INTELLIA THERAPEUTICS, INC.

2024 ANNUAL REPORT

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

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2024

☐ **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 $1,916,954,312 as of June 30, 2024 (based on a closing price of $22.38 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 103,517,460 shares of Common Stock, $0.0001 par value per share, outstanding as of February 14, 2025.

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 2025 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, 2024. 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, 2024

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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 nexiguran ziclumeran ("nex-z," also referred to as NTLA-2001), our program for the treatment of transthyretin ("ATTR") amyloidosis, including the ability to successfully complete our global Phase 3 study for ATTR amyloidosis with cardiomyopathy ("ATTR-CM"), to complete our global Phase 3 study for hereditary ATTR amyloidosis with polyneuropathy ("ATTRv-PN"), file a biologics license application ("BLA") or comparable marketing application within a certain time period, 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 global Phase 3 study, generate results supporting the potential of NTLA-2002 to be a functional cure for HAE, file a BLA or comparable marketing application within a certain time period, or the success of such program;
- 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 applicable 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;
- 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;
- 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 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 resulting product, 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 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 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 activities and 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 may damage public perception of the safety of our product candidates 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.
- 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 have licensed intellectual property from third parties for use in our programs, and termination or modification of any of these licenses could result in the loss of those intellectual property rights, which could harm our business.
- 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 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, 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.
- 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 would be harmed.

- Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches or compromises, 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

Intellia Therapeutics, Inc. ("we," "us," "our," "Intellia," or the "Company") is a leading clinical-stage gene editing company focused on revolutionizing medicine with CRISPR-based therapies. CRISPR is a gene editing technology which is also sometimes referred to as CRISPR/Cas or CRISPR/Cas9 when referring to the use of CRISPR technology with the Cas9 enzyme. Since its inception, Intellia has focused on leveraging gene editing technology to develop novel, first-in-class medicines that address important unmet medical needs and advance the treatment paradigm for patients. Intellia's deep scientific, technical and clinical development experience, along with its people, are helping set the standard for a new class of medicine. To harness the full potential of gene editing, Intellia continues to expand the capabilities of its CRISPR-based platform with novel editing and delivery technologies.

Our mission is to transform the lives of people with severe diseases by developing potentially curative genome editing treatments.

Our lead *in vivo* product candidates, nexiguran ziclumeran ("nex-z", also referred to as NTLA-2001) for the treatment of transthyretin ("ATTR") amyloidosis and NTLA-2002 for the treatment of hereditary angioedema ("HAE"), are the first CRISPR-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 *ex vivo* programs, wholly owned and in collaboration with partners, to develop product candidates for the treatment of immuno-oncology and autoimmune diseases, and multiple *in vivo* programs, also wholly owned and in collaboration with partners, to address diseases with significant unmet medical need by delivering gene editing therapeutics to organs outside the liver.

For over a decade, we have been applying novel technologies, such as CRISPR-based gene editing technologies and lipid nanoparticle ("LNP") delivery technologies, to develop *in vivo* and *ex vivo* product candidates. Our *in vivo* product candidates address genetic diseases by deploying our technologies, including CRISPR/Cas9 delivered by LNPs, as the therapy for diseases with high unmet need. For our *ex vivo* product candidates, we apply our technologies to create engineered cell therapies to address immuno-oncology and autoimmune diseases. Our deep scientific, technical and clinical development experience have enabled us to develop first-in-class therapeutic applications of CRISPR/Cas9 and our other technologies, opening a new frontier in genetic medicine.

Treating—and potentially curing—a broad range of severe diseases requires the application of multiple technologies. With our proprietary technologies at the core of our platform, we continue to research and develop new gene editing and delivery technologies to expand our therapeutic opportunities, furthering progress on the frontier of genetic medicine and generating additional development candidates.

Strategy

Our strategy is to develop and commercialize our product candidates and further our gene editing technology to develop new product candidates, expanding the application of gene editing medicine. Our approach to realizing the broad potential of genome editing includes:

Focusing on Developing and Commercializing Our Lead* In Vivo *Product Candidates, Enabling the Potential of the CRISPR/Cas9 System. We are focused on successfully completing late-stage clinical development of our lead product candidates, nex-z for the treatment of ATTR amyloidosis and NTLA-2002 for the treatment of HAE. As the only *in vivo* genome editing product candidates in Phase 3 clinical trials, our lead product candidates are positioned at the forefront of genomic medicine. Our strategy involves building a foundation designed to position us for the successful commercial launch of our product candidates.

Progressing* Ex Vivo *Therapeutic Programs. We are researching proprietary engineered cell therapies to treat various cancers and autoimmune diseases. We are deploying our LNP-based cell engineering platform and a proprietary allogeneic technology, a first-of-its-kind solution designed to avoid immune rejection by both T cells and natural killer ("NK") cells, 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.

Advancing the Science of Genome Editing. Since our founding, we have been at the scientific forefront of genome editing. Our scientific co-founder, Dr. Jennifer Doudna, and her collaborators developed the Nobel Prize-winning CRISPR/Cas9 system. The versatility of this groundbreaking genome editing system opened the door to numerous scientific breakthroughs and provided the foundation of our genome editing therapeutics, including those that led to our first-in-class clinical product candidates. The versatility of the CRISPR/Cas9 system is exemplified by the diverse types of edits it can facilitate, including knockouts, repairs and insertions, which can be accomplished solely by the endonuclease activity of the Cas9 enzyme or by fusing variants of the Cas9 enzyme to other proteins that can edit double-stranded deoxyribonucleic acid ("DNA") at specific locations in various ways. CRISPR/Cas9 systems comprise a Cas9 enzyme, or a variant thereof, and a ribonucleic acid ("RNA") molecule, called a guide RNA ("gRNA"). The complex formed by the Cas9 enzyme and the gRNA enable CRISPR/Cas9 systems' features by precisely targeting and binding a specific sequence in double-stranded DNA.

We continue to advance the science of genome editing, and therapeutic applications of CRISPR/Cas9 systems, in order to maximize our opportunity to develop clinically successful products. In executing this research strategy, we have applied a risk-mitigated approach to selecting indications with significant unmet medical needs based on four primary criteria:

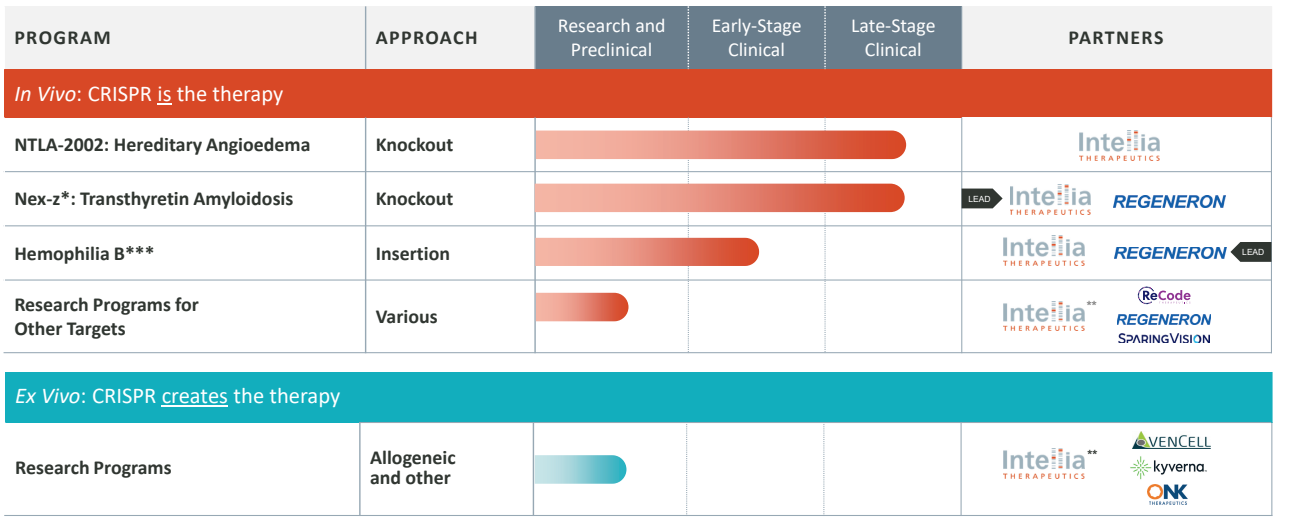
- the type of edit: knockout, repair or insertion;
- the delivery modality for *in vivo* and *ex vivo* applications;
- the existence of efficient regulatory pathways to approval; and
- the potential for the CRISPR/Cas9 system to provide improved therapeutic benefits over existing therapeutic options.

