15, "Notes to Consolidated Financial Statements," of this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of December 31, 2023, we had cash equivalents, restricted cash equivalents and marketable securities of $921.6 million consisting of interest-bearing money market accounts, corporate and financial institution debt securities, U.S. Treasury and other government securities and asset-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are primarily in marketable securities. Due to the short-term duration of our investment portfolios and the low risk profile of our investments, we do not believe an immediate change of 100 basis points, or one percentage point, would have a material effect on the fair market value of our investment portfolio. Declines in interest rates, however, would reduce future investment income.

We do not have any foreign currency or derivative financial instruments. Inflation generally affects us by increasing our cost of labor, preclinical and clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the year ended December 31, 2023.

Item 8. Financial Statements and Supplementary Data

The information required by this item is presented at the end of this report beginning on page F-1.

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

The Company has established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2023.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's 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 and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- 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
- 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. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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 our internal control over financial reporting as of December 31, 2023. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework* (2013 framework) ("COSO"). Based on its assessment, management believes that, as of December 31, 2023, our internal control over financial reporting is effective based on those criteria.

Deloitte & Touche LLP, our independent registered public accounting firm, has issued an attestation report on the effectiveness of our internal control over financial reporting, which is included below.

Changes in Internal Controls over Financial Reporting

No change in the Company's internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended December 31, 2023 that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Intellia Therapeutics, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of Intellia Therapeutics, Inc. and subsidiary (the "Company") as of December 31, 2023, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2023, of the Company and our report dated February 22, 2024, expressed an unqualified opinion on those financial statements.

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/ Deloitte & Touche LLP

Boston, Massachusetts
February 22, 2024

Item 9B. Other Information

Rule 10b5-1 Trading Plans

During the three months ended December 31, 2023, none of the Company's directors or officers adopted, materially modified, or terminated any contract, instruction, or written plan for the purchase or sale of Company securities that was intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) or any non-Rule 10b5-1 trading arrangement.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and is incorporated by reference from our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, which we expect to file with the SEC no later than April 29, 2024.

Item 10. Directors, Executive Officers and Corporate Governance

Information regarding our directors, including the audit committee and audit committee financial experts, and executive officers and compliance with Section 16(a) of the Exchange Act will be included in our 2024 Proxy Statement and is incorporated herein by reference.

We have adopted a Code of Business, Conduct and Ethics for all of our directors, officers and employees as required by Nasdaq governance rules and as defined by applicable SEC rules. Stockholders may locate a copy of our Code of Business Conduct and Ethics on our website at www.intelliatx.com or request a copy without charge from:

Intellia Therapeutics, Inc.
Attention: Investor Relations
40 Erie Street, Suite 130
Cambridge, MA 02139

We will post to our website any amendments to the Code of Business, Conduct and Ethics, and any waivers that are required to be disclosed by the rules of either the SEC or Nasdaq.

Item 11. Executive Compensation

The information required by this item regarding executive compensation will be included in our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item regarding security ownership of certain beneficial owners and management and securities authorized for issuance under equity compensation plans will be included in our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item regarding certain relationships and related transactions and director independence will be included in our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

Information about aggregate fees billed to us by our independent principal accountant, Deloitte & Touche LLP (PCAOB ID No. 34), located in Boston, Massachusetts, will be presented in our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders under the caption “Audit Committee Matters — Principal Accounting Firm Fees” and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are included in this Annual Report on Form 10-K:

1. The following Report and Consolidated Financial Statements of the Company are included in this Annual Report:

   Report of Independent Registered Public Accounting Firm (PCAOB ID No.34)

   Consolidated Balance Sheets

   Consolidated Statements of Operations and Comprehensive Loss

   Consolidated Statements of Stockholders' Equity

   Consolidated Statements of Cash Flows

   Notes to Consolidated Financial Statements

2. All financial schedules have been omitted because the required information is either presented in the consolidated financial statements or the notes thereto or is not applicable or required.

3. The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index are incorporated by reference herein.

Item 16. Form 10-K Summary

The Company has elected not to include summary information.

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INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Intellia Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Intellia Therapeutics, Inc. and subsidiary (the "Company") as of December 31, 2023 and 2022, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2023, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023, in conformity with accounting principles generally accepted in the United States of America.

We have also 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, 2023, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 22, 2024, expressed an unqualified opinion on the Company's internal control over financial reporting.

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 critical audit matters does not alter in any way our opinion on the 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.

Revenue Recognition — Collaboration Arrangements – Refer to Note 9 to the financial statements.

Critical Audit Matter Description

The Company recognizes collaboration revenue on license and collaboration agreements as they fulfill their performance obligations and transfer control of goods and services to the customer. During 2023, a customer exercised an extension (the "Extension") for one of the customer's collaboration agreements, which resulted in management applying judgment in determining the accounting for the modified agreement, and in particular, in identifying if the promised performance obligations were distinct.

Auditing the Company's accounting for revenues pertaining to the Extension required an increased extent of effort and a high degree of auditor judgment, due to the complex and judgmental nature of evaluating the terms and assumptions of the related Extension and the appropriate accounting for the modification under the guidance in ASC 606, *Revenue from Contracts with Customers*.

How the Critical Audit Matter Was Addressed in the Audit

Our principal audit procedures related to the Company's revenue recognition for the Extension included the following:

- We tested the effectiveness of controls over the Company's processes for assessing the accounting treatment of modifications to existing collaboration agreements.
- Obtained and read the Extension agreement along with the original and amended collaboration agreements and the Company's accounting position paper for the Extension.
- We tested and evaluated, among other things, the performance obligations identified and the Company's conclusion that the promised goods and services under the Extension are not distinct from the combined performance obligations identified in the existing arrangement.
- Performed corroborative inquiries with those overseeing the work relating to the Extension.
- We tested the mathematical accuracy of management's calculations of revenue and the associated timing of revenue recognized in the financial statements.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 22, 2024

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

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(Amounts in thousands except share and per share data)

	December 31, 2023	December 31, 2022
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 226,748	$ 523,506
Marketable securities	685,475	669,116
Accounts receivable ($0.2 million and $0.3 million, respectively, from related party)	36,456	3,768
Prepaid expenses and other current assets	49,651	20,407
Total current assets	998,330	1,216,797
Marketable securities - noncurrent	99,864	69,338
Property and equipment, net	32,760	27,921
Operating lease right-of-use assets	115,375	133,076
Equity method investment	11,765	32,455
Investments and other assets	42,883	40,527
Total Assets	$ 1,300,977	$ 1,520,114
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 7,452	$ 5,154
Accrued expenses ($1.0 million and $1.6 million, respectively, from related party)	67,017	60,876
Current portion of operating lease liability	18,599	16,685
Current portion of deferred revenue ($0 and $19.9 million, respectively, from related party)	22,140	43,839
Total current liabilities	115,208	126,554
Deferred revenue, net of current portion	38,853	19,932
Long-term operating lease liability	96,747	114,018
Contingent consideration liability	-	24,026
Total liabilities	250,808	284,530
Commitments and contingencies (Note 8)		
Stockholders' Equity:		
Common stock, $0.0001 par value; 240,000,000 and 120,000,000 shares authorized at December 31, 2023 and December 31, 2022, respectively; 92,997,158 and 87,103,007 shares issued and outstanding at December 31, 2023 and December 31, 2022, respectively	9	9
Additional paid-in capital	2,710,797	2,420,223
Accumulated other comprehensive loss	(2,258)	(7,461)
Accumulated deficit	(1,658,379)	(1,177,187)
Total stockholders' equity	1,050,169	1,235,584
Total Liabilities and Stockholders' Equity	$ 1,300,977	$ 1,520,114

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

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(Amounts in thousands except per share data)

	Year Ended December 31,		
	2023	2022	2021
Collaboration revenue [1]	$ 36,275	$ 52,121	$ 33,053
Operating expenses:			
Research and development	435,069	419,979	229,807
General and administrative	116,497	90,306	71,096
Total operating expenses	551,566	510,285	300,903
Operating loss	(515,291)	(458,164)	(267,850)
Other income (expense), net:			
Interest income	49,832	8,542	1,283
Loss from equity method investment	(15,633)	(11,079)	(1,325)
Change in fair value of contingent consideration	(100)	(13,485)	-
Total other income (expense), net	34,099	(16,022)	(42)
Net loss	$ (481,192)	$ (474,186)	$ (267,892)
Net loss per share, basic and diluted	$ (5.42)	$ (6.16)	$ (3.78)
Weighted average shares outstanding, basic and diluted	88,770	76,972	70,894
Other comprehensive loss:			
Unrealized gain (loss) on marketable securities	3,635	(1,637)	(2,126)
Other comprehensive gain (loss) from equity method investment	1,568	(3,192)	(507)
Comprehensive loss	$ (475,989)	$ (479,015)	$ (270,525)
[1] Including the following revenue from related party (see Notes 9 and 16):	$ 12,832	$ 21,134	$ 6,072

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

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(Amounts in thousands, except share data)

	Common		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Equity
Balance at December 31, 2020	66,234,056	$ 7	$ 962,173	$ 1	$ (435,109)	$ 527,072
Issuance of common stock through follow-on offerings, net of issuance costs of $284	4,758,620	-	648,315	-	-	648,315
Issuance of common stock through at-the-market offerings, net of issuance costs of $52	641,709	-	45,255	-	-	45,255
Exercise of stock options	2,700,886	-	41,094	-	-	41,094
Vesting of restricted stock units	119,715	-	-	-	-	-
Issuance of shares under employee stock purchase plan	30,897	-	2,024	-	-	2,024
Stock-based compensation	-	-	47,009	-	-	47,009
Other comprehensive loss - unrealized loss on marketable securities	-	-	-	(2,126)	-	(2,126)
Other comprehensive loss - equity method investment	-	-	-	(507)	-	(507)
Net loss	-	-	-	-	(267,892)	(267,892)
Balance at December 31, 2021	74,485,883	7	1,745,870	(2,632)	(703,001)	1,040,244
Issuance of common stock through follow-on offerings, net of issuance costs of $253	7,532,751	1	337,891	-	-	337,892
Issuance of common stock through at-the-market offerings, net of issuance costs of $164 - 2019 Sale Agreement	579,788	1	38,885	-	-	38,886
Issuance of common stock through at-the-market offerings, net of issuance costs of $125 - 2022 Sale Agreement	3,395,339	-	189,011	-	-	189,011
Exercise of stock options	883,954	-	14,517	-	-	14,517
Vesting of restricted stock units	147,674	-	-	-	-	-
Issuance of shares under employee stock purchase plan	77,618	-	2,649	-	-	2,649
Stock-based compensation	-	-	91,400	-	-	91,400
Other comprehensive loss - unrealized loss on marketable securities	-	-	-	(1,637)	-	(1,637)
Other comprehensive loss - equity method investment	-	-	-	(3,192)	-	(3,192)
Net loss	-	-	-	-	(474,186)	(474,186)
Balance at December 31, 2022	87,103,007	9	2,420,223	(7,461)	(1,177,187)	1,235,584
Issuance of common stock through at-the-market offerings, net of issuance costs of $376 - 2022 Sale Agreement	4,122,824	-	121,870	-	-	121,870
Contingent consideration paid to Rewrite Holders	567,045	-	24,126	-	-	24,126
Exercise of stock options	385,130	-	6,599	-	-	6,599
Vesting of restricted stock units	677,055	-	-	-	-	-
Issuance of shares under employee stock purchase plan	142,097	-	3,929	-	-	3,929
Stock-based compensation	-	-	134,050	-	-	134,050
Other comprehensive gain - unrealized gain on marketable securities	-	-	-	3,635	-	3,635
Other comprehensive gain - equity method investment	-	-	-	1,568	-	1,568
Net loss	-	-	-	-	(481,192)	(481,192)
Balance at December 31, 2023	92,997,158	$ 9	$ 2,710,797	$ (2,258)	$ (1,658,379)	$ 1,050,169

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

INTELLIA THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands)