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.

We have built a broad genome editing toolbox, which enables us to select the best tools to develop novel product candidates for each therapeutic application. We continue to invest selectively 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 lead *in vivo* programs are the only Phase 3 genome editing product candidates designed to address unmet need in patients with ATTR amyloidosis and HAE. Our *in vivo* research efforts focus on pursuing additional targets within the liver and expanding delivery technology to enable product candidates for diseases outside the liver.

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 a wholly owned, investigational *in vivo* CRISPR-based therapy designed to knock out the *kallikrein B1 ("KLKB1")* gene in the liver, with the goal of achieving lifelong control of HAE attacks after a single dose. It also aims to eliminate the significant treatment burden associated with currently available HAE therapies.

About the NTLA-2002 Clinical Program

In October 2024, we announced the initiation of the Phase 3 HAELO study of NTLA-2002. HAELO is a global, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of NTLA-2002 in 60 adults with Type I or Type II HAE. Patients will be randomized 2:1 to receive a single 50 mg infusion of NTLA-2002 or placebo. Patients randomized to the placebo arm will be eligible for optional crossover to NTLA-2002 at week 28. The primary endpoint is the number of HAE attacks from week 5 through week 28. In January 2025, we announced that the first patient had been dosed in the global Phase 3 study. We expect to complete enrollment in the second half of 2025 and submit a biologics license application ("BLA") in the second half of 2026 to support plans for a potential United States ("U.S.") launch in 2027.

Also in October 2024, we presented positive Phase 2 data from the ongoing Phase 1/2 study of NTLA-2002, with results continuing to support the potential of NTLA-2002 to be a functional cure for HAE in most patients. Eight of 11 patients in the 50 mg arm ceased having any attacks during the 16-week primary observation period after a single dose of NTLA-2002. These eight patients continued to be attack-free as of the cutoff date. NTLA-2002 was well tolerated. The most frequent adverse events ("AEs") were headache, fatigue and nasopharyngitis. There have been no serious AEs, and all AEs were either Grade 1 or 2. These interim data were published in The New England Journal of Medicine and presented at the 2024 American College of Allergy, Asthma & Immunology ("ACAAI") Scientific Meeting in Boston, Massachusetts.

We expect to present longer-term data from the ongoing Phase 1/2 study in 2025, which will include patients in the Phase 2 portion who initially received a 25 mg dose or placebo and were subsequently given the 50 mg dose of NTLA-2002 selected for the Phase 3 study.

We have received five regulatory designations for NTLA-2002, including orphan designation in the European Union ("EU") granted by the European Commission ("EC") in November 2023. NTLA-2002 was also granted orphan designation and Regenerative Medicine Advanced Therapy ("RMAT") designation by the U.S. Food and Drug Administration ("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.

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 250,000 and 500,000 people may suffer from ATTRwt with cardiomyopathy ("ATTRwt-CM").

Limitations of Current Treatment Options

Currently, there are three marketed therapies for the treatment of ATTRv-PN approved in the 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 are two therapies approved for ATTR amyloidosis with cardiomyopathy ("ATTR-CM") (including both ATTRv-CM and ATTRwt-CM) which have 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

Nex-z is an investigational CRISPR-based therapy designed to inactivate the *TTR* gene in liver cells, thereby preventing the production of TTR protein for the treatment of ATTR amyloidosis. Delivered with our *in vivo* LNP technology, nex-z 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 Nex-z Clinical Program

ATTR Amyloidosis with Cardiomyopathy ("ATTR-CM"):

In 2024, we initiated the pivotal Phase 3 MAGNITUDE trial. The MAGNITUDE trial is a randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of nex-z in adults with ATTR-CM. The primary endpoint of the study is a composite of cardiovascular ("CV")-related mortality and events. Patients will be randomized 2:1 nex-z:placebo, with a single 55 mg infusion of nex-z administered. In March 2024, the first patients in the U.S. and globally were dosed. The MAGNITUDE trial is currently enrolling and we anticipate enrollment to exceed 550 total patients by the end of 2025.

In November 2024, we presented new data from the ATTR-CM arm of the ongoing Phase 1 study. Across all patients (n=36), a single dose of nex-z led to consistently rapid, deep and sustained serum TTR reduction, regardless of baseline levels, through the latest follow-up. At month 12, the mean serum TTR reduction was 90%, and the mean absolute residual serum TTR concentration was 17 µg/mL. With 11 patients who had reached 24 months of follow-up as of November 2024, all patients continued to show a sustained response with no evidence of a waning effect over time. The consistently low levels of serum TTR are anticipated to reduce the rate of ongoing amyloid formation and potentially allow for amyloid clearance and improvement in cardiac function. Nex-z was generally well tolerated across all patients.

Hereditary ATTR Amyloidosis with Polyneuropathy ("ATTRv-PN"):

In November 2024, we announced that the FDA has cleared our nex-z Investigational New Drug ("IND") application to initiate the MAGNITUDE-2 pivotal Phase 3 trial for ATTRv-PN. MAGNITUDE-2 is an international, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of nex-z in 50 adults with ATTRv-PN. Patients will be randomized 1:1 to receive a single 55 mg infusion of nex-z or placebo. Patients randomized to the placebo arm will be eligible for optional crossover to receive nex-z following month 18. The primary endpoints are the change from baseline in modified Neuropathy Impairment Score +7 (mNIS+7) at month 18 and serum TTR at day 29. The mNIS+7 scale is a validated measure specifically designed to assess and quantify polyneuropathy impairment, including muscle weakness, muscle stretch reflexes, sensory loss and autonomic impairment. We are actively screening patients for the Phase 3 MAGNITUDE-2 study and are on track to dose the first patient in the first quarter of 2025.

In November 2024, we presented new data from the ATTRv-PN arm of the ongoing Phase 1 study. Across patients who received a dose of 0.3 mg/kg or higher (n=33), the mean serum TTR reduction was 91% and the mean absolute residual serum TTR concentration was 20 µg/mL at month 12. With 16 patients who had reached 24 months of follow-up as of November 2024, all patients continued to show a sustained response with no evidence of a waning effect over time. It is anticipated that greater TTR reduction may lead to a greater clinical benefit in patients with ATTRv-PN. Nex-z was generally well tolerated across all patients and at all dose levels tested.

Nex-z has received orphan drug designation for the treatment of ATTR amyloidosis by both the FDA and the EC and has received RMAT designation from the FDA for the treatment of ATTRv-PN.

We expect to present longer-term data from both ATTR-CM and ATTRv-PN patients in the Phase 1 study in 2025, which will include updated measures of clinical efficacy and safety.

Nex-z is the subject of a co-development and co-promotion ("Co/Co") agreement (the "ATTR Co/Co") with Regeneron Pharmaceuticals, Inc. ("Regeneron"), 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 and has an option to enter into a co-promotion agreement for the U.S. commercialization. For more information regarding our collaboration with Regeneron, see the section below entitled "**Collaborations - *Regeneron Pharmaceuticals, Inc.*"**

Ex Vivo *Programs*

We and our collaboration partners are advancing preclinical programs utilizing our allogeneic platform for the treatment of immuno-oncology and autoimmune diseases. Our proprietary allogeneic cell engineering platform avoids both T cell- and NK cell-mediated rejection in preclinical models, an unsolved challenge with other investigational allogeneic approaches. Cell therapies engineered with our allogeneic platform, combined with edits to enhance cell function, could offer a new approach to target both hematological and solid tumors. Our proprietary cell engineering 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, and could be used to treat patients with cancer.

- We are developing an allogeneic CAR T cell therapy, which uses cells derived from unrelated donors and modified outside of the human body to allow them to be administered to and persist in an unrelated patient. Preclinical data based on our differentiated allogeneic engineering platform applied a novel combination of gene edits, including knockout of specific human leukocyte antigen ("HLA") Class I and II proteins to avoid rejection by T cells while retaining and matching one select HLA protein that is important for blocking NK cells. This strategy led to persistent allogeneic T cells, comparable to autologous T cells, in preclinical models. With our approach, we may be 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 could address the majority of the patient population with only a small set of donors.
- 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, such as our collaborations with AvenCell Therapeutics, Inc., Kyverna Therapeutics, Inc., and ONK Therapeutics, Ltd.

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 LNP-based approach has been used in multiple *ex vivo* candidates in development by us and our collaborators.

Our Research Programs

We are expanding the range of diseases that can be targeted with our CRISPR-based technologies by expanding our genome editing and delivery technologies to develop new product candidates. This includes advancing gene editing programs in tissues outside the liver, either independently or in collaboration with partners, and using new gene editing technologies, including DNA writing.

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.

We have applied our comprehensive genome editing platform to discover and develop multiple product candidates with complex compositions, including LNPs comprising messenger RNA and gRNA as well as adeno-associated virus ("AAV") vectors when required for insertion. The product candidates we discovered and developed, both wholly owned and together with our collaborators, apply a broad spectrum of genome editing approaches, including the knockout, insertion, and/or modification of genes. Based on both non-human primate ("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 have also 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 addition, we have developed a leading LNP platform that has proven to be critical to the initial success of our, and our collaborators', liver-focused product candidates, where we deliver the CRISPR/Cas9 therapy intravenously to patients using our

proprietary LNP platform. In our research programs, we are focusing on applying those learnings from our initial *in vivo* applications in the liver, to expand our delivery technology to develop product candidates that require delivery to tissues other than the liver. We believe that our proprietary LNP platform provides distinct advantages over other delivery technologies because, *inter alia*, our LNPs provide our product candidates with stability, selective delivery, improved pharmacologic properties and controlled circulation time. 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.

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. As currently amended, the technology collaboration, and related target selection rights, under the 2016 Regeneron Agreement extends until April 2026. In addition, the 2016 Regeneron Agreement has been amended to (a) increase the number of exclusive *in vivo* targets to which Regeneron may develop CRISPR/Cas-based therapeutic products to fifteen and (b) grant Regeneron a non-exclusive license under certain of our intellectual property ("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 leverages 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; 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. Under the 2016 Regeneron Agreement, we will be eligible to receive up to $320.0 million per *in vivo* target in development and commercial milestone payments, as well as up to mid-single-digit royalties on potential future sales.

In 2018, we entered into the ATTR Co/Co agreement with Regeneron. In May 2020, we entered into co-development and co-funding agreements for the treatment of hemophilia A and hemophilia B (the "Hemophilia Co/Co") agreements. We terminated the hemophilia B Co/Co agreement in September 2024. We will continue to support Regeneron with the development of gene editing products directed to hemophilia B, as applicable, under the 2016 Regeneron Agreement.

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 the fourth quarter of 2024, AvenCell completed a Series B financing which resulted in our equity interest being reduced to below 10%.

We have one option to enter into an additional co-development and co-funding agreement for a payment of $30.0 million to 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.

In December 2024 SparingVision provided notice to us to terminate one of their three ocular targets due to a reprioritization strategy, effective in November 2024.

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.

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.

Rewrite Therapeutics Inc. ("Rewrite")

On February 2, 2022, we entered into an Agreement and Plan of Merger with, *inter alia*, Rewrite (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 14, 2024, we entered into a license, collaboration and option agreement with ReCode (the "ReCode LCA"), a clinical-stage genetic medicines company, to develop novel genomic medicines for the treatment of cystic fibrosis ("CF"). The ReCode LCA leverages our proprietary CRISPR-based gene editing platform, including our DNA writing technology, and ReCode's proprietary Selective Organ Targeting ("SORT") LNP delivery platform to precisely correct one or more CF disease-causing gene mutations. As part of the agreement, ReCode and Intellia 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. We 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 and worldwide commercialization for certain programs arising from the collaboration 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 also have an option to lead commercialization in the U.S. for certain programs (the "Co/Co option").

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.

We have a broad portfolio of wholly owned and in-licensed patents and patent applications, including foundational filings on the use of CRISPR/Cas9 systems for genome editing, as well as improvement to CRISPR/Cas9 systems, such as base editor and DNA writing technologies, and delivery technologies, including LNP technologies. We co-own some of these patent portfolios with our collaboration partners, such as Regeneron, and we have licensed some of these patent portfolios from licensors, including Caribou Biosciences, Inc. ("Caribou") and others. If issued, patents resulting from our wholly owned patent portfolio, which may claim our product candidates, 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 Caribou License includes 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. Any patents that grant or have granted from these applications will expire in or after 2034, assuming payment of necessary maintenance fees.

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.

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. As noted above, under the Caribou License, we have an exclusive, worldwide sublicense to UC/Vienna's interest in this foundational CRISPR/Cas9 patent family in 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.

Since 2015, certain U.S. patents and patent applications within the UC/Vienna/Charpentier IP and a patent portfolio owned by the Broad Institute, Massachusetts Institute of Technology, and the President and Fellows of Harvard College (collectively, the "Broad Institute patent family" or the "Broad") have been involved in interferences at the United States Patent and Trademark Office ("USPTO")'s Patent Trial and Appeal Board (the "PTAB"). The most recent interference began in 2019 (the "Broad Interference") and its subject matter pertain to 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. As of December 31, 2024, 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 patent interference, finding that the involved patents and application in the Broad Institute patent family have priority over the patent applications in the UC/Vienna/Charpentier IP with respect to the subject matter of the interference. Both parties appealed to the U.S. Court of Appeals for the Federal Circuit, which held a hearing in May 2024.

In addition, the PTAB has instituted and completed the motions phase in two interferences involving the same UC/Vienna/Charpentier patent applications involved in the Broad Interference—one interference involving certain patent rights owned by ToolGen, Inc. ("ToolGen") and another involving 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 U.S. 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.

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. 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 good manufacturing practice ("GMP") compliant facilities and by processes that comply with FDA and other regulatory agency requirements.

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 nex-z 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., Bayer AG, Ionis Pharmaceuticals, Inc., Metagenomi Technologies, LLC, Novo Nordisk A/S, Pfizer, Inc. and YolTech Therapeutics.

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., CSL Limited, Ionis Pharmaceuticals, Inc., KalVista Pharmaceuticals, Inc., Pharming Group N.V., Pharvaris N.V. and Takeda Pharmaceutical Company Limited.