	Year Ended December 31,		
	2023	**2022**	**2021**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (481,192)	$ (474,186)	$ (267,892)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	8,976	7,572	6,891
Loss (gain) on disposal of property and equipment	72	(162)	-
Stock-based compensation	134,050	91,400	47,009
(Accretion) amortization of investment discounts and premiums	(25,897)	4,003	7,604
Loss from equity method investment	15,633	11,079	1,325
Deferral of equity method investment intra-entity profit on sales	6,624	11,405	2,937
Change in fair value of contingent consideration	100	13,485	-
In-process research and development expense	-	55,990	-
Changes in operating assets and liabilities:			
Accounts receivable	(32,688)	(1,737)	99
Prepaid expenses and other current assets	(27,168)	(2,160)	(9,798)
Operating lease right-of-use assets	19,011	13,121	9,349
Other assets	(707)	(1,091)	117
Accounts payable	2,522	(4,584)	529
Accrued expenses	6,024	15,924	17,260
Deferred revenue	(2,778)	(63,464)	(31,355)
Operating lease liabilities	(16,668)	(9,882)	(9,105)
Net cash used in operating activities	(394,086)	(333,287)	(225,030)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(13,985)	(13,558)	(12,756)
Purchases of marketable securities	(904,464)	(429,032)	(1,020,620)
Maturities of marketable securities	887,102	647,581	485,598
Proceeds from sale of property and equipment	-	150	-
Acquired in-process research and development, net of cash acquired of $287	-	(44,832)	-
Investment in Kyverna Therapeutics, Inc.	-	-	(3,000)
Net cash (used in) provided by investing activities	(31,347)	160,309	(550,778)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Net proceeds from issuance of common stock through follow-on offerings, net of issuance costs	-	337,892	648,315
Net proceeds from issuance of common stock through at-the-market offerings, net of issuance costs	119,795	227,897	45,255
Proceeds from options exercised	6,599	14,517	41,094
Issuance of shares through employee stock purchase plan	3,929	2,649	2,024
Net cash provided by financing activities	130,323	582,955	736,688
Net (decrease) increase in cash and cash equivalents and restricted cash equivalents	(295,110)	409,977	(39,120)
Cash, cash equivalents and restricted cash equivalents, beginning of period	535,463	125,486	164,606
Cash, cash equivalents and restricted cash equivalents, end of period	$ 240,353	$ 535,463	$ 125,486
Reconciliation of cash, cash equivalents and restricted cash equivalents to consolidated balance sheet:			
Cash and cash equivalents	$ 226,748	$ 523,506	$ 123,406
Restricted cash equivalents, included in investments and other assets	13,605	11,957	2,080
Total cash, cash equivalents and restricted cash equivalents	$ 240,353	$ 535,463	$ 125,486
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Purchases of property and equipment unpaid at period end	$ 1,525	$ 1,623	$ 667
Shares issued for Rewrite contingent consideration	24,126	-	-
Right-of-use assets acquired under operating leases	1,311	67,053	49,378
Proceeds from at-the-market offerings unpaid at period end	2,075	-	-
Contingent consideration liability assumed in asset acquisition	-	10,541	-
Non-cash trade-in of property and equipment	-	200	-
Non-cash contribution of intellectual property to AvenCell Therapeutics, Inc.	-	-	62,900
Non-cash contribution of intellectual property to SparingVision SAS	-	-	14,759
Non-cash contribution of intellectual property to Kyverna Therapeutics, Inc.	-	-	7,000

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

1. Nature of Operations

Organization

Intellia Therapeutics, Inc. ("Intellia" or the "Company") is a leading clinical-stage gene editing company, focused on developing potentially curative therapeutics using CRISPR/Cas9-based technologies. CRISPR/Cas9, an acronym for Clustered, Regularly Interspaced Short Palindromic Repeats ("CRISPR")/CRISPR associated 9 ("Cas9"), is a technology for genome editing, the process of altering selected sequences of genomic deoxyribonucleic acid ("DNA"). To fully realize the transformative potential of CRISPR/Cas9-based technologies, the Company is building a full-spectrum gene editing company, by leveraging its modular platform, to advance *in vivo* and *ex vivo* therapies for diseases with high unmet need by pursuing two primary approaches. For *in vivo* applications to address genetic diseases, the Company deploys CRISPR/Cas9 as the therapy. The Company's *in vivo* programs use CRISPR to enable precise editing of disease-causing genes directly inside the human body. In addition, the Company is advancing *ex vivo* applications to address immuno-oncology and autoimmune diseases, where it uses CRISPR/Cas9 as the tool to create the engineered cell therapy. For its *ex vivo* programs, CRISPR/Cas9 is used to engineer human cells outside the body. The Company's deep scientific, technical and clinical development experience, along with its robust intellectual property ("IP") portfolio, have enabled it to unlock broad therapeutic applications of CRISPR/Cas9 and related technologies to create new classes of genetic medicine.

The Company was founded and commenced active operations in 2014. The Company will require substantial additional capital to fund its research and development. The Company is subject to risks and uncertainties common to clinical-stage companies in the biotechnology industry, including, but not limited to, development by competitors of more advanced or effective therapies, dependence on key executives, protection of and dependence on proprietary technology, compliance with government regulations and ability to secure additional capital to fund operations. Programs currently in development or moving into development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

Liquidity

Since its inception through December 31, 2023, the Company has raised an aggregate of $2,534.1 million to fund its operations through its initial public offering ("IPO") and concurrent private placements, follow-on public offerings, at-the-market offerings and the sale of convertible preferred stock, as well as through its collaboration agreements. The Company expects that its cash, cash equivalents and marketable securities as of December 31, 2023 will enable the Company to fund its ongoing operating expenses and capital expenditure requirements for at least the twelve-month period following the issuance of these consolidated financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements include the accounts of Intellia Therapeutics, Inc. and its wholly owned, controlled subsidiary, Intellia Securities Corp. All intercompany balances and transactions have been eliminated in consolidation. Comprehensive loss is comprised of net loss and gain/loss on marketable securities and equity method investments.

In February 2022, the Company entered into an agreement to acquire Rewrite Therapeutics, Inc., a Delaware corporation ("Rewrite"). On the effective date of the agreement, Rewrite became a wholly owned subsidiary of the Company. In September 2022, Rewrite merged into Intellia, with Intellia the surviving entity.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") requires management to make estimates, judgments and assumptions that affect the amounts reported in the financial statements and accompanying notes. Significant estimates in these consolidated financial statements have been made in connection with the calculation of revenues, research and development expenses, valuation and determination of impairment of equity and fair value method investments, contingent consideration and stock-based compensation expense. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances at the time such estimates are made. Actual results could differ from those estimates. The Company periodically reviews its estimates in light of changes in circumstances, facts and experience.

The effects of material revisions in estimates are reflected in the consolidated financial statements prospectively from the date of the change in estimate.

Fair Value Measurements

The Company's financial instruments include cash equivalents, restricted cash equivalents, marketable securities, accounts receivable, non-marketable securities, accounts payable and accrued expenses. Certain of the Company's financial assets, including cash equivalents, restricted cash equivalents and marketable securities, have been initially valued at the transaction price, and subsequently revalued at the end of each reporting period, utilizing third party pricing services or other observable market data. The pricing services utilize industry standard valuation models and observable market inputs to determine value. Investments in non-marketable securities are accounted for using the measurement alternative at cost minus impairment, adjusted for changes in observable prices.

Refer to Note 4 for further information regarding the Company's fair value measurements.

Other financial instruments, including accounts receivable, accounts payable and accrued expenses, are carried at cost, which approximate fair value due to the short duration and term to maturity.

Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less when purchased to be cash equivalents. As of December 31, 2023, cash equivalents consisted of interest-bearing money market accounts, U.S. Treasury bills and other government securities. As of December 31, 2022, cash equivalents consisted of interest-bearing money market accounts and reverse purchase agreements.

Restricted Cash Equivalents

The Company has restricted cash equivalents made up of money market funds held in collateral accounts that are restricted to secure letters of credit in accordance with certain of its leases. As of December 31, 2023, these restricted cash equivalents amounted to $13.6 million. As of December 31, 2022, these restricted cash equivalents amounted to $12.0 million. The letters of credit are required to be maintained throughout the term of the leases; in some cases, the Company is able to reduce the amounts held over time. These restricted cash equivalents are long-term in nature and are included in "Investments and other assets" in the Company's consolidated balance sheets.

Marketable Securities

The Company's marketable securities are accounted for as available-for-sale and recorded at fair value with the related unrealized gains and losses included in accumulated other comprehensive (loss)/income, a component of stockholders' equity.

The Company reviews its investment portfolio to identify and evaluate investments that have an indication of possible other-than-temporary impairment. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition and near-term prospects of the investee, and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in market value.

Refer to Note 3 for further information regarding the Company's marketable securities.

Asset Acquisitions

At the time of acquisition, the Company determines if a transaction should be accounted for as a business combination or acquisition of assets. The Company measures and recognizes asset acquisitions that are not deemed to be business combinations based on the cost to acquire the assets, which includes transaction costs, and the consideration is allocated to the items acquired based on a relative fair value methodology. Goodwill is not recognized in asset acquisitions. In an asset acquisition, the cost allocated to acquire in-process research and development with no alternative future use is charged to research and development expense at the acquisition date.

Non-Marketable Equity Securities

The Company periodically invests in equity securities of companies whose securities are not publicly traded and where fair value is not readily available. These investments are accounted for using the measurement alternative at cost minus impairment adjusted for changes in observable prices. The Company monitors these investments to evaluate whether there are any indicators of impairment, and if so determines the fair value of the investment and compares to the recorded balance, to determine if there is an impairment, or if the investment has a readily determinable fair value. These investments are included in "Investments and other assets" in the Company's consolidated balance sheets. Refer to Note 10 for further information regarding the Company's investments in non-marketable equity securities.

Concentrations of Credit Risk

The Company's cash, cash equivalents, restricted cash equivalents and marketable securities may potentially be subject to concentrations of credit risk. The Company generally maintains balances in various accounts in excess of federally insured limits with financial institutions that management believes to be of high credit quality.

Accounts receivable represents amounts due from collaboration partners and joint ventures. The Company monitors economic conditions to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection. As of December 31, 2023, the Company's accounts receivable were related to its collaborations with Regeneron Pharmaceuticals, Inc. ("Regeneron"), SparingVision SAS ("SparingVision"), AvenCell Therapeutics, Inc. ("AvenCell"), and Kyverna Therapeutics, Inc. ("Kyverna"). As of December 31, 2022, the Company's accounts receivable were related to its collaborations with Regeneron, AvenCell, SparingVision and ONK Therapeutics, Ltd. ("ONK").

Property and Equipment

The Company records property and equipment at cost and recognizes depreciation and amortization using the straight-line method over the following estimated useful lives of the respective assets:

Asset Category	Useful Life
Laboratory equipment	5 years
Office furniture and equipment	5 years
Computer software	3 years
Computer equipment	3 years
Leasehold improvements	Shorter of useful life or remaining lease term

Expenditures for repairs and maintenance of assets are expensed as incurred. Upon retirement or sale, the cost of assets disposed and the corresponding accumulated depreciation are removed from the related accounts and any resulting gain or loss is reflected in the results of operations.

Impairment of Long-Lived Assets

The Company tests long-lived assets to be held and used, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of assets or asset groups may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets.

Evaluation of recoverability of the asset or asset group is based on an estimate of undiscounted future cash flows resulting from the use of the asset or asset group and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the asset or asset group, the assets are written down to their estimated fair values. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any material impairment losses on long-lived assets.

Contingent Consideration

The Company accounts for contingent consideration identified in an asset acquisition, that is payable in cash and does not meet the definition of a derivative under Accounting Standard Codification ("ASC") 815, *Derivatives and Hedging*, when the contingency is resolved and the consideration is paid or becomes payable.

The Company accounts for contingent consideration identified in an asset acquisition that is settled in shares of common stock under ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480"). The contingent consideration liability will be recorded at fair value at the end of each reporting period with changes in estimated fair values recorded in other (expense) income in the consolidated statements of operations and comprehensive loss.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences attributable to differences between carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax reporting purposes and for operating loss and tax credit carryforwards. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes.

The Company's deferred tax assets and liabilities are measured using enacted tax rates expected to apply in the years in which these temporary differences are expected to be recovered or settled. A valuation allowance is recorded to reduce deferred tax assets if it is determined that it is more likely than not that all or a portion of the deferred tax asset will not be realized. The Company considers many factors when assessing the likelihood of future realization of deferred tax assets, including recent earnings results, expectations of future taxable income, carryforward periods available and other relevant factors. The Company records changes in the required valuation allowance in the period that the determination is made.

The Company assesses its income tax positions and records tax benefits for all years subject to examination based upon management's evaluation of the facts, circumstances and information available as of the reporting date. For those tax positions where it is more likely than not that a tax benefit will be sustained, the Company records the largest amount of tax benefit with a greater than 50% likelihood of being realized upon ultimate settlement with a taxing authority having full knowledge of all relevant information. For those income tax positions where it is not more likely than not that a tax benefit will be sustained, the Company does not recognize a tax benefit in the financial statements. The Company records interest and penalties related to uncertain tax positions, if applicable, as a component of income tax expense.

Revenue Recognition

The Company recognizes revenue in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers (Topic 606)* and its related amendments (collectively known as "ASC 606").