Our platform and product foci are on the development of therapies using CRISPR-based technologies. Genome editing companies focused on CRISPR-based technologies include: Arbor Biotechnologies, Inc., Beam Therapeutics Inc., Caribou Biosciences, Inc., CRISPR Therapeutics AG, EdiGene, Inc., Editas Medicine, Inc., Emendo Biotherapeutics, Inc., Ensoma, Inc., Excision Biotherapeutics, Inc., Integra Therapeutics, S.L., Mammoth Biosciences, Inc., Metagenomi Technologies, LLC, Modalis Therapeutics Inc., nChroma Bio (formerly Chroma Medicine, Inc.), Prime Medicine, Inc., Scribe Therapeutics, Inc., Tessera Therapeutics, Inc., ToolGen, Inc., Tune Therapeutics, Inc., Verve Therapeutics, Inc. and YolTech Therapeutics.

There are also companies developing therapies using additional genome editing technologies, which include Allogene Therapeutics, Inc., bluebird bio, Inc., Cellectis S.A., Editas Medicine, Inc., Life Edit Therapeutics (an ElevateBio Company), Myeloid Therapeutics, Inc., Poseida Therapeutics, Inc. (acquired by Roche Holdings, Inc.), Precision Biosciences, Inc., Prime Medicine, Inc., Sangamo Therapeutics, Inc., Seamless Therapeutics, Inc., Stylus Medicine, Inc. and Tessera 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 Atara Biotherapeutics, Inc., Allogene Therapeutics, Inc., BRL Medicine, Inc., Caribou Biosciences, Inc., CARSgen Therapeutics Corporation, Cellectis S.A., CRISPR Therapeutics AG, Legend Biotech USA, Inc., Poseida Therapeutics, Inc. (acquired by Roche Holdings, Inc.), Precision BioSciences, Inc., and Sana Biotechnology, Inc. For *in vivo*, these companies include Beam Therapeutics Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Ensoma, Inc.,

Metagenomi Technologies, LLC, Orna Therapeutics, Inc., Precision Biosciences, Inc., Prime Medicine, Inc., Tessera Therapeutics, Inc., Vertex Pharmaceuticals, 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, clinical trial applications ("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 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 RMAT. 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 Centers for Medicare & 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 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. The law also created a new state regulatory agency that is vested with the authority to implement and enforce the CCPA.

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. Further, in addition to comprehensive laws at the state level, some states have been proposing or passing laws that target particular aspects of privacy. For example, the state of Washington has enacted a wide-ranging law that protects the privacy of medical and health-related information that is not covered by HIPAA and a small number of states have passed laws specifically focused on biometric information.

At the federal level, regulators and legislators in the U.S. are increasingly scrutinizing and restricting certain personal data transfers and transactions involving foreign countries. For example, the Biden Administration's executive order Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government-Related Data by Countries of Concern, as implemented by Department of Justice regulations issued in December 2024, prohibits data brokerage transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and/or civil sanctions and may result in exclusion from participation in federal and state programs.

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 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 a product with an orphan designation.

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.

All of 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, and, in April 2024, the European Parliament proposed amendments to the legislative proposals. 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.

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 editing 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. An EU 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. 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.
- At a federal level, President Trump reversed some of President Biden's executive orders including rescinding Executive Order 14087 entitled "Lowering Prescription Drug Costs for Americans." President Trump may issue new

executive orders designed to impact drug pricing, and/or rescind or modify the previous administration's efforts to address drug costs. A number of these and other proposed measures may require authorization through additional legislation to become effective. Congress and the Trump administration 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 who bring high integrity, innovative ideas, and creative solutions to Intellia. In order to attract and retain such highly skilled employees with desired expertise and experience, we support programs that foster our company values, as well as employee engagement, growth and development, while providing competitive compensation and benefits.

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 and directors, are required to abide by, review and confirm compliance to our Code of Business Conduct and Ethics and other internal policies that outline our high expectations.

Many of our employees actively participate in our employee engagement programs, which are designed as a grassroots approach to employee engagement with support and guidance from our executive leadership team. Our engagement programs are an expression of our company values—ONE, EXPLORE, DISRUPT, and DELIVER. Our employee resource groups, including groups focused on mentorship, career development, social activities, and affinity 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 our collaborative workplace. Our employee engagement groups are led by employee volunteers, supported by executive sponsors, and all of our employees are invited to participate to support their colleagues.

As we build our company and execute our strategy, we continue to support a culture that celebrates diverse expertise and experiences and fosters collaboration inside the organization and in our community. We believe in enabling and supporting a collaborative environment that allows our employees' varying voices to be heard and reinforces our company values. As part of our efforts to foster a collaborative environment, support employee engagement, and attract top talent, we provide several types of development trainings for our management teams, including our human resources recruiting team, such as bias awareness training. In addition, we have sponsored career fairs and conferences at organizations focused on scientists and other highly skilled biotechnology professionals with diverse experiences and backgrounds.

We are committed to equitable pay, irrespective of gender, race, ethnicity, sexual orientation, marital status, veteran status, disability or any other legally protected status 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.

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 need to find success now and in the future. Of particular importance is fostering leadership with a wide variety of development programming for our employees, including seminars and tools focused on career development within the organization. We also have an internal mentorship program for our research and development employees, who can work with more senior employees to learn new skills.

Employees

As of February 14, 2025, we had 403 full-time employees, 303 of whom were primarily engaged in research and development activities and 109 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, Nominating and Corporate Governance Committee, and Science and Technology 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, 2024 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.

We are focused on developing novel therapeutics 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.

The approaches we are taking to discover and develop novel therapeutics using CRISPR/Cas9 systems are unproven and may never lead to marketable products.

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 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 nex-z 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 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 uncertain.

If we are unable to develop viable product candidates, achieve regulatory approval for any such product candidate or market and sell any resulting product, we may never achieve profitability.

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-based therapies, 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 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, which would affect our ability to market and sell our product candidates and achieve profitability.

Clinical development involves a lengthy and expensive process, with an uncertain outcome.

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.

We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.

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, clinical trial sites or investigators 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 Risk Evaluation and Mitigation Strategy ("REMS") 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, 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 study 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 for gene and genome editing therapy products has 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 and the draft guidance document titled "Frequently Asked Questions — Developing Potential Cellular and Gene Therapy Products" published in November 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 modified 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 are still at a clinical stage, with only one *ex vivo* CRISPR-based therapeutic product approved in the U.S. and EU. We have ongoing clinical trials in various countries for nex-z for transthyretin ("ATTR") amyloidosis and NTLA-2002 for hereditary angioedema ("HAE"). 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. 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 nex-z and NTLA-2002 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 that they will approve amendments to our INDs or equivalent regulatory filings, including for nex-z and NTLA-2002, 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 nex-z or Phase 1/2 study of NTLA-2002. Interim data from clinical trials that have not been completed are subject to the risk that the later results may be materially different as patient enrollment continues. 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 may damage public perception of the safety of our product candidates 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, and only one *ex vivo* genome editing product, 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 disease such as 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 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 genome editing 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 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 uncertain 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 nex-z for ATTR amyloidosis, NTLA-2002 for HAE, or to our other preclinical stage product candidates 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 nex-z, NTLA-2002 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, which may include warnings or other information about possible unintended DNA changes;
- 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, which may include availability of adequate facilities and equipment;
- 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, research, development, and/or commercialization 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, development, and commercialization efforts. As our product candidates advance through development, as research in the fields in which we work expands, and as more patents are issued, the risk increases that our product candidates, or the resulting products, may give rise to claims of infringement of patent rights owned or controlled by third parties. Our product 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, virus or virus-like particles, or formulation components, such as lipids and lipid nanoparticles. We cannot guarantee that any of these components of our technology, processes, or future product candidates, or the commercialization or 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/or commercialize our product candidates, or the resulting products, 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, research, develop, and/or commercialize. For example, on July 8, 2024, BlueAllele Corp. ("BlueAllele") filed a complaint alleging infringement by Intellia of various patents in the U.S. District Court for the District of Delaware, as more fully discussed in the Legal Proceedings section below. 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 obtain a court order, or other form of relief, blocking our ability to commercialize, manufacture, import, and/or use the applicable product candidate, or resulting products, in the applicable jurisdiction(s) 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, or obtaining such a license may result in significant costs or delays. Even if we were able to obtain a license, it could be limited in scope or geography or it could be non-exclusive, i.e., our competitors may be able to obtain a similar license on substantially the same or better terms. If we are unable to obtain a license on reasonable terms, we could be forced, including by court order, to cease commercializing, manufacturing, importing, and/or using the infringing technology or product, or to redesign our infringing products, which could result in significant costs or delays. 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. Any of the foregoing assertions or results could materially harm our business, cause significant costs or delays to our plans, and/or prevent us from further developing and commercializing the affected product candidates or products, thereby causing us significant harm.

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 obtain 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 intellectual property rights. As discussed above, legal proceedings asserting that we infringe, do not own, or do not have the right to exploit intellectual property rights of a third party could result in legal orders, such as injunctions or other equitable relief, that could effectively block our ability to further develop and commercialize our product candidates or products that we develop, or require us to obtain a license to such third party's intellectual property rights, resulting in significant costs or delays. In addition, as discussed above, such legal proceedings could affect product candidates or products developed with our collaborators, which may also require us to defend and/or indemnify 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 patent portfolio for human therapeutic, prophylactic and palliative uses, including companion diagnostics, except for anti-fungal and anti-microbial uses. 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." In addition, we have granted further sublicenses to this portfolio to our collaborators in certain fields of use. The UC/Vienna/Charpentier 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.

Third parties could assert, and have in the past asserted, that our licensors do not have rights to the licensed patents and/or patent applications (such as, in the case of the Caribou License, the UC/Vienna/Charpentier patent family), including inventorship and ownership rights to currently issued or allowable patents. In addition, third parties could assert, and have asserted, that our licensors, or any rights owned by our licensors, such as UC/Vienna/Charpentier, are limited. If such third parties were found to have rights to patents or patent applications covering our licensed technology (such as CRISPR/Cas9 technology), they could assert that we infringe such patents and, as discussed above, we may be required to obtain rights from such parties (e.g., by obtaining a license) or cease our development and commercialization efforts. Even if such third parties are not ultimately successful in their claims, such assertions could result in significant costs or delays to our programs.

For example, various patent applications within the UC/Vienna/Charpentier patent family and the Broad Institute patent family have been involved in patent interferences and other patent challenges in the U.S. and other jurisdictions, in which the respective owners have alleged, and are alleging, that they invented and/or own intellectual property claiming overlapping aspects of CRISPR/Cas9 systems. Specifically, certain patent applications within the UC/Vienna/Charpentier patent family, licensed to us under the Caribou License, covering certain aspects of CRISPR/Cas9 systems to edit genes in eukaryotic cells, including human cells (collectively, the "UC/Vienna/Charpentier eukaryotic patent family") have been the subject of patent interferences involving patents and patent application co-owned by the Broad Institute, Massachusetts Institute of Technology, the President and Fellows of Harvard College and the Rockefeller University (collectively, the "Broad Institute") that also claim CRISPR/Cas9 systems to edit genes in eukaryotic cells (collectively, the "Broad Institute patent family"). For example, 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 (the "Interference Appeal"), and the oral argument occurred on May 7, 2024.

In addition, on December 14, 2020, the PTAB declared an interference between the same 14 allowable patent applications in the UC/Vienna/Charpentier eukaryotic 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 eukaryotic 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 Interference Appeal. The Sigma-Aldrich interference is in its motions phase, and an order scheduling oral argument issued on October 24, 2022. In addition, other third parties, such as Vilnius University (whose patents we have sublicensed under our Caribou Agreement) 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 either the Broad Institute, ToolGen or Sigma-Aldrich were to succeed in any of their respective interferences, or if other third parties, such as Vilnius University or Harvard University, pursue claims and succeed in such claims, the prevailing party or parties could assert its issued patents against us based on our CRISPR/Cas9-based activities, including research, development, and commercialization of our product candidates or resulting products. In addition, such claims could result in the loss of rights to certain patents and patent applications in the UC/Vienna/Charpentier patent family and, thus, we (and our sublicensees) could lose the benefits that we obtained under our Caribou License to the UC/Vienna/Charpentier patent family. The prevailing party may also 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. As discussed above, such allegations or litigation may affect our ability to market and sell CRISPR/Cas9-based human therapeutics and may result in significant costs or delays to our programs.

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/or commercializing all or some of our product candidates, or the resulting products, 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. For example, the BlueAllele litigation described above has required us to divert resources to the defense of BlueAllele's allegations.

We have licensed intellectual property from third parties for use in our programs, and termination or modification of any of these licenses could result in the loss of those intellectual property rights, which could 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.

Disputes have and may arise between us and our licensors (e.g., Caribou), our licensors (e.g., Caribou) and their licensors (e.g., UC/Vienna), or us and third parties that co-own intellectual property with our licensors or their licensors, regarding the scope of our rights to intellectual property that is subject to a license agreement, including those relating to:

- the scope of rights, if any, granted under the license agreement (e.g, the Caribou License) and other issues related to the terms of the license agreement;
- whether and the extent to which our technology, products and processes infringe, or derive from, intellectual property of the licensor that is not subject to the license agreement;
- whether our licensor or its licensor in the case of a sublicense (e.g., UC/Vienna as Caribou's licensor in the case of our Caribou License) 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 in-licensed 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. As discussed above, 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"). U.S. law also provides for other procedures to challenge patents, including *inter partes* reviews, post-grant reviews and, in certain circumstances, interference or derivation proceedings, that add uncertainty to the possibility of challenge to our developed or licensed patents and patent applications in the future. See the above risk factor entitled **"*Third party claims of intellectual property infringement against us, our licensors or our collaborators may prevent or delay our product discovery, research, development and/or commercialization 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, and may file in the future, challenges to the validity of patents we own or license (e.g., patents or patent applications in the UC/Vienna/Charpentier patent family). If we or the owners of patents we license (e.g., UC/Vienna/Charpentier) fail in defending the validity of these patents, we (and our sublicensees) may lose the benefit of patents and patent applications we own or license (e.g., patents and patent applications licensed under the Caribou License), as discussed above. 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 (including CMOs and CROs), and collaborators, and we also rely on federal and state laws requiring our directors, employees, consultants, contractors (including CMOs and CROs), 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 preclinical development or clinical trials. 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 $519.0 million for the year ended December 31, 2024. As of December 31, 2024, we had an accumulated deficit of $2,177.4 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.

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, complex and difficult to manufacture.*

The manufacturing processes used to produce CRISPR/Cas9-based *in vivo* genome editing product candidates and *ex vivo* engineered cell therapy product candidates are novel and complex. In addition, our manufacturing processes 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 (or, if approved commercial) 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.

We could experience manufacturing problems that result in delays in the development, approval or commercialization of our product candidates or otherwise harm our business.

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 product candidates or 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 exists for approval of gene therapy products, including genome editing products, the limited precedent for genome editing products make 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 European Commission 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, the World Health Organization ("WHO") has established or recommended standards and registries for research using genome editing technologies. 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 trials of nex-z and NTLA-2002, and may in the future conduct clinical trials for our other product candidates 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 nex-z 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 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 European Commission ("EC") 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 EC 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 nex-z for the treatment of ATTR amyloidosis and from the FDA and 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, proposed amendments to EU regulations regarding orphan medicines are under consideration 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 nex-z for the treatment of ATTRv-PN and for NTLA-2002 for the treatment of HAE, and may in the future seek such designation for some of our other 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 nex-z for the treatment of ATTRv-PN and 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.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates.