At inception, the Company determines whether contracts are within the scope of ASC 606 or other topics. For contracts that are determined to be within the scope of ASC 606, revenue is recognized when a customer obtains control of promised goods or services. The amount of revenue recognized reflects the consideration to which the Company expects to be entitled to receive in exchange for these goods and services. To achieve this core principle, the Company applies the following five steps: (i) identify the contract with the customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when or as the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when 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.

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 and are distinct in the context of the contract. To the extent a contract includes multiple promised goods and services, the Company applies judgment to determine whether promised goods and services are both 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.

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, the Company estimates the amount of variable consideration that should be included in the transaction price utilizing either the expected value method or the most likely amount method, depending on the nature of the variable consideration. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Any estimates, including the effect of the constraint on variable consideration, are evaluated at each reporting period for any changes. Determining the transaction price requires significant judgment, which is discussed in further detail for each of the Company's collaboration agreements in Note 9. In addition, none of the Company's contracts as of December 31, 2023 or 2022 contained a significant financing component.

If the contract contains a single performance obligation, the entire transaction price is allocated to the single performance obligation. Contracts that contain multiple performance obligations require an allocation of the transaction price to each performance obligation on a relative standalone selling price basis unless the transaction price 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. The Company typically determines standalone selling prices using an adjusted market assessment approach model.

The Company satisfies performance obligations either over time or at a point in time. Revenue is recognized over time if either (i) the customer simultaneously receives and consumes the benefits provided by the entity's performance, (ii) the entity's performance creates or enhances an asset that the customer controls as the asset is created or enhanced, or (iii) 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. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

As of December 31, 2023, the Company's revenue recognized is solely related to collaboration agreements with third parties which are either within the scope of ASC 606, under which the Company licenses certain rights to its product candidates to third parties, or within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808") if it involves a joint operating activity pursuant to which the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement. For the collaboration arrangements under the scope of ASC 606, as discussed in further detail in Note 9, the terms of these arrangements typically include payment to the Company of one or more of the following: nonrefundable, upfront fees; development, regulatory, and commercial milestone payments; research and development funding payments; and royalties on the net sales of licensed products. Additionally, the terms of certain arrangements may include an equity interest in the other company. Each of these payments results in collaboration revenues, except for revenues from royalties on the net sales of licensed products, which are classified as royalty revenues. For arrangements within the scope of ASC 808, the terms of these arrangements typically include payments received or made under the cost sharing provisions which are recognized as a component of revenues in the consolidated statements of operations and comprehensive loss.

Licenses of intellectual property: If the license to the Company's IP is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from consideration allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the licenses. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue.

Milestone payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates the probability of reaching the milestones and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur in the future, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore revenue recognized is constrained as management is unable to assert that a reversal of revenue would not be probable. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenues and earnings in the period of adjustment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on levels of sales, if the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its collaboration agreements.

The Company receives payments from its customers based on billing schedules or upon the achievement of milestones established in each contract. The Company's contract liabilities consist of deferred revenue. Upfront payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until the Company satisfies its obligations under these arrangements.

The Company also considers the nature and contractual terms of an arrangement and assesses whether the arrangement involves a joint operating activity pursuant to which the Company is an active participant and is exposed to significant risks and rewards with respect to the arrangement. If the Company is an active participant and is exposed to the significant risks and rewards with respect to the arrangement, the Company accounts for the arrangement under ASC 808. Based on this consideration, the Company accounts for its co-development agreements with Regeneron and AvenCell under ASC 808. Because ASC 808 does not provide recognition and measurement guidance for collaborative arrangements, the Company has analogized to ASC 606. Refer to Note 9 for additional information regarding the Company's collaboration agreements.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development costs consist of expenses incurred in performing research and development activities, such as salaries, stock-based compensation and benefits of employees, allocated facility-related expenses, overhead expenses, license, sublicense and milestone fees, contract research, clinical trial costs, development and manufacturing services, and other related costs.

The Company records payments made for research and development services prior to the services being rendered as prepaid expenses on the consolidated balance sheet and expenses them as the services are provided. Contracts for multi-year research and development services are recorded on a straight-line basis over each annual contractual period based on the total contractual fee when the services rendered are expected to be substantially equivalent over the term of the arrangement. The cost of obtaining licenses for certain technology or IP is recorded to research and development expense when incurred if the licensed technology or IP has not yet reached technological feasibility and has no alternative future use.

Stock-Based Compensation

The Company's stock-based compensation cost is measured at the grant date based on the fair value of the award and is recognized as an expense over the requisite service period.

The fair value of stock option grants is estimated using the Black-Scholes option pricing model. Use of the valuation model requires management to make certain assumptions with respect to selected model inputs. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant for a term consistent with the expected life of the stock options. Volatility assumptions are calculated based on historical volatility of the Company's stock. The Company estimates the expected term of options using the simplified method. In addition, an expected dividend yield of zero is used in the option valuation model because the Company does not pay cash dividends and does not expect to pay any cash dividends in the foreseeable future. Forfeitures are recorded as they occur. The fair value of market-based restricted stock units is determined using a Monte Carlo simulation model, which uses multiple input variables to determine the probability of satisfying the market condition requirements.

For awards with service conditions only, the Company recognizes stock-based compensation expense on a straight-line basis over the requisite service period. For awards with service and performance-based conditions, the Company recognizes stock-based compensation expense using the graded vesting method over the requisite service period. For awards with market-based conditions, the Company recognizes stock-based compensation expense using the accelerated attribution method over the requisite service period. Estimates of stock-based compensation expense for an award with performance conditions are based on the probable outcome of the performance conditions and the cumulative effect of any changes in the probability outcomes are recorded in the period in which the changes occur.

The Company classifies stock-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified.

(Loss) Earnings per Share

The Company calculates basic (loss) earnings per share by dividing net (loss) income for each respective period by the weighted average number of common shares outstanding for each respective period. The Company computes diluted (loss) earnings per share after giving consideration to the dilutive effect of stock options and unvested restricted stock that are outstanding during the period, except where such securities would be anti-dilutive.

Segment Information

The Company's chief executive officer, its chief operating decision maker, manages the Company's operations as a single segment for the purpose of assessing performance and making operating decisions. The Company's one business segment is the development of genome editing-based therapies. All of the Company's assets are held in the U.S. and all of the Company's revenue has been generated in the U.S.

Variable Interest Entity

The Company evaluates at the inception of each arrangement, and whenever a reconsideration event occurs, whether an entity in which the Company holds an investment or in which the Company has other variable interests is considered a variable interest entity ("VIE") in accordance with FASB ASC *Topic 810, Consolidation* ("ASC 810"). If the entity meets the criteria to qualify as a VIE, the Company assesses whether or not the Company is the primary beneficiary of that VIE based on a number of factors, including (i) which party has the power to direct the activities that most significantly affect the VIE's economic performance, (ii) the parties' contractual rights and responsibilities pursuant to any contractual agreements and (iii) which party has the obligation to absorb losses or the right to receive benefits from the VIE. If the Company is deemed the primary beneficiary of a VIE, the Company consolidates such entity and reflects the non-controlling interest of other beneficiaries of that entity. If the Company is not the primary beneficiary, no consolidation is necessary, and the Company accounts for the investment or other variable interest in accordance with applicable U.S. GAAP.

Equity Method of Accounting

In circumstances where the Company has the ability to exercise significant influence, but not control, over the operating and financial policies of an entity in which the Company has a common stock or in-substance common stock investment, the Company utilizes the equity method of accounting for recording related investment activity. In assessing whether the Company exercises significant influence, the Company considers the nature and magnitude of the investment, the voting and protective rights the Company holds, any participation in the governance of the other entity and other relevant factors such as the presence of a collaborative or other business relationship.

Under the equity method of accounting, the Company's investments are initially recorded at cost on the consolidated balance sheets. Upon recording an equity method investment, the Company evaluates whether there are basis differences between the carrying value and fair value of the Company's proportionate share of the investee's underlying net assets. Typically, the Company amortizes basis differences identified on a straight-line basis over the underlying assets' estimated useful lives when calculating the attributable earnings or losses, excluding the basis differences attributable to in-process research and development ("IPR&D") that has no alternative future use. If the Company is unable to attribute all of the basis difference to specific assets or liabilities of the investee, the residual excess of the cost of the investment over the proportional fair value of the investee's assets and liabilities is considered to be Equity Method Goodwill and is recognized within the equity investment balance, which is tracked separately within the Company's memo accounts. The Company subsequently records in the consolidated statements of operations and comprehensive loss its share of income or loss of the other entity within other income/expense. If the share of losses exceeds the carrying value of the Company's investment, the Company will suspend recognizing additional losses and will continue to do so unless it commits to providing additional funding; however, if there are intra-entity profits this can cause the investment balance to go negative.

The Company evaluates its equity method investments for impairment whenever events or changes in circumstance indicate that the carrying amounts of such investments may be impaired and considers qualitative and quantitative factors including the investee's financial metrics, product and commercial outlook and cash usage. If a decline in the value of an equity method investment is determined to be other than temporary, a loss is recorded in earnings in the current period and the investment is written down to fair value.

At December 31, 2023 and 2022, the Company accounted for its investment in AvenCell under the equity method of accounting and no impairment charges were recognized during the years ended December 31, 2023 or 2022. Refer to Note 10 for further details.

Recently Adopted Accounting Pronouncements

There were no accounting pronouncements adopted by the Company in 2023.

Recent Issued Accounting Pronouncements Not Yet Effective

In November 2023, the FASB issued ASU No. 2023-07, "Segment Reporting - Improvements to Reportable Segment Disclosures." The amendments require disclosure of incremental segment information on an annual and interim basis. The amendments also require companies with a single reportable segment to provide all disclosures required by this amendment and all existing segment disclosures in ASC 280, "Segment Reporting." The amendments are effective for fiscal years beginning after December 15, 2023, and interim periods beginning after December 15, 2024. The Company is currently evaluating the impact of adopting this ASU on its consolidated financial statements and disclosures.

In December 2023, the FASB issued ASU No. 2023-09, "Income Taxes (Topic 740): Improvements to Income Tax Disclosures." This ASU updates income tax disclosure requirements primarily by requiring specific categories and greater disaggregation within the rate reconciliation and disaggregation of income taxes paid by jurisdiction. This ASU is effective for annual periods beginning after December 15, 2024 and is applicable to the Company's fiscal year beginning January 1, 2025, with early application permitted. The Company is currently evaluating the impact of adopting this ASU on its consolidated financial statements and disclosures.

3. Marketable Securities

The following table summarizes the Company's available-for-sale marketable securities:

	December 31, 2023			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Marketable securities:				
U.S. Treasury and other government-backed securities	$ 382,260	$ 302	$ (254)	$ 382,308
Financial institution debt securities	246,270	92	(243)	246,119
Corporate debt securities	97,490	53	(135)	97,408
Other asset-backed securities	59,453	75	(24)	59,504
Total	$ 785,473	$ 522	$ (656)	$ 785,339

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Marketable securities:				
U.S. Treasury and other government-backed securities	$ 244,562	$ 62	$ (1,938)	$ 242,686
Financial institution debt securities	380,891	-	(1,030)	379,861
Corporate debt securities	102,059	-	(509)	101,550
Other asset-backed securities	14,703	-	(346)	14,357
Total	$ 742,215	$ 62	$ (3,823)	$ 738,454

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At December 31, 2023 and 2022, the balance in the Company's accumulated other comprehensive loss was composed of activity related to the Company's available-for-sale marketable securities and equity method investment. There were no material realized gains or losses in the years ended December 31, 2023, 2022 or 2021. The Company did not reclassify any amounts out of accumulated other comprehensive loss during these periods. The Company generally does not intend to sell any investments prior to recovery of their amortized cost basis for any investment in an unrealized loss position. As such, the Company has classified these unrealized losses as temporary in nature.

The Company's available-for-sale securities that are classified as current marketable securities in the consolidated balance sheet mature within one year or less as of the balance sheet date. Available-for-sale securities that are classified as noncurrent marketable securities in the consolidated balance sheet are those that mature after one year but within five years from the balance sheet date and that the Company does not intend to dispose of within the next twelve months. At December 31, 2023 and 2022, the Company did not hold any investments that matured beyond five years of the balance sheet date.

Accrued interest on marketable securities is included in "Prepaid expenses and other current assets" on the Company's consolidated balance sheets.

4. Fair Value Measurements

The Company classifies fair value-based measurements using a three-level hierarchy that prioritizes the inputs used to measure fair value. This hierarchy requires entities to maximize the use of observable inputs and minimize the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows: Level 1, quoted market prices in active markets for identical assets or liabilities; Level 2, observable inputs other than quoted market prices included in Level 1, such as quoted market prices for markets that are not active or other inputs that are observable or can be corroborated by observable market data; and 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, including certain pricing models, discounted cash flow methodologies and similar techniques that use significant unobservable inputs.