In June 2024, the U.S. Supreme Court overruled the *Chevron* doctrine, which gave deference to regulatory agencies' statutory interpretations in litigation against federal government agencies, such as the FDA and Centers for Medicare & Medicaid Services ("CMS"), agencies within the U.S. Department of Health and Human Services, where the law is ambiguous. This decision may result in more lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, which could undermine the FDA's authority, lead to uncertainties in the industry, and disrupt the FDA's normal operations, any of which could delay the FDA's review of our regulatory submissions. We cannot predict the full impact of this decision, future judicial challenges brought against the FDA, or the nature or extent of government regulation that may arise from future legislation or administrative action. In addition, the leadership, personnel, policies, and/or priorities of government departments and agencies responsible for establishing and operating programs and regulations related to pharmaceutical products, such as the U.S. Department of Health and Human Services, FDA and CMS, may change. New leadership, personnel, policies, priorities, and/or regulations may affect our industry and/or products. For example, FDA or CMS policies and practices concerning gene and cell therapies may change in a way that disparately impacts our product candidates, such as reducing the staff of these agencies or not retaining experienced staff at these agencies who have expertise relevant to our industry and/or products. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

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. In addition, as discussed above, the U.S. Supreme Court's June 2024 decision to overturn established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays, and/or changes. 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.

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." In addition, on July 31, 2024, Massachusetts passed the Frances Perkins Workplace Equity Act, requiring disclosure of the pay range for a particular job under certain circumstances, including job postings, promotions, or when an employee requests. 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 these laws.

For example, the Massachusetts non-compete law limits the terms under which employers can enter into non-competition agreements with employees. Further, other jurisdictions in which our employees may work limit enforcement of non-competition agreements. Additionally, 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.

Inadequate funding for, substantial changes in leadership, personnel, policies or priorities of, or other 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 ("SEC"), have had to furlough critical FDA, SEC and other government employees and stop critical activities.

A prolonged government shutdown in the U.S. or other jurisdictions where we plan to conduct our clinical trials, manufacturing, or other operations, or substantial changes in leadership, personnel, policies or priorities 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 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 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 are manufacturing and processing product candidate components on a clinical scale and may not be able to successfully continue to do so. We are optimizing and will continue to optimize the manufacturing process for late-stage clinical and commercial supply, 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.

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 EU General Data Protection Regulation ("EU GDPR") and the EU GDPR in such form as incorporated into the laws of the U.K. ("U.K. GDPR," collectively with EU GDPR referred to as "GDPR"), we could be subject to substantial fines and other penalties, including fines of up to 20.0 million Euros (17.5 million GBP for the U.K. GDPR) or up to 4% of our total worldwide annual turnover for the preceding financial year, whichever is higher. The GDPR also confers a private right of action on data subjects and consumer

associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations.

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.

Public health concerns and measures taken in response by U.S. or other governments may significantly impact 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, incidents, or compromises, which could result in a 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 cybersecurity incidents, breaches or compromises 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 incidents, breaches, compromises 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. We and 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 incidents, compromises or 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. Cybersecurity incidents, breaches, compromises, 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, incidents or compromises 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. We have a process that assesses risks and opportunities for AI deployed at Intellia.

A growing number of legislators and regulators are adopting laws and regulations and have focused enforcement efforts on the adoption of AI, and use of such technologies in compliance with ethical standards and societal expectations. These developments may increase our compliance burden and costs in connection with use of AI and lead to legal liability if we fail to meet evolving legal standards or if use of such technologies results in harms or other causes of action we did not predict. For example, the EU's Artificial Intelligence Act ("AI Act") entered into force on August 1, 2024, with most provisions becoming effective on August 2, 2026. This legislation imposes significant obligations on providers and deployers of AI systems, and encourages providers and deployers of AI systems to account for EU ethical principles in their development and use of these systems. The scope of

requirements depends on legal and risk determinations that rely on novel legal provisions that have not yet been interpreted by courts or regulators, and non-compliance can lead to significant fines.

Likewise, in the U.S., several states, including Colorado and California, passed laws that will take effect in 2026, to regulate various uses of AI, including to make consequential decisions. In addition, various federal regulators have issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The FDA, for example, issued guidance on the use of AI in medical devices, requiring detailed risk management and review processes to obtain approvals. If we use AI systems governed by these laws or regulations, we will need to meet higher standards of data quality, transparency, monitoring and human oversight, and we would need to adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements, with the potential for significant enforcement or litigation in the event of any perceived non-compliance.

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

Our vendors may in turn incorporate AI tools into their offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI, to engage in illegal activities involving the theft and misuse of personal information, confidential information and IP. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

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 nex-z 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., Bayer AG, Ionis Pharmaceuticals, Inc., Metagenomi Technologies, LLC, Novo Nordisk A/S, Pfizer, Inc. and YolTech Therapeutics.

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., CSL Limited, Ionis Pharmaceuticals, Inc., KalVista Pharmaceuticals, Inc., Pharming Group N.V., Pharvaris N.V. and Takeda Pharmaceutical Company Limited.

Our platform and product foci are on the development of therapies using CRISPR-based technologies. Genome editing companies focused on CRISPR-based technologies include: Arbor Biotechnologies, Inc., Beam Therapeutics Inc., Caribou Biosciences, Inc., CRISPR Therapeutics AG, EdiGene, Inc., Editas Medicine, Inc., Emendo Biotherapeutics, Inc., Ensoma, Inc., Excision Biotherapeutics, Inc., Integra Therapeutics, S.L., Mammoth Biosciences, Inc., Metagenomi Technologies, LLC, Modalis Therapeutics Inc., nChroma Bio (formerly Chroma Medicine, Inc.), Prime Medicine, Inc., Scribe Therapeutics, Inc., Tessera Therapeutics, Inc., ToolGen, Inc., Tune Therapeutics, Inc., Verve Therapeutics, Inc. and YolTech Therapeutics.

There are also companies developing therapies using additional genome editing technologies, which include Allogene Therapeutics, Inc., bluebird bio, Inc., Cellectis S.A., Editas Medicine, Inc., Life Edit Therapeutics (an ElevateBio Company),

Myeloid Therapeutics, Inc., Poseida Therapeutics, Inc. (acquired by Roche Holdings, Inc.), Precision Biosciences, Inc., Prime Medicine, Inc., Sangamo Therapeutics, Inc., Seamless Therapeutics, Inc., Stylus Medicine, Inc. and Tessera 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 Atara Biotherapeutics, Inc., Allogene Therapeutics, Inc., BRL Medicine, Inc., Caribou Biosciences, Inc., CARSgen Therapeutics Corporation, Cellectis S.A., CRISPR Therapeutics AG, Legend Biotech USA, Inc., Poseida Therapeutics, Inc. (acquired by Roche Holdings, Inc.), Precision BioSciences, Inc., and Sana Biotechnology, Inc. For *in vivo*, these companies include Beam Therapeutics Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Ensoma, Inc., Metagenomi Technologies, LLC, Orna Therapeutics, Inc., Precision Biosciences, Inc., Prime Medicine, Inc., Tessera Therapeutics, Inc., Vertex Pharmaceuticals, 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, Edward J. Dulac III, our Executive Vice President, Chief Financial Officer and Treasurer, James Basta, our Executive Vice President, General Counsel and Corporate Secretary, Eliana Clark, our Executive Vice President and Chief Technical Officer, Michael P. Dube, our Chief Accounting Officer, David Lebwohl, our Executive Vice President and Chief Medical Officer and Birgit Schultes, 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.

To help attract, retain, and motivate qualified employees in senior roles, we use equity-based awards and performance-based cash incentive awards. Sustained declines in our stock price, or lower stock price performance relative to competitors, can reduce the retention value of our equity-based awards, which can impact the competitiveness of our compensation. There can be no assurance that we will be successful in retaining existing personnel or recruiting new personnel.

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 uptake.

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 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-insurance or 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, 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 entitled "**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:

- 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 went into effect on January 1, 2023, and substantially modified the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information, 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, effective as of March 31, 2024, that regulates health and medical information that is not subject to HIPAA. Similar laws have been passed in Connecticut and Nevada. Additionally, 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 European Economic Area ("EEA"), the collection and use of personal data is regulated by the GDPR and the member states' related data protection and privacy laws. As the GDPR 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. The GDPR imposes strict requirements, including requirements to ensure an appropriate legal basis or condition applies to the processing of personal data, special protections for "sensitive" personal data which includes health and genetic information of individuals in the EEA or the U.K.; 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. The GDPR 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, the GDPR includes strict requirements on, and prohibits, the transfer of personal data subject to GDPR to jurisdictions that have not been deemed by competent authorities to offer "adequate" privacy protections ("third countries"), unless a derogation exists or a valid GDPR 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 the GDPR, 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 developments related to the U.K.'s withdrawal from the EU ("Brexit") 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 introduced a Data Use and Access 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 GDPR 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 GBP 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 GDPR, 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 addition, significant uncertainty exists in the U.S. and certain other jurisdictions regarding the provision and financing of healthcare because the elected administrations in such countries 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.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

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. Even if the allegations against us are unfounded or we ultimately are not held liable, we may experience related negative publicity resulting in damage to our reputation. 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.

Our executive officers, directors, 5% or greater stockholders and their affiliates beneficially own a significant percentage 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. In addition, although the U.S. Department of Treasury, the Federal Deposit Insurance Corporation ("FDIC") and Federal Reserve Board previously provided loans and other programs to mitigate the risk of potential losses from uninsured deposits, there is no guarantee that the U.S. Department of Treasury, FDIC and Federal Reserve Board will provide access to such programs 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 and "at-the-market" offerings, could result in additional dilution of the percentage ownership of stockholders and could cause our stock price to fall.

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

Given the volatility in the capital markets, we may not be willing or able to continue to raise equity capital. 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.

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. 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, 2024, we had federal and state NOLs of $1,088.4 million and $1,079.2 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, 2024, we had federal and state research and development and other credit carryforwards of approximately $139.3 million and $77.9 million, which begin to expire in 2034 and 2029, respectively. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (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. The analysis did not result in a material limitation to our tax attributes and the results of this analysis are reflected herein. We have not completed an analysis through December 31, 2024. To the extent there was a change in control during 2023 and 2024, 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 is integrated within our enterprise risk management program.

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, security assessments, vendor risk management, regular system maintenance including application of security patches as appropriate, regular penetration testing and implementation of enhancements to security measures used to protect our systems and data. We employ third parties, including assessors, consultants and auditors, in our cyber risk management program as appropriate, e.g., training, assessment, auditing, benchmarking, and penetration testing.

Our CSIRP 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 related to identified cybersecurity incidents, including a framework for identifying and addressing material 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, incidents or compromises, which could result in a 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 Information Technology ("IT"), periodically reports to the full Board of Directors to inform them of potential cybersecurity risks and threats, the status of projects to further develop our information security systems, and the emerging cybersecurity threat landscape.

Our Head of IT has primary responsibility for day-to-day management of our cybersecurity risk management program, including leading a dedicated team of IT professionals to monitor and assess cybersecurity risks, and is responsible for strategic leadership of our cybersecurity risk management program. The Head of IT role is currently held by an individual who has close to twenty years of professional IT management experience in the life sciences industry. 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. Under our CSIRP and other applicable policies and procedures, we have established a framework for responding to cybersecurity incidents based on severity of the incident, which includes escalation to our executive leadership team and other management committees and assessment of materiality of cybersecurity incidents individually and in the aggregate.

Item 2. Properties

In aggregate, the Company leases approximately 370,000 square feet of real estate, including office, laboratory and manufacturing space in Cambridge, Massachusetts and the surrounding areas.

Our headquarters are located at 40 Erie Street in Cambridge, Massachusetts, where we occupy approximately 65,000 square feet of office and laboratory space, which expires in 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, approximately 39,000 square feet of office and laboratory space at 281 Albany Street in Cambridge, Massachusetts, which expires in 2030 with an option to extend the lease for two successive five-year terms, approximately 62,000 square feet of office and laboratory space at 640 Memorial Drive, Cambridge, Massachusetts, which expires in 2027, approximately 14,000 square feet of office space at 17 Tudor Street in Cambridge, Massachusetts, which expires in 2025 and approximately 38,000 square feet of office and laboratory space at 730 Main Street, Cambridge, Massachusetts, which expires in 2032 with an option to extend the lease for one five-year term. We have subleased approximately 13,000 square feet of the property at 730 Main Street for office and laboratory use through March 2026.

We also lease approximately 140,000 square feet of office, general laboratory and manufacturing space at 840 Winter Street, Waltham, Massachusetts. In February 2025, we entered into a Second Amendment to Lease (the "Winter Street Amendment"). Pursuant to the Winter Street Amendment, the 840 Winter Street lease will terminate on or before June 30, 2028, as described in Note 16, "Subsequent Events."

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.

BlueAllele Corp. v. Intellia Therapeutics, Inc.

On July 8, 2024, BlueAllele Corp. ("BlueAllele") filed a complaint alleging infringement by Intellia of various patents in the U.S. District Court for the District of Delaware. Specifically, BlueAllele alleges that our experimentation, basic research, identification, optimization, manufacturing and/or use of bi-directional insertion template technology infringes the asserted patents and seeks, *inter alia*, unspecified compensatory damages and an injunction against the alleged infringing activities. On September 12, 2024, we filed a motion to dismiss the complaint, and on December 9, 2024, the court denied the motion to dismiss and discovery began. On January 6, 2025, we filed our answer and counterclaims, and BlueAllele filed a motion to dismiss our counterclaims on January 27, 2025. On February 21, 2025, the court substantially denied BlueAllele's motion to dismiss, and granted the motion with respect to one counterclaim.

Gonzalez v. Intellia Therapeutics, Inc.

On February 11, 2025, a purported stockholder of the Company filed a lawsuit, captioned *Gonzalez v. Intellia Therapeutics, Inc.*, No. 1:25-cv-01353 (D. Mass.), in the U.S. District Court for the District of Massachusetts against the Company and certain of our officers on behalf of a putative class of stockholders who purchased Company shares from July 30, 2024 through January 8, 2025. The complaint alleges claims under Sections 10(b) and 20(a) and Rule 10b-5 of the Securities Exchange Act of 1934 (the "Exchange Act") premised upon statements relating to the Company's NTLA-3001 program and the demand for viral-based editing. The complaint seeks unspecified damages, interest, reasonable attorneys' fees and other costs. We intend to defend vigorously against the claims.

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."