The Company's financial assets and liabilities recognized at fair value on a recurring basis consisted of the following:

	Fair Value as of December 31, 2023			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Assets				
Cash equivalents and restricted cash equivalents	$ 136,254	$ 136,254	$ -	$ -
Marketable securities:				
U.S. Treasury and other government-backed securities	382,308	120,556	261,752	-
Financial institution debt securities	246,119	-	246,119	-
Corporate debt securities	97,408	-	97,408	-
Other asset-backed securities	59,504	-	59,504	-
Total marketable securities	785,339	120,556	664,783	-
Total	$ 921,593	$ 256,810	$ 664,783	$ -

	Fair Value as of December 31, 2022			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Assets				
Cash equivalents and restricted cash equivalents	$ 534,581	$ 534,581	$ -	$ -
Marketable securities:				
U.S. Treasury and other government-backed securities	242,686	172,939	69,747	-
Financial institution debt securities	379,861	-	379,861	-
Corporate debt securities	101,550	-	101,550	-
Other asset-backed securities	14,357	-	14,357	-
Total marketable securities	738,454	172,939	565,515	-
Total	$ 1,273,035	$ 707,520	$ 565,515	$ -
Liabilities				
Contingent consideration	$ 24,026	$ -	$ -	$ 24,026

Certain of the Company's financial assets, including cash equivalents, restricted cash equivalents and marketable securities, have been initially valued at the transaction price, and subsequently revalued at the end of each reporting period, utilizing third party pricing services or other observable market data. The pricing services utilize industry standard valuation models and observable market inputs to determine value.

Other financial instruments, including accounts receivable, accounts payable and accrued expense, are carried at cost, which approximates fair value due to the short duration and term to maturity.

Level 3 Assets and Liabilities

Equity-Method Investments

The Company's equity-method investment in AvenCell is classified as a Level 3 asset and is not included in the fair value table above as it is not valued at fair value on a recurring basis. Refer to Note 10 for further details. The carrying value of the Company's equity-method investment as of December 31, 2023 and 2022 was $11.8 million and $32.5 million, respectively.

Other Investments

The Company's other investments are classified as Level 3 assets and are not included in the fair value table above as they are not valued at fair value on a recurring basis .

The Company's investment in SparingVision was initially recorded at fair value, determined according to Level 3 inputs in the fair value hierarchy described above. The SparingVision investment is included in "Investments and other assets" on the consolidated balance sheets. This investment is accounted for using the measurement alternative at cost minus impairment adjusted for changes in observable prices. There were no changes in observable prices or impairment of this investment as of December 31, 2023 or 2022. The carrying value of the SparingVision investment was $14.8 million as of December 31, 2023 and 2022. Refer to Note 10 for further details.

The Company's investment in Kyverna was initially recorded at cost, which is representative of fair value. The Kyverna investment is included in "Investments and other assets" on the consolidated balance sheets. This investment is accounted for using the measurement alternative at cost minus impairment adjusted for changes in observable prices. There were no changes in observable prices or impairment of this investment as of December 31, 2023 or 2022. The carrying value of the Kyverna investment was $10.0 million as of December 31, 2023 and 2022. Refer to Note 10 for further details.

Contingent Consideration

As discussed further in Note 11, as part of its acquisition of Rewrite, the Company made a $25.0 million research milestone payment in February of 2023, payable in a combination of $0.9 million in cash and the remainder in the Company's common stock. The milestone payable in the Company's common stock resulted in liability classification under ASC 480. This contingent consideration liability was carried at fair value which was estimated by applying a probability-based model, which utilized inputs based on timing of achievements that were unobservable in the market. The contingent consideration liability was classified within Level 3 of the fair value hierarchy until it was settled in February of 2023.

The following table reconciles the change in fair value of the contingent consideration liability based on the level 3 inputs listed below for the years ended December 31, 2023 and 2022 (in thousands):

Balance at February 2, 2022 (at inception)	$ 10,541
Change in fair value	13,485
Balance at December 31, 2022	24,026
Change in fair value	100
Payment of contingent consideration	(24,126)
Balance at December 31, 2023	$ -

	As of inception (February 2, 2022)	As of December 31, 2022
Discount rate	7%	10.1%
Probability of achievement	50%	100%
Projected year of achievement	2024	2023

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
	2023	2022
	(In thousands)	
Laboratory equipment	$ 63,970	$ 51,911
Office furniture and equipment	2,633	2,633
Computer equipment	982	1,785
Leasehold improvements	3,134	3,066
Computer software	1,902	1,725
Total property and equipment	72,621	61,120
Less: accumulated depreciation and amortization	(39,861)	(33,199)
Property and equipment, net	$ 32,760	$ 27,921

Depreciation and amortization expense was $9.0 million, $7.6 million and $6.9 million for the years ended December 31, 2023, 2022 and 2021, respectively.

6. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2023	2022
	(In thousands)	
Accrued research and development	$ 27,411	$ 32,684
Employee compensation and benefits	26,615	21,778
Accrued legal and professional expenses	2,063	1,457
Accrued construction costs	6,891	-
Accrued other	4,037	4,957
Total accrued expenses	$ 67,017	$ 60,876

7. Income Taxes

The Company did not record net income tax benefits for the operating losses incurred during the periods presented due to the uncertainty of realizing a tax benefit from those losses. Accordingly, any benefit recorded related to these deferred tax assets was offset by a valuation allowance reflecting management's conclusion that realization of those assets was not more likely than not.

A reconciliation of the federal statutory income tax rate and the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2023	2022	2021
Federal statutory income tax rate	(21.0)%	(21.0)%	(21.0)%
State income taxes	(8.6)	(8.3)	(16.6)
Research and development tax credits	(6.9)	(5.3)	(8.7)
Stock-based compensation	1.6	(0.1)	(16.8)
Non-deductible officers' compensation	-	0.1	0.2
In-process research and development	-	2.5	-
Change in valuation allowance	34.9	32.1	62.9
Effective income tax rate	—%	—%	—%

The Company's net deferred tax assets (liabilities) consisted of the following:

	December 31,	
	2023	2022
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 258,664	$ 229,375
Research and development credit carryforwards	151,333	101,326
Section 174 capitalized research	150,993	78,873
Operating lease liability	31,183	35,386
Deferred revenue	9,633	13,189
Stock-based compensation	30,408	22,512
Accruals and allowances	6,244	4,968
Prepaid rent	1,190	1,367
Equity investment adjustments	7,580	3,358
Intangibles, including in-process research and development	1,017	930
Capitalized start-up costs	249	296
Gross deferred tax assets	648,494	491,580
Deferred tax asset valuation allowance	(616,082)	(454,793)
Total deferred tax assets	32,412	36,787
Deferred tax liabilities:		
Fixed assets	(1,221)	(759)
Operating lease right-of-use assets	(31,191)	(36,028)
Total deferred tax liabilities	(32,412)	(36,787)
Net deferred tax asset (liability)	$ -	$ -

The Tax Cuts and Jobs Act ("TCJA") requires taxpayers to capitalize and amortize, rather than deduct, research and development expenditures under section 174 for tax years beginning after December 31, 2021. These rules became effective for the Company during the year ended December 31, 2022. As a result, the Company has capitalized research and development costs of $322.6 million and $365.8 million for the years ended December 31, 2022 and December 31, 2023, respectively. The Company will amortize these costs for tax purposes over 5 years if the research and development was performed in the U.S. and over 15 years if the research and development was performed outside the U.S.

As of December 31, 2023 and 2022, the Company had federal net operating loss carryforwards of $954.0 million and $852.1 million, respectively, which may be available to offset future income tax liabilities.

Approximately $36.9 million of the federal net operating losses generated prior to 2018 will begin to expire in 2034, unless previously utilized. Losses incurred prior to 2018 will generally be deductible to the extent of the lesser of a corporation's net operating loss carryover or 100% of a corporation's taxable income and be available for twenty years from the period the loss was generated. The federal net operating losses generated after 2017 of approximately $917.1 million will be carried over indefinitely, but will generally

limit the net operating loss deduction to the lesser of the net operating loss carryforward or 80% of a corporation's taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended). Also, there will be no carryback for losses incurred after 2017.

As of December 31, 2023 and 2022, the Company also had state net operating loss carryforwards of $922.8 million and $797.8 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2034.

As of December 31, 2023 and 2022, the Company had federal tax credit carryforwards of approximately $100.7 million and $63.4 million, respectively, which begin to expire in 2034. As of December 31, 2023 and 2022, the Company had state research and development and other credit carryforwards of approximately $64.1 million and $48.0 million, which begin to expire in 2029.

The Company evaluated the expected realizability of its net deferred tax assets and determined that there was significant negative evidence due to its net operating loss position and insufficient positive evidence to support the realizability of these net deferred tax assets. The Company concluded it is more likely than not that its net deferred tax assets would not be realized in the future; therefore, the Company has provided a full valuation allowance against its net deferred tax asset balance as of December 31, 2023 and 2022. The valuation allowance increased by $161.3 million in 2023, $150.0 million in 2022, and $163.9 million in 2021.

Ownership changes may limit the amount of net operating loss carryforwards or research and development tax credit carryforwards that can be utilized to offset future taxable income or tax liability. In general, an ownership change, as defined by Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. If the Company has experienced a change of control, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382 and 383 of the Code. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. During 2022, the Company completed an assessment of the available net operating loss carryforwards and other tax attributes under Section 382 that covered the period from inception through December 31, 2022. The analysis did not result in a material limitation to the Company's tax attributes and the results of this analysis are reflected herein. The Company has not completed an analysis through December 31, 2023. To the extent there was a change in control during 2023, the Company's tax attributes could be subject to limitation. However, a full valuation allowance has been provided against the deferred tax assets related to the Company's net operating loss and tax credit carryforwards and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance.

As of December 31, 2023, the Company had not identified any unrecognized tax benefits. The Company will recognize interest and/or penalties related to uncertain tax benefits in income tax expense if they arise.

The Company files income tax returns in the U.S. federal tax jurisdiction and Massachusetts and various other state tax jurisdictions. The Company is subject to examination by the Internal Revenue Service, Massachusetts taxing authorities and state taxing authorities for tax year 2020 through present. To the extent that the Company has tax attribute carryforwards, the tax year in which the attributes were generated may still be adjusted upon examination by the Internal Revenue Service or State taxing authorities to the extent utilized in a future period. The returns in these jurisdictions since inception remain open for examination; however, there are currently no pending tax examinations.

8. Commitments and Contingencies

Litigation

From time to time, the Company is involved in legal and administrative proceedings and claims of various types. In some actions, the claimants seek damages, as well as other relief, which, if granted, would require significant expenditures. The Company records a liability in its consolidated financial statements for these matters when a loss is known or considered probable and the amount can be reasonably estimated. The Company reviews these estimates each accounting period as additional information is known and adjusts the loss provision when appropriate. If a matter is both probable to result in a liability to the Company and the amount of the loss can be reasonably estimated, the Company estimates and discloses the possible loss or range of loss. If the loss is not probable or cannot be reasonably estimated, a liability is not recorded in its consolidated financial statements.

During the year ended December 31, 2023, there have been no material changes to any outstanding litigation, nor is the Company a party to any significant new litigation.

License Agreements

The Company is party to license agreements, which include contingent payments. These payments will become payable if and when certain development, regulatory and commercial milestones are achieved. As of December 31, 2023, the satisfaction and timing of the contingent payments is uncertain and not reasonably estimable.

9. Collaborations and Other Arrangements

To accelerate the development and commercialization of CRISPR/Cas9-based products in multiple therapeutic areas, the Company has formed, and intends to seek other opportunities to form, strategic alliances with collaborators who can augment its leadership in CRISPR/Cas9 therapeutic development. As of December 31, 2023, the Company's accounts receivable were related to its collaborations with Regeneron, SparingVision, AvenCell and Kyverna and the Company's contract liabilities were related to its collaborations with Regeneron and SparingVision. As of December 31, 2022, the Company's accounts receivable were related to its collaborations with Regeneron, AvenCell, SparingVision and ONK and the Company's contract liabilities were related to its collaborations with Regeneron, AvenCell, SparingVision and Kyverna.

The following table presents changes in the Company's accounts receivable and contract liabilities (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Year Ended December 31, 2023				
Accounts receivable	$ 3,768	$ 51,421	$ (18,733)	$ 36,456
Contract liabilities - deferred revenue	$ 63,771	$ 40,312	$ (43,090)	$ 60,993

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Year Ended December 31, 2022				
Accounts receivable	$ 2,031	$ 12,453	$ (10,716)	$ 3,768
Contract liabilities - deferred revenue	$ 127,235	$ -	$ (63,464)	$ 63,771

The Company recognized the following revenues as a result of changes in the contract liability balance (in thousands):

Revenue recognized in the period from:	Year Ended December 31, 2023	Year Ended December 31, 2022	Year Ended December 31, 2021
Amounts included in the contract liability at the beginning of the period	$ 23,462	$ 52,060	$ 22,544

Costs to obtain and fulfill a contract

The Company has not incurred significant expenses to obtain collaboration agreements and costs to fulfill those contracts do not generate or enhance resources of the Company. As such, no costs to obtain or fulfill a contract have been capitalized in any period.

Regeneron Pharmaceuticals, Inc.

In April 2016, the Company entered into a license and collaboration agreement with Regeneron (as amended from time to time, the "2016 Regeneron Agreement"). The 2016 Regeneron Agreement has two principal components: i) a product development component under which the parties will research, develop and commercialize CRISPR/Cas-based therapeutic products primarily focused on genome editing in the liver, and ii) a technology collaboration component, pursuant to which the Company and Regeneron will engage in research-related activities aimed at discovering and developing novel technologies and improvements to CRISPR/Cas technology to enhance the Company's genome editing platform. Under this agreement, the Company also may access the Regeneron Genetics Center and proprietary mouse models to be provided by Regeneron for a limited number of the Company's liver programs. At the inception of the 2016 Regeneron Agreement, Regeneron selected the first of its 10 targets, transthyretin ("ATTR") amyloidosis, which is subject to a co-development and co-promotion agreement between the Company and Regeneron (the "ATTR Co/Co").

In connection with the 2016 Regeneron Agreement, the Company received a nonrefundable upfront payment of $75.0 million. In addition, on Regeneron programs that are not subject to Co/Co agreements, the Company may be eligible to earn, on a per-licensed target basis, (i) up to $25.0 million in development milestones, including for the dosing of the first patient in each of Phase I, Phase II and Phase III clinical trials, (ii) up to $110.0 million in regulatory milestones, including for the acceptance of a regulatory filing in the U.S., and for obtaining regulatory approval in the U.S. and in certain other identified countries, and (iii) up to $185.0 million in sales-based milestone payments. The Company is also eligible to earn royalties ranging from the high-single digits to low teens, in each case, on a per-product basis, which royalties are potentially subject to various reductions and offsets and incorporate the Company's existing

low- to mid-single-digit royalty obligations under a license agreement with Caribou. In connection with the 2016 Regeneron Agreement, Regeneron purchased $50.0 million of the Company's common stock in a private placement under a stock purchase agreement concurrent with the Company's IPO.

In May 2020, the Company entered into (i) amendment no. 1 (the "2020 Regeneron Amendment") to the 2016 Regeneron Agreement, (ii) co-development and co-funding agreements for the treatment of hemophilia A and hemophilia B (the "Hemophilia Co/Co") agreements and (iii) a stock purchase agreement. The collaboration expansion builds upon the jointly developed targeted transgene insertion capabilities designed to durably restore missing therapeutic protein, and to overcome the limitations of traditional gene therapy. The technology collaboration was extended until April 2024, at which point Regeneron would have an option to renew for an additional two years. The 2020 Regeneron Amendment also granted Regeneron exclusive rights to develop products for five additional *in vivo* CRISPR/Cas-based therapeutic liver targets and non-exclusive rights to independently develop and commercialize up to 10 *ex vivo* gene edited products made using certain defined cell types.

As part of the consideration for the 2020 Regeneron Amendment, Regeneron paid the Company an upfront payment of $70.0 million, which included the $25.0 million fee to extend the Technology Collaboration Term, as defined in the 2016 Regeneron Agreement, to April 2024. The potential future milestones and royalties remain unchanged from the 2016 Regeneron Agreement. In addition, on May 30, 2020, the Company and Regeneron entered into the 2020 Stock Purchase Agreement. Under the 2020 Stock Purchase Agreement, the Company sold to Regeneron 925,218 shares of its common stock, par value $0.0001 per share, for aggregate cash consideration of $30.0 million, or $32.42 per share (the "Equity Transaction"), representing a 100% premium over the volume-weighted average trading price of the Company's common stock during the 30-day period prior to the closing of the Equity Transaction. Under the 2020 Stock Purchase Agreement, Regeneron will not dispose of any shares of common stock it beneficially owns in the Company until the termination of the Technology Collaboration Term.

In October 2023, Regeneron notified the Company that it was exercising its one-time option to extend the Technology Collaboration Term for an additional two years (the "2024 Technology Collaboration Extension"), until April 2026, in exchange for a nonrefundable payment of $30.0 million due in April 2024.

2024 Technology Collaboration Extension: Accounting Analysis. The 2024 Technology Collaboration Extension was accounted for as a contract modification. The promised goods and services under the 2024 Technology Collaboration Extension are not distinct from the combined performance obligations identified in the 2020 Regeneron Amendment, which was only partially satisfied at the date of option exercise. A cumulative catch-up adjustment was recorded during the fourth quarter of 2023 resulting in a charge of $10.3 million against revenue previously recognized.

The transaction price of the 2024 Technology Collaboration Extension was determined to be $51.7 million, which is comprised of the $11.4 million remaining consideration under the 2020 Regeneron Amendment as of the modification date, the $30.0 million extension fee and the $10.3 million cumulative catch-up adjustment. The $51.7 million transaction price was allocated to the performance obligations including the licenses to targets and associated research activities and evaluation plans and the combined performance obligation including the technology collaboration and associated research activities, on a relative standalone selling price basis.

As a result of this evaluation, the Company allocated $48.3 million to the combined performance obligation including the licenses to targets and associated research activities and evaluation plans and $3.4 million to the combined performance obligation including the technology collaboration and associated research activities, which are being recognized using a time elapsed inputs method from the October 2023 extension date through April 2026, the remaining period of the collaboration.

ATTR and Hemophilia Co/Co Agreements: Accounting Analysis. The Company concluded that the ATTR Co/Co and Hemophilia Co/Co agreements meet the definition of a collaborative arrangement per ASC 808, which is outside of the scope of ASC 606. Since ASC 808 does not provide recognition and measurement guidance for collaborative arrangements, the Company has analogized to ASC 606. As such, the Company classifies cumulative amounts paid or received under the cost sharing provisions of the ATTR Co/Co and the Hemophilia Co/Co agreements as a component of revenues in the consolidated statements of operations and comprehensive loss, to the extent that this does not result in a cumulative "negative revenue" amount, in which case the cumulative shortfall would be reclassified as an expense.

In September 2023, Regeneron and Intellia further expanded the research collaboration (the "2023 Regeneron Amendment") to develop additional *in vivo* CRISPR-based gene editing therapies focused on neurological and muscular diseases. The collaboration will leverage Intellia's proprietary Nme2 CRISPR/Cas9 genome editing systems adapted for viral vector delivery and designed to precisely modify a target gene and Regeneron's proprietary antibody-targeted adeno-associated virus vectors and delivery systems. Under the terms of the expanded research collaboration, the companies will initially research two *in vivo* non-liver targets. Intellia will lead the design of the editing methodology and Regeneron will lead the design of the targeted viral vector delivery approach and the parties will share research costs equally. Each party will have the opportunity to lead potential development and commercialization for one product candidate, and

the party that is not leading development and commercialization will have the option to enter into a co-development and co-promotion agreement for the target.

2023 Regeneron Amendment: Accounting Analysis. The Company concluded that the accounting for the 2023 Regeneron Amendment is within the scope of ASC 606. The Company identified one performance obligation, the transfer of the license and performance of collaborative research and development activities. There is no upfront consideration related to the 2023 Regeneron Amendment. As the 2023 Regeneron Amendment progresses, the Company and Regeneron will share research costs equally. Any cost reimbursements received from Regeneron will be recorded as a component of revenue and any payments made to Regeneron will be recorded as a reduction of revenue.

Since December 31, 2022, there have been no material changes to the key terms of the 2016 Regeneron Agreement, ATTR Co/Co or Hemophilia Co/Co (the "Regeneron Agreements"), other than as described above. For further information on the terms and conditions of these agreements, see the notes to the consolidated financial statements included in the Company's Annual Report for the year ended December 31, 2022.

Revenue Recognition: Collaboration Revenue. The Company recognized $21.0 million, $24.1 million and $25.7 million of collaboration revenue in the years ended December 31, 2023, 2022 and 2021, respectively, in the consolidated statements of operations and comprehensive loss. This includes $19.6 million, $11.9 million, and $5.9 million, respectively, primarily representing payments due from Regeneron pursuant to the ATTR Co/Co agreement. These revenues are offset in part by contra-revenue related to the Hemophilia Co/Co agreements amounting to approximately $10.7 million in the year ended December 31, 2023, $10.4 million in the year ended December 31, 2022 and $2.7 million in the year ended December 31, 2021.

As of December 31, 2023, there was approximately $47.1 million of the aggregate transaction price remaining to be recognized that will be recognized through April 2026, the remaining period of the collaboration.

As of December 31, 2023 and 2022, the Company had accounts receivable of $35.7 million and $3.2 million, respectively, and deferred revenue of $47.1 million and $28.8 million, respectively, related to the Regeneron Agreements.

AvenCell Therapeutics, Inc.

In July 2021, the Company entered into two agreements with AvenCell, a privately held chimeric antigen receptor T ("CAR-T") cell therapy company formed on that date in a joint venture between the Company, Cellex Cell Professionals GmbH ("Cellex") and funds managed by Blackstone Life Sciences Advisors L.L.C. ("BXLS"): (i) a license and collaboration agreement (the "AvenCell LCA"), under which the Company will collaborate to develop allogeneic universal CAR-T cell therapies and which granted AvenCell a license to develop and commercialize genome edited universal CAR-T cell therapies (limited to its use with their switchable, universal CAR-T cell UniCAR and RevCAR platforms); and (ii) a co-development and co-funding agreement (the "AvenCell Co/Co"), under which the Company will co-develop and co-commercialize allogeneic universal CAR-T cell products for an immuno-oncology indication.

In November 2022, the Company decided to re-prioritize its *ex vivo* programs and terminated the AvenCell Co/Co, effectively turning over control of the program to AvenCell. The Company's obligations under the terminated agreement were completed in the second quarter of 2023. Since December 31, 2022, there have been no other material changes to the key terms of the AvenCell LCA and AvenCell Co/Co agreements.

Revenue Recognition – Collaboration Revenue. The Company recognized $13.2 million, $22.8 million and $5.9 million in revenue related to the AvenCell LCA for the years ended December 31, 2023, 2022 and 2021, respectively, after eliminating $6.6 million, $11.4 million and $2.9 million in intra-entity profits during those respective periods, which will be deferred and recognized if and when AvenCell commercializes a product with the Company's license or abandons the related project. Until such time, this revenue is indefinitely deferred and excluded from the results of operations of the Company. The Company also recognized $0.2 million and $0.3 million related to materials shipped in accordance with the AvenCell LCA in the years ended December 31, 2023 and 2022, respectively. The Company recognized $0.6 million and $2.0 million in contra-revenue in the years ended December 31, 2023 and 2022, respectively, related to the AvenCell Co/Co agreement. The Company recognized $0.2 million in revenues related to the AvenCell Co/Co agreement for the year ended December 31, 2021.

As of December 31, 2023, there was no remaining transaction price of the AvenCell LCA to be recognized.

The Company had $0.2 million in accounts receivable and no deferred revenue related to the AvenCell agreements as of December 31, 2023. As of December 31, 2022, the Company had $0.3 million in accounts receivable and deferred revenue of $19.9 million related to the AvenCell agreements.

SparingVision SAS

In October 2021, the Company and SparingVision, a genomic medicine company developing vision saving treatments for ocular diseases, entered into a license and collaboration agreement (the "SparingVision LCA") to develop novel genomic medicines utilizing CRISPR/Cas9 technology for the treatment of ocular diseases.

Since December 31, 2022, there have been no material changes to the key terms of the SparingVision LCA. For further information on the terms and conditions of these agreements, see the notes to the consolidated financial statements included in the Company's Annual Report for the year ended December 31, 2022.

Revenue Recognition: Collaboration Revenue. The Company recognized $1.8 million and $0.2 million in revenue related to the SparingVision LCA for the years ended December 31, 2023 and 2022, respectively. The Company did not recognize collaboration revenue in the year ended December 31, 2021 related to the SparingVision LCA. As of December 31, 2023 and 2022, the Company had $0.5 million and $0.1 million in accounts receivable, respectively, related to the SparingVision LCA. As of December 31, 2023 and 2022, the Company had deferred revenue of $13.9 million and $14.7 million related to the SparingVision LCA, respectively, which is expected to be recognized over a six to nine year period from the signing of the agreement.

Kyverna Therapeutics, Inc.

In December 2021, the Company and Kyverna, a cell therapy company engineering a new class of therapies for autoimmune and inflammatory diseases, entered into a licensing and collaboration agreement (the "Kyverna LCA"), for the development of an allogeneic CD19 CAR-T cell therapy for the treatment of a variety of B cell-mediated autoimmune diseases.

Since December 31, 2022, there have been no material changes to the key terms of the Kyverna LCA. For further information on the terms and conditions of this agreement, see the notes to the consolidated financial statements included in the Company's Annual Report for the year ended December 31, 2022.

Revenue Recognition: Collaboration Revenue. The Company had recognized revenue from the Kyverna LCA in full as of March 31, 2023, including $0.4 million and $6.6 million in revenue for the years ended December 31, 2023 and 2022, respectively. The Company recognized approximately $0.1 million in revenue in the year ended December 31, 2023 related to materials shipped to Kyverna. The Company did not recognize any revenue for the year ended December 31, 2021 related to the Kyverna LCA. As of December 31, 2023, the Company had $0.1 million in accounts receivable related to the Kyverna LCA. As of December 31, 2022, the Company did not have accounts receivable related to the Kyverna LCA. As of December 31, 2023, the Company did not have deferred revenue related to the Kyverna LCA. As of December 31, 2022 the Company had deferred revenue of $0.4 million related to the Kyverna LCA.

ONK Therapeutics, Ltd.

On February 12, 2022 the Company entered into a license, collaboration and option agreement (the "ONK LCA") with ONK, an innovative company dedicated to developing optimally engineered natural killer ("NK") cell therapies to cure patients with cancer.

Since December 31, 2022, there have been no material changes to the key terms of the ONK LCA.

Revenue Recognition: Collaboration Revenue. The Company recognized $0.2 million and $0.1 million in revenue for the years ended December 31, 2023 and 2022, respectively, related to materials shipped in accordance with the ONK LCA. As of December 31, 2023, the Company did not have accounts receivable related to the ONK LCA. As of December 31, 2022, the Company had $0.1 million in accounts receivable related to the ONK LCA.

10. Equity-Method Investment and Other Investments

AvenCell Therapeutics, Inc.

In July 2021, the Company, Cellex and BXLS established AvenCell, a joint venture and privately held company. In exchange for contributing an exclusive license to the joint venture, the Company entered into a Preferred Stock Purchase Agreement with AvenCell for a 33.33% equity interest in AvenCell at the time of the initial closing. Cellex and BXLS each equally owned the remaining 66.67% at that time.

The Company has significant influence over, but does not control, AvenCell through its noncontrolling representation on AvenCell's Board of Directors and the Company's equity interest in AvenCell. The Company has determined that the preferred stock it owns is in-substance common stock. The Company is not the primary beneficiary as it does not have the power to direct the activities of AvenCell that most significantly impact AvenCell's economic performance. Accordingly, the Company does not consolidate the financial statements of AvenCell and accounts for its investment using the equity method of accounting.

The Company recorded the initial investment in AvenCell of $62.9 million in "Equity method investments" on its consolidated balance sheet. Due to the timing and availability of AvenCell's financial information, the Company records its share of losses from AvenCell on a quarterly basis on a one-quarter lag. The Company evaluates material events occurring during the quarter lag to determine whether the effects of any such events should be disclosed in the financial statements. The Company's share of AvenCell's losses were $14.1 million, $14.3 million and $1.8 million for the years ended December 31, 2023, 2022 and 2021, respectively, and are reflected in its operating results and comprehensive loss. The Company eliminated intra-entity profit of $6.6 million, $11.4 million and $2.9 million for the years ended December 31, 2023, 2022 and 2021, respectively (see Note 9). The carrying value of the Company's investment in AvenCell was $11.8 million and $32.5 million as of December 31, 2023 and 2022, respectively. In February 2024, AvenCell notified the Company that it is evaluating the valuation of its intangible assets for potential impairment which may result in the reduction of the Company's equity method investment. AvenCell's financial statements for the three months ended December 31, 2023, had not been finalized at the time the Company's financial statements were issued. At December 31, 2023, the maximum exposure to loss is limited to the Company's equity investment in the joint venture as adjusted for intra-entity profits that have been deferred to date.

SparingVision SAS

In connection with the SparingVision LCA (see Note 9), the Company received 83,316 shares of Series A2 Preferred Stock ("Series A2"). Attached to each share of Series A2, the Company received three warrants for the right to purchase additional Series A2 shares at designated prices that are subject to certain vesting conditions (collectively referred to as the "SparingVision investments"). The Company accounts for the SparingVision investments using the measurement alternative as SparingVision is a private company and there is no readily observable transaction price. The Company recorded the initial investment in SparingVision of $14.8 million in "Investments and other assets" on its consolidated balance sheet. There have been no changes in the valuation of the investment in SparingVision as of December 31, 2023.

Kyverna Therapeutics, Inc.

In connection with the Kyverna LCA (see Note 9), the Company received 3,739,515 shares of Series B Preferred Stock with a fair value of $7.0 million. The Company separately made an additional investment in Kyverna, purchasing 1,602,649 shares of Series B Preferred Stock in exchange for $3.0 million in cash (collectively referred to as the "Kyverna investments"). As of December 31, 2023, the Company accounted for the Kyverna investments using the measurement alternative as Kyverna was a private company with no readily observable transaction price. The Company recorded the initial investment in Kyverna of $10.0 million in "Investments and other assets" on its condensed consolidated balance sheet. There have been no changes in the valuation of the investment in Kyverna as of December 31, 2023. In February 2024, Kyverna announced the completion of its IPO and its common stock began trading on the Nasdaq Global Select Market under the ticker symbol "KYTX".

11. Rewrite Acquisition

In February 2022, the Company entered into an Agreement and Plan of Merger by and among the Company, Rewrite, RW Acquisition Corp. and Shareholder Representative Services, LLC as Securityholder representative (the "Rewrite Merger Agreement"). Under the Rewrite Merger Agreement, the Company paid Company Securityholders (as defined in the Rewrite Merger Agreement) (the "Rewrite Holders") upfront consideration in an aggregate amount of $45.0 million, excluding customary purchase price adjustments and closing costs, payable in cash. Pursuant to the Rewrite Merger Agreement, the Company acquired all of the issued and outstanding shares of Rewrite. The Rewrite transaction resulted in the acquisition of certain know-how and IP assets related to Rewrite's proprietary DNA writing technology. The Company's management determined that the acquired assets do not meet the definition of a business pursuant to ASC 805, *Business Combinations*, as substantially all of the fair value of the acquired assets is concentrated into one identifiable asset, the DNA writing technology. As of the date of closing of the transactions contemplated by the Rewrite Merger Agreement (the "Rewrite Merger Agreement Date"), the asset acquired had no alternative future use and had not reached a stage of technological feasibility. As a result, all payment obligations were recorded as research and development expense in the condensed consolidated statements of operations and other comprehensive loss in the amount of $56.0 million. The total transaction price was allocated to the assets acquired and liabilities assumed on a relative fair value basis.

In addition, the Rewrite Holders are eligible to receive up to an additional $155.0 million, including $55.0 million upon the achievement of pre-specified research milestones and $100.0 million upon the achievement of a regulatory approval milestone, payable through a mixture of $130.0 million in cash and $25.0 million in a combination of cash and the Company's common stock which would be valued using the volume-weighted average price of the Company's Common Stock over the ten consecutive trading day period ending on and including the trading day that is two trading days immediately prior to the issuance of the consideration issued in connection with the applicable milestone. In September 2022, Rewrite merged into Intellia, with Intellia the surviving entity.

In January 2023, the $25.0 million research milestone noted above was achieved and, in February 2023, the Company paid the Rewrite Holders $0.9 million in cash and issued 567,045 shares of Intellia common stock in order to fulfill its obligation under the Rewrite Merger Agreement. The cash obligation was recorded as research and development expense in the consolidated statement of operations

and other comprehensive loss in the first quarter of 2023. The Company had determined that the research milestone settled in the Company's common stock would be classified as a contingent consideration liability under ASC 480 and, therefore, the Company initially recorded a liability for this milestone payment as of the Rewrite Merger Agreement Date at its original fair value of $10.5 million. The contingent consideration liability was remeasured at fair value each financial reporting period, with the resulting impact reflected in the Company's consolidated statements of operations and other comprehensive loss, presented within other income (expense). The remaining milestones to be settled in cash would be recorded when the contingency is resolved and the consideration is paid or becomes payable.

The transaction price on the Rewrite Merger Agreement Date was determined and allocated as follows (in thousands):

Transaction Price		
Upfront cash consideration	$	43,730
Research contingent consideration liabilities		10,541
Transaction costs		1,838
Total transaction price	$	56,109
Transaction Price Allocated		
In-process research and development	$	55,990
Cash acquired		287
Other current assets acquired		153
Other liabilities assumed		(321)
Total transaction price	$	56,109

12. Leases

Property Leases - Commenced

The Company leases approximately 230,000 square feet of real estate, including laboratory and office space in Cambridge, Massachusetts, and the surrounding areas. The Company's leases have remaining terms ranging from one to approximately nine years. Certain leases include options to renew, exercised at the Company's sole discretion, with varying renewal terms that can extend the lease term for an additional three to five years. All of the Company's leases qualify as operating leases.

In January 2023, the Company executed a sublease for approximately 13,000 square feet of space of laboratory and office space in Cambridge, Massachusetts for a term of approximately three years. The sublease agreement grants an option to renew the term for one additional year.

Property Leases – Not Yet Commenced

In February 2022, the Company entered into an agreement to lease approximately 140,000 square feet of office, general laboratory and planned good manufacturing practice ("GMP") manufacturing space at 840 Winter Street in Waltham, Massachusetts (the "840 Winter Lease"). The Company has committed to making at least $146.0 million in rental payments over a lease term of 144 months estimated to begin in the second half of 2024. The Company has the option to extend the 840 Winter Lease for two five-year terms.

In June 2023, the Company executed an amendment to the 840 Winter Lease, which outlines the Company's and the landlord's responsibilities regarding the construction of the leased space. The Company will be responsible for the oversight of the construction of the tenant improvements, which will be primarily funded by a tenant improvement allowance of up to $400 per rentable square foot, a portion of which would be repaid over the term of the lease with interest. The Company will also be responsible for certain future construction costs to the extent that they exceed the tenant improvement allowance. The Company anticipates a phased move-in process during the second half of 2024. As of December 31, 2023, the Company had not taken control of the premises and therefore there are no right of use assets or liabilities recorded related to the 840 Winter Lease under ASC 842, *Leases (Topic 842)* ("ASC 842").

Throughout the term of its leases, the Company is responsible for paying certain costs and expenses, in addition to the rent, as specified in the lease, including a proportionate share of applicable taxes, operating expenses and utilities. The variable portion of these costs are expensed as incurred and are disclosed as variable lease costs.

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's operating leases:

	Year Ended December 31,	
	2023	2022
	(In thousands)	
Lease cost		
Operating lease cost	$ 27,849	$ 18,031
Variable lease cost	6,991	4,443
Sublease income	(1,439)	-
Net lease cost	$ 33,401	$ 22,474

	Year Ended December 31,	
	2023	2022
	(In thousands)	
Other information		
Operating cash flows used for operating leases	$ 25,456	$ 14,656
Operating lease liabilities arising from obtaining right-of-use assets	1,311	67,053

	As Of December 31,	
	2023	2022
Lease term and discount rate		
Weighted average remaining lease term	6.2 years	6.9 years
Weighted average discount rate	7.37%	7.20%

The table below reconciles the undiscounted cash flows for each of the next five years and total of the remaining years to the operating lease liabilities recorded in the consolidated balance sheet as of December 31, 2023:

Future Operating Lease Payments	
Year Ending December 31,	**(in thousands)**
2024	$ 26,395
2025	25,933
2026	25,110
2027	17,548
2028	12,300
Thereafter	39,260
Total lease payments	$ 146,546
Less: imputed interest	(31,200)
Total operating lease liabilities at December 31, 2023	$ 115,346

13. Stock-Based Compensation

Stock-based compensation expense is classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31,		
	2023	2022	2021
		(In thousands)	
Research and development	$ 82,211	$ 56,279	$ 26,712
General and administrative	51,839	35,121	20,297
Total	$ 134,050	$ 91,400	$ 47,009

Amended and Restated 2015 Stock Option and Incentive Plan

In April 2016, the Company adopted the Amended and Restated 2015 Stock Option and Incentive Plan (the "2015 Plan"). The 2015 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards ("RSAs"), restricted stock units ("RSUs") and other stock-based awards. Recipients of incentive stock options and non-qualified stock options are eligible to purchase shares of the Company's common stock at an exercise price equal to the fair value of such stock on the grant date.

The Company maintains a retirement policy for equity awards granted to all employees (the "Retirement Policy"), which applies to all equity awards granted after July 1, 2022 to employees who meet certain retirement eligibility criteria set forth in the Retirement Policy

(the "Retirees"). Pursuant to the terms of the Retirement Policy, upon a Retiree's eligible retirement: (i) all stock options held by the Retiree will continue to vest following the Retiree's retirement date according to the original vesting schedule of the option until fully vested and all vested stock options held by such Retiree will remain exercisable until the earlier of the five-year anniversary of the Retiree's retirement date or the original expiration date of the option, (ii) all unvested time-based RSUs held by the Retiree will vest in full on the Retiree's retirement date and (iii) all unvested performance-based awards held by the Retiree will remain outstanding following the Retiree's retirement date and the Retiree will remain eligible to earn a pro-rated portion of such performance-based awards at the end of the performance period based on actual performance during the performance period.

As of December 31, 2023, there were 3,875,539 shares available for future issuance under the 2015 Plan. The number of shares reserved for issuance under the 2015 Plan will be cumulatively increased on each January 1st by four percent of the number of shares of stock issued and outstanding on the immediately preceding December 31st or such lesser number of shares of stock as determined by the board of directors.

Restricted Stock Units

The following table summarizes the Company's RSU activity for the year ended December 31, 2023:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock units as of December 31, 2022	1,941,379	$ 70.70
Granted	3,047,544	41.30
Vested	(677,055)	68.04
Cancelled	(270,115)	49.41
Unvested restricted stock units as of December 31, 2023	4,041,753	$ 50.40

In March 2023, the Company granted 2,195,135 RSUs with a service condition to employees as part of their annual grant, which have the potential to vest over a period of three years. The weighted average grant date fair value of these RSUs was $40.75 and the vesting start date for these RSUs was January 1, 2023.

Also in March 2023, 181,743 market-based RSUs were granted to senior executives as part of their annual grant. These RSUs have the potential to vest after a period of three years, with a vesting start date of January 1, 2023, and the number of shares to be delivered will depend on the Company's Total Shareholder Return ("TSR"), a market condition, over that period relative to a defined group of biotechnology companies. The grant date fair value for these RSUs, calculated using a Monte Carlo valuation model, was $68.55. The following assumptions were used to determine the grant date fair value: risk free interest rate: 4.60%; expected dividend yield: 0.0%; expected volatility: 84.34%; expected term (in years): 2.84.

In March 2022, the Company granted 794,424 RSUs with a service condition to employees as part of their annual grant, which have the potential to vest over a period of three years. The weighted average grant date fair value of these RSUs was $79.85 and the vesting start date for these RSUs was January 1, 2022.

Also in March 2022, 55,144 RSUs were granted to senior executives as part of their annual grant. These RSUs have the potential to vest after a period of 3 years, with a vesting start date of January 1, 2022, and the number of shares to be delivered will depend on the Company's TSR, a market condition, over that period relative to a defined group of biotechnology companies. The grant date fair value for these RSUs, calculated using a Monte Carlo valuation model, was $126.49. The following assumptions were used to determine the grant date fair value: risk free interest rate: 1.44%; expected dividend yield: 0.0%; expected volatility: 82.53%; expected term (in years): 2.84.

The Company also granted 66,296 performance-based RSUs in March 2022 to certain non-executive employees that would vest upon obtaining certain scientific milestones. There were two separate tranches, each attached to a different set of milestones. The milestone related to the first tranche, made up of 21,878 RSUs, was achieved in the first quarter of 2023 and these RSUs vested. The remaining performance milestones were considered not probable of achievement as of December 31, 2023 and, therefore, no related stock-based compensation was recorded during the period then ending for those RSUs.

RSUs granted under the 2015 Plan in 2023 generally vest as to one-third on the first anniversary of the original vesting date, with the balance vesting annually over the remaining two years.

The weighted-average grant date fair value of RSUs granted for the years ended December 31, 2023, 2022 and 2021 was $41.30, $70.90 and $73.81, respectively. The total fair value of RSUs vested (measured on the date of vesting) for the years ended December 31, 2023, 2022 and 2021 was $24.9 million, $10.4 million and $14.1 million, respectively.

As of December 31, 2023, there was $125.2 million of unrecognized stock-based compensation expense related to RSUs that are expected to vest; these costs are expected to be recognized over a weighted average remaining vesting period of 1.7 years.

Stock Options

The weighted average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $28.92, $57.23 and $54.09 per option for options granted during the years ended December 31, 2023, 2022 and 2021, respectively.

Weighted average assumptions used to apply this pricing model were as follows:

	Year Ended December 31,		
	2023	2022	2021
Risk-free interest rate	4.4%	1.9%	1.0%
Expected life of options	6.0 years	5.9 years	6.0 years
Expected volatility of underlying stock	78.7%	76.2%	72.9%
Expected dividend yield	0.0%	0.0%	0.0%

Risk-free Interest Rate. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant with maturities approximately equal to the option's expected term.

Expected Term. The expected term represents the period that stock option awards are expected to be outstanding. For option grants that are considered to be "plain vanilla," the Company determines the expected term using the simplified method. The simplified method deems the term to be the average of the time-to-vesting and the contractual life of the options. The Company uses the simplified method because it does not have sufficient historical option exercise data to provide a reasonable basis upon which to estimate the expected term.

Expected Volatility. Beginning in the first quarter of 2023, expected volatility is estimated based on actual movements in the Company's stock price over the most recent historical periods, over the expected term of their stock option grants. Prior to 2023, the expected volatility was derived from a blend of the Company's historical volatility and an average of the historical stock volatilities of several peer companies within the Company's industry, both over a period equivalent to the expected term of the stock option grants.

Expected Dividend Yield. The expected dividend yield assumption is based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends.

Stock options granted under the 2015 Plan in 2023 generally vest as to one-third on the first anniversary of the original vesting date, with the balance vesting monthly over the remaining two years, unless they contain specific performance-based vesting provisions. The maximum term of stock options granted under the 2015 Plan is ten years.

The Company uses the market closing price of its common stock as reported on the Nasdaq Global Select Market to determine the fair value of the shares of common stock underlying stock options.

The following is a summary of stock option activity for the year ended December 31, 2023:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2022	5,471,675	$ 49.86		
Granted	569,821	41.00		
Exercised	(385,130)	17.13		
Forfeited	(197,367)	73.90		
Outstanding at December 31, 2023	5,458,999	$ 50.38	6.65	$ 35,922
Exercisable at December 31, 2023	4,017,227	$ 43.63	6.14	$ 34,790

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during the years ended December 31, 2023, 2022 and 2021 was $7.6 million, $42.8 million, and $262.0 million, respectively.

As of December 31, 2023, there was $56.1 million of unrecognized compensation cost related to stock options that have not yet vested; these costs are expected to be recognized over a weighted average remaining vesting period of 1.4 years.

2016 Employee Stock Purchase Plan

In May 2016, the Company adopted the 2016 Employee Stock Purchase Plan (the "2016 Plan"). The 2016 Plan allows eligible employees to purchase shares of the Company's common stock on the last day of each predetermined six-month offering period at 85% of the lower of the fair market value per share at the beginning or end of the applicable offering period. The 2016 Plan provides for six-month offering periods beginning in January and July of each year.

As of December 31, 2023, there were 1,077,487 shares available for future issuance under the 2016 Plan. The number of shares reserved for issuance under the 2016 Plan shall be cumulatively increased by the lesser of a) one percent of the number of shares of common stock issued and outstanding on the immediately preceding December 31, b) 500,000 shares of common stock, or c) such lesser number of shares of common stock as determined by the board of directors.

During the years ended December 31, 2023, 2022, and 2021, the Company issued 142,079, 77,618, and 30,897 shares of common stock under the 2016 Plan, respectively. The weighted-average purchase prices of shares issued under the 2016 Plan were $27.65, $34.15 and $65.51 per share for the years ended December 31, 2023, 2022, and 2021, respectively.

The fair value of the awards issued under the 2016 Plan to employees was estimated at the beginning of the offering period using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2023	2022	2021
Risk-free interest rate	4.7%-5.53%	0.22%-2.52%	0.05%-0.09%
Expected term (in years)	0.5 years	0.5 years	0.5 years
Expected volatility of underlying stock	60.4%-69.2%	63.6%-95.3%	77.5%-109.2%
Expected dividend yield	0.0%	0.0%	0.0%

14. Loss Per Share

Basic and diluted loss per share was calculated as follows:

	Year Ended December 31,		
	2023	2022	2021
		(In thousands)	
Net loss	$ (481,192)	$ (474,186)	$ (267,892)
Weighted average shares outstanding, basic and diluted	88,770	76,972	70,894
Net loss per share, basic and diluted	$ (5.42)	$ (6.16)	$ (3.78)

The following common stock equivalents were excluded from the calculation of diluted loss per share because their inclusion would have been anti-dilutive:

	Year Ended December 31,		
	2023	2022	2021
		(In thousands)	
Unvested restricted stock units	4,042	1,941	453
Stock options	5,459	5,472	6,305
	9,501	7,413	6,758

15. Stockholders' Equity

At-the-Market Offering Programs

2019 Sale Agreement

In August 2019, the Company entered into an Open Market Sale Agreement (the "2019 Sale Agreement") with Jefferies LLC ("Jefferies"), under which Jefferies was able to offer and sell, from time to time in "at-the-market" offerings, common stock having aggregate gross proceeds of up to $150.0 million. The Company agreed to pay cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2019 Sale Agreement. Under the 2019 Sale Agreement, the Company issued 3,778,889 shares of its common stock.

During the first quarter of 2022, the Company issued 579,788 shares of its common stock, in a series of sales, at an average price of $69.43 per share, in accordance with the 2019 Sale Agreement for aggregate net proceeds of $38.9 million, after payment of cash commissions and legal, accounting and other fees in connection with the sales. The 2019 Sale Agreement expired in the third quarter of 2022.

2022 Sale Agreement

In March 2022, the Company entered into an Open Market Sale Agreement (the "2022 Sale Agreement") with Jefferies, under which Jefferies is able to offer and sell, from time to time in "at-the-market" offerings, shares of the Company's common stock having aggregate gross proceeds of up to $400.0 million. The Company agreed to pay cash commissions of 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement. Through December 31, 2023, the Company issued 7,518,163 shares of its common stock under the 2022 Sale Agreement.

During the year ended December 31, 2023, the Company issued 4,122,824 shares of its common stock, in a series of sales, at an average price of $30.57 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of $121.9 million, after payment of cash commissions and legal, accounting and other fees in connection with the sales.

During the year ended December 31, 2022, the Company issued 3,395,339 shares of its common stock, in a series of sales, at an average price of $57.43 per share, in accordance with the 2022 Sale Agreement for aggregate net proceeds of $189.0 million, after payment of cash commissions and legal, accounting and other fees in connection with the sales. As of December 31, 2023, $2.1 million of these proceeds are included in "Prepaid expenses and other current assets" on the Company's consolidated balance sheet, representing offerings with trade dates in December 2023 that were settled in January 2024.

As of December 31, 2023, $79.0 million in shares of common stock remain eligible for sale under the 2022 Sale Agreement.

Follow-on Offerings

On June 29, 2021, the Company entered into an underwriting agreement related to a public offering of 4,758,620 shares of its common stock, par value $0.0001 per share, including the exercise in full by the underwriters of their option to purchase an additional 620,689 shares at a public offering price of $145.00 per share. The offering closed on July 2, 2021 and the Company received net proceeds of $648.3 million, after deducting the underwriting discount, commissions and offering expenses.

In November 2022, the Company entered into an underwriting agreement related to a public offering of 6,550,219 shares of its common stock, par value $0.0001 per share, at a public offering price of $45.80 per share. In addition, the Company granted the underwriter an option exercisable for 30 days from the date of the agreement to purchase, at the public offering price less any underwriting discounts and commissions, up to an additional 982,532 shares. The offering closed on December 2, 2022 and the Company received net proceeds of $337.9 million, including the exercise in full of the underwriters' option to purchase additional shares, after deducting the underwriting discount, commissions and offering expenses.

Approval of Additional Authorized Shares

In June 2023, the Company filed a Certificate of Amendment to the Company's Second Amended and Restated Certificate of Incorporation to increase the number of authorized shares of common stock from 120,000,000 to 240,000,000. The increase in the number of authorized shares was approved by the holders of a majority of the outstanding shares of the Company's common stock at its Annual Meeting of Stockholders held on June 14, 2023.

16. Related Party Transactions

In the ordinary course of business, the Company may purchase materials or supplies from entities that are associated with a party that meets the criteria of a related party of the Company. These transactions are reviewed quarterly and to date have not been material to the Company's consolidated financial statements.

The Company and AvenCell are parties to the AvenCell LCA, as described in Note 9. The Company's relationship with AvenCell is considered to be as a related party due to the Company's 33.33% investment in AvenCell being accounted for under the equity method. The Company recognized $13.2 million, $22.8 million and $5.9 million in revenue related to the AvenCell LCA for the years ended December 31, 2023, 2022 and 2021, respectively, after eliminating $6.6 million, $11.4 million and $2.9 million in intra-entity profits during those respective periods. The elimination of intra-entity profits results in the deferral of revenue that will be recognized if and when AvenCell commercializes a product with the Company's license or abandons the related project. Until such time, this revenue is indefinitely deferred and excluded from the results of operations of the Company. The Company also recognized $0.2 million and $0.3 million related to materials shipped in accordance with the AvenCell LCA in the years ended December 31, 2023 and 2022, respectively.

The Company and AvenCell were also parties to the AvenCell Co/Co, under which the Company would co-develop and co-commercialize allogeneic universal CAR-T cell products for an immuno-oncology indication. This agreement was terminated by the Company, and all obligations under the terminated agreement were completed in the second quarter of 2023. The Company recognized $0.6 million and $2.0 million in contra-revenue in the years ended December 31, 2023 and 2022, respectively, related to the AvenCell Co/Co agreement. The Company recognized $0.2 million in revenues related to the AvenCell Co/Co agreement for the year ended December 31, 2021.

As of December 31, 2023, there was no remaining transaction price of the AvenCell LCA to be recognized.

17. 401(k) Plan

In 2015, the Company established the Intellia Therapeutics, Inc. 401(k) Plan (the "401(k) Plan") for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. The Company makes matching contributions of 50% of the first 6% of employee contributions. The Company made matching contributions of $3.3 million, $2.7 million and $1.6 million for the years ended December 31, 2023, 2022 and 2021, respectively.

18. Subsequent Event

On February 15, 2024, the Company announced a strategic collaboration with ReCode Therapeutics, Inc. ("ReCode"), a clinical-stage genetic medicines company, to develop novel genomic medicines for the treatment of cystic fibrosis ("CF"). CF is a genetic disease caused by mutations in the *CFTR* gene, leading to the accumulation of thick mucus in the lungs, digestive systems and other organs. CF can result in life-threatening infections, respiratory failure and other serious complications.

The collaboration will leverage the Company's proprietary CRISPR-based gene editing platform, including its DNA writing technology, and ReCode's proprietary Selective Organ Targeting ("SORT") lipid nanoparticle delivery platform to precisely correct one or more CF disease-causing gene mutations. As part of the agreement, the companies will focus initial research efforts on therapeutic approaches that address CF for patients who have limited or no treatment options available, with the opportunity to expand the scope of the collaboration in later phases. The Company will be responsible for the design of the editing strategy and research-grade components for the investigational therapies. ReCode will lead the subsequent preclinical and clinical development. ReCode will also lead worldwide commercialization for certain programs arising from the collaboration. The Company will be eligible to receive pre-specified development and commercial milestone payments, as well as royalties on potential sales. The Company may also exercise an option to lead commercialization in the U.S. for certain programs.

EXHIBIT INDEX

Exhibit No.	Exhibit Index
3.1*	Second Amended and Restated Certificate of Incorporation of the Registrant
3.2	Second Amended and Restated By-laws of the Registrant (1)
4.1	Description of Certain Registrant's Securities (15)
10.1#	2015 Amended and Restated Stock Option and Incentive Plan and forms of award agreements thereunder (3)
10.2#	Senior Executive Cash Incentive Bonus Plan (5)
10.3†	License Agreement dated as of July 16, 2014 by and between the Registrant (as successor in interest of Intellia Therapeutics, LLC) and Caribou Biosciences, Inc. (4)
10.4†	Services Agreement dated as of July 16, 2014 by and between the Registrant (as successor in interest of Intellia Therapeutics, LLC) and Caribou Biosciences, Inc. (4)
10.5#	Form of Indemnification Agreement (3)
10.6	Lease Agreement, by and between the Registrant and MIT 130 Brookline LLC, dated as of October 21, 2014 (5)
10.7	Lease Agreement, by and between the Registrant and BMR-Sidney Research Campus LLC, dated as of January 6, 2016 (5)
10.8#	2016 Employee Stock Purchase Plan (3)
10.9†	Amendment No. 1 to License Agreement dated as of February 2, 2016 by and between the Registrant and Caribou Biosciences, Inc. (5)
10.10†	Addendum to License Agreement dated as of February 2, 2016 by and between the Registrant and Caribou Biosciences, Inc. (5)
10.11†	License and Collaboration Agreement dated as of April 11, 2016 by and between the Registrant and Regeneron Pharmaceuticals, Inc. (2)
10.12	Common Stock Purchase Agreement dated as of April 26, 2016 between the Registrant and Regeneron Pharmaceuticals, Inc. (3)
10.13#	Form of Employment Agreement for Executive Officers (3)
10.14†	Consent to Assignments, Licensing and Common Ownership and Invention Management Agreement dated December 15, 2016 by and between the Registrant, CRISPR Therapeutics AG, The Regents of the University of California, University of Vienna, ERS Genomics Ltd., TRACR Hematology Ltd., Caribou Biosciences, Inc., and Dr. Emmanuelle Charpentier (17)
10.15#	Form of Amended and Restated Employment Agreement (7)
10.16†	Letter Agreement, dated as of July 20, 2018, by and between the Company and Regeneron Pharmaceuticals, Inc. and the corresponding Form of Co-Development and Co-Promotion Agreement, by and between the Company and Regeneron Pharmaceuticals, Inc. (8)
10.17	First Amendment to Lease, dated as of April 5, 2019, by and between the Company and MIT 130 Brookline Leasehold LLC. (10)
10.18#	Fifth Amended and Restated Non-Employee Director Compensation Policy (4)
10.19	Lease Agreement, by and between the Registrant and 281-295 Albany Street Leasehold LLC, dated as of March 12, 2020 (12)
10.20	Second Amendment to Lease, dated as of March 12, 2020, by and between the Company and MIT 130 Brookline Leasehold LLC. (12)
10.21†	Amendment No. 1 to the License and Collaboration Agreement, dated as of May 30, 2020 by and between the Company and Regeneron Pharmaceuticals, Inc. (13)

10.22	Stock Purchase Agreement, dated as of May 30, 2020 by and between the Company and Regeneron Pharmaceuticals, Inc. (13)
10.23#*	Second Amended and Restated Corporate Bonus Plan, effective November 30, 2023
10.24†	Agreement and Plan of Merger, by and among Intellia Therapeutics, Inc., Rewrite Therapeutics, Inc., RW Acquisition Corp., and Shareholder Representative Services, LLC, as securityholder representative, dated as of February 2, 2022 (17)
10.25	Lease Agreement by and between the Registrant and Are-Winter Street Property, LLC, dated as of February 22, 2022 (17)
10.26#	Amended and Restated Retirement Policy for Equity Awards, effective December 6, 2022 (11)
10.27	Amendment to Lease Agreement by and between the Registrant and Are-Winter Street Property, LLC, dated as of June 20, 2023 (14)
10.28	Letter Agreement (Second Amendment) to License and Collaboration Agreement by and between Registrant and Regeneron Pharmaceuticals, Inc., dated November 22, 2022. (18)
10.29	Third Amendment to License and Collaboration Agreement by and between Registrant and Regeneron Pharmaceuticals, Inc., dated September 29, 2023. (18)
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm
31.1*	Certification of Chief Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Chief Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by John M. Leonard, M.D., President and Chief Executive Officer of the Company, and Glenn Goddard, Executive Vice President, Chief Financial Officer of the Company (19)
97.1#*	Intellia Therapeutics, Inc. Compensation Recovery Policy
101.INS*	Inline XBRL Instance Document.
101.SCH*	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents.
104*	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101*)

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10) of Regulation S-K.
* Filed herewith.
# Indicates a management contract or any compensatory plan, contract or arrangement

(1) Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37766) filed with the Securities and Exchange Commission on May 7, 2020
(2) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on May 5, 2016
(3) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 27, 2016
(4) Incorporated by reference to the Registration Statement on Registrant's Quarterly Report on Form 10-Q (File No. 001-37766) filed with the Securities and Exchange Commission on May 5, 2022
(5) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 11, 2016
(6) Incorporated by reference to the Registration Statement on Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 12, 2016
(7) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on April 17, 2018

(8) Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37766) filed with the Securities and Exchange Commission on October 31, 2018
(9) Incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-37766) filed with the Securities and Exchange Commission on February 27, 2019
(10) Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37766) filed with the Securities and Exchange Commission on May 2, 2019
(11) Incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-37766) filed with the Securities and Exchange Commission on February 23, 2023
(12) Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37766) filed with the Securities and Exchange Commission on May 7, 2020
(13) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on June 1, 2020
(14) Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37766) filed with the Securities and Exchange Commission on August 3, 2023
(15) Incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-37766) filed with the Securities and Exchange Commission on February 27, 2020
(16) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on June 17, 2021
(17) Incorporated by reference to the Registrant's Annual Report on Form 10-K (File No. 001-37766) filed with the Securities and Exchange Commission on February 24, 2022
(18) Incorporated by reference to the Registrant's Quarterly Report on Form 10-Q (File No. 001-37766) filed with the Securities and Exchange Commission on November 9, 2023
(19) The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

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.

INTELLIA THERAPEUTICS, INC.

By: /s/ John M. Leonard
John M. Leonard, M.D.
President and Chief Executive Officer

Dated: February 22, 2024

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ John M. Leonard John M. Leonard, M.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 22, 2024
/s/ Glenn Goddard Glenn Goddard	Executive Vice President, Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 22, 2024
/s/ Muna Bhanji Muna Bhanji	Director	February 22, 2024
/s/ Bill Chase Bill Chase	Director	February 22, 2024
/s/ Fred Cohen Fred Cohen, M.D.	Director	February 22, 2024
/s/ Jesse Goodman Jesse Goodman, M.D.	Director	February 22, 2024
/s/ Georgia Keresty Georgia Keresty	Director	February 22, 2024
/s/ Frank Verwiel Frank Verwiel, M.D.	Director	February 22, 2024

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INTELLIA THERAPEUTICS, INC. CORPORATE AND OTHER INFORMATION

Board Of Directors

John Leonard, M.D.
President and Chief Executive Officer

Frank Verwiel, M.D.
Chairman of the Board of Directors

Muna Bhanji, R.Ph.
Founder and Principal, TIBA Global Access, LLC

William Chase
Director

Fred Cohen, M.D., D. Phil.
Founder of Monograph Capital Partners, co-founder and senior managing director at Vida Ventures

Jesse Goodman, M.D., M.P.H.
Director of the Center on Medical Product Access, Safety and Stewardship, and professor of medicine and attending physician in infectious diseases at Georgetown University

Georgia Keresty, Ph.D., M.P.H.
Director

Executive Officers

John Leonard, M.D.
President and Chief Executive Officer

Glenn Goddard
Executive Vice President, Chief Financial Officer and Treasurer

James Basta, J.D.
Executive Vice President, General Counsel and Corporate Secretary

Eliana Clark, Ph.D.
Executive Vice President, Chief Technical Officer

Derek Hicks
Executive Vice President, Chief Business Officer

David Lebwohl, M.D.
Executive Vice President, Chief Medical Officer

Laura Sepp-Lorenzino, Ph.D
Executive Vice President, Chief Scientific Officer

Board Committees

Audit Committee
Compensation and Talent Development Committee
Nominating and Corporate Governance Committee
Science and Technology Committee

Annual Meeting

The 2024 Annual Meeting of Stockholders will be held online, on the day and time as set forth in the notice of the meeting, proxy statement and form of proxy that will be mailed to stockholders in advance of the meeting.

Form 10-K Report

The Company's Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission, is printed as part of this Annual Report. Additional copies are available without charge upon written request to:

Attention: Investor Relations/Corporate Secretary
Intellia Therapeutics, Inc.
40 Erie Street, Suite 130
Cambridge, MA 02139

Transfer Agent

Computershare Trust Company, N.A.
150 Royall Street, Suite 101
Canton, MA 02021
1 (855) 879-3967
https://www.computershare.com/us

Investor Relations

IRcontact@intelliatx.com

Stock Exchange

Intellia Therapeutics, Inc.'s common shares are listed on the Nasdaq Global Market under the trading symbol "NTLA."

Visit us on the Web

https://www.intelliatx.com