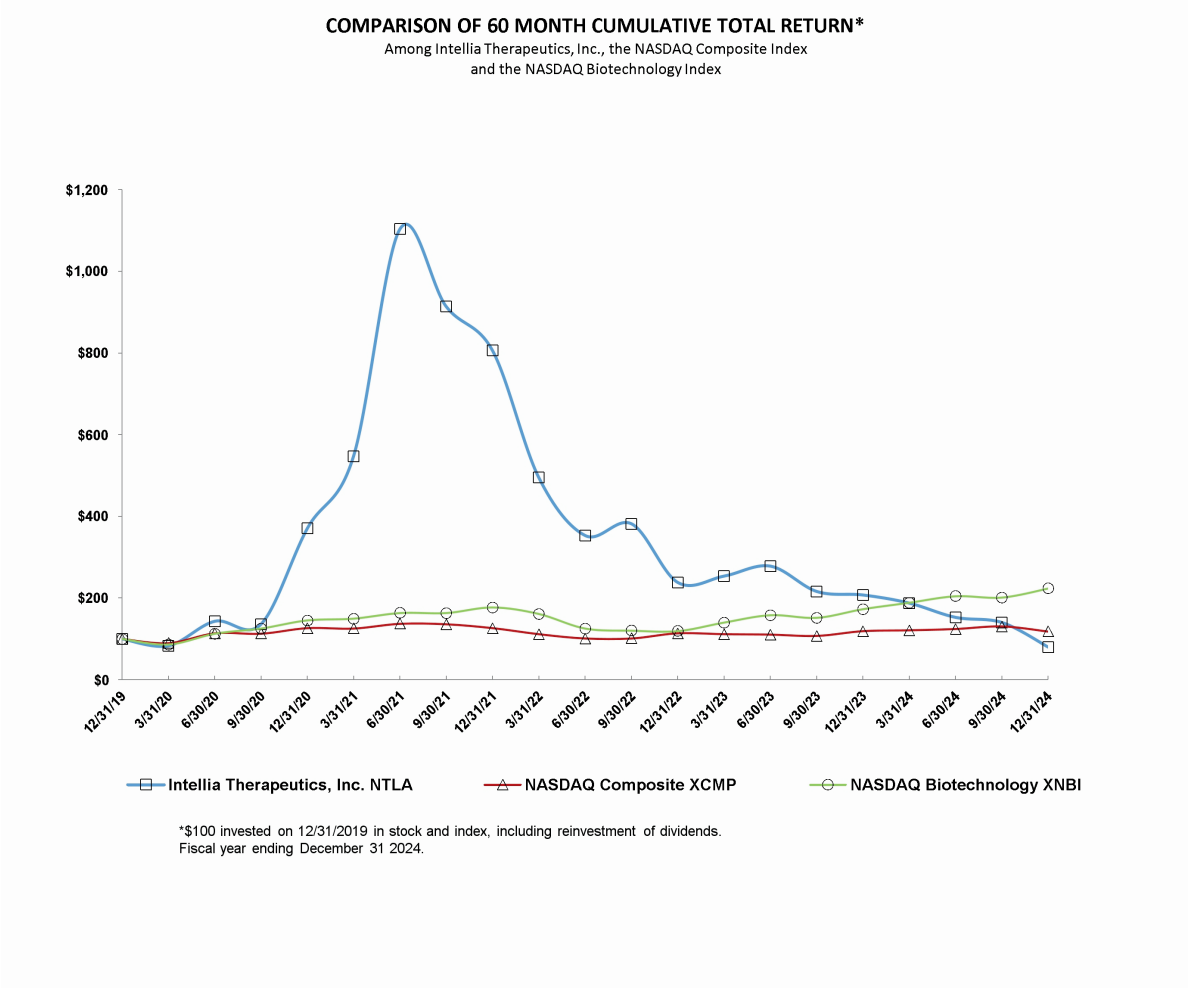
As of February 14, 2025, the number of holders of record of our common stock was 13. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other 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, 2019 through December 31, 2024, 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 2022 was included in our Annual Report on Form 10-K for the year ended December 31, 2023 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 22, 2024.

Management Overview

Intellia Therapeutics, Inc. ("we," "us," "our," "Intellia," or the "Company") is a leading clinical-stage gene editing company focused on revolutionizing medicine with CRISPR-based therapies. CRISPR is a gene editing technology which is also sometimes referred to as CRISPR/Cas or CRISPR/Cas9 when referring to the use of CRISPR technology with the Cas9 enzyme. Since its inception, Intellia has focused on leveraging gene editing technology to develop novel, first-in-class medicines that address important unmet medical needs and advance the treatment paradigm for patients. Intellia's deep scientific, technical and clinical development experience, along with its people, are helping set the standard for a new class of medicine. To harness the full potential of gene editing, Intellia continues to expand the capabilities of its CRISPR-based platform with novel editing and delivery technologies. 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 license and collaboration agreements.

Research and Development

Research and development expenses 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

During the year ended December 31, 2024, other income (expense), net consists of interest income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities and change in the fair value of our investments. During the year ended December 31, 2023, other income (expense), net consisted of interest income earned on our cash, cash equivalents, restricted cash equivalents and marketable securities, loss from our 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 Year Ended December 31, 2024 and 2023

The following table summarizes our results of operations:

	Year Ended December 31,		Period-to-Period Change
	2024	2023	
	(In thousands)		
Collaboration revenue	$ 57,877	$ 36,275	$ 21,602
Operating expenses:			
Research and development	466,311	435,069	31,242
General and administrative	125,829	116,497	9,332
Total operating expenses	592,140	551,566	40,574
Operating loss	(534,263)	(515,291)	(18,972)
Other income (expense), net:			
Interest income	47,807	49,832	(2,025)
Change in fair value of investments, net	(32,565)	-	(32,565)
Loss from equity method investment	-	(15,633)	15,633
Change in fair value of contingent consideration	-	(100)	100
Total other income (expense), net	15,242	34,099	(18,857)
Net loss	$ (519,021)	$ (481,192)	$ (37,829)

Collaboration Revenue

Collaboration revenue increased by $21.6 million to $57.9 million during the year ended December 31, 2024, as compared to $36.3 million during the year ended December 31, 2023. The increase in collaboration revenue during the year ended December 31, 2024 is primarily due to the recognition of $21.0 million of previously eliminated intra-entity profit under our license and collaboration agreement with AvenCell Therapeutics, Inc. (the "AvenCell LCA") and a $12.8 million increase in revenue related to Regeneron Pharmaceuticals, Inc. ("Regeneron"), offset by a $12.3 million decrease in revenue related to the AvenCell LCA. 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 $31.2 million to $466.3 million during the year ended December 31, 2024, as compared to $435.1 million during the year ended December 31, 2023.

The following table summarizes our research and development expenses, together with the changes in those items in dollars and the respective percentages of change:

	Year Ended December 31,		Period-to-Period Change	Percent Change
	2024	2023		
	(In thousands)			
External development expenses by program:				
Nex-z	$ 69,793	$ 54,454	$ 15,339	28%
NTLA-2002	42,173	24,560	17,613	72%
NTLA-3001	8,709	17,312	(8,603)	-50%
Unallocated research and development expenses:				
Employee-related expenses	127,383	136,628	(9,245)	-7%
Research materials and contracted services	60,661	60,726	(65)	0%
Rewrite research milestone	-	874	(874)	-100%
Facility-related expenses	59,397	53,141	6,256	12%
Stock-based compensation	94,230	82,211	12,019	15%
Other	3,965	5,163	(1,198)	-23%
Total research and development expenses	$ 466,311	$ 435,069	$ 31,242	7%

The increase in research and development expenses for the year ended December 31, 2024 compared to the year ended December 31, 2023 was primarily attributable to:

- a $15.3 million increase in external costs related to the development of nexiguran ziclumeran ("nex-z", also referred to as NTLA-2001), one of our lead product candidates, primarily due to an increase in spend on contracted services and consulting fees, offset in part by a decrease in drug components;
- a $17.6 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 fees;
- an $8.6 million decrease in external costs related to NTLA-3001, primarily related to initial manufacturing activities in 2023, offset in part by an increase in spend on contracted services;
- a $9.2 million decrease in employee-related expenses, primarily driven by a workforce reduction in January 2024;
- a $6.3 million increase in facility-related expenses primarily related to depreciation, facility maintenance costs, technology expense allocated to research and development, and rent; and
- a $12.0 million increase in stock-based compensation.

General and Administrative

General and administrative expenses increased by $9.3 million to $125.8 million during the year ended December 31, 2024, compared to $116.5 million during the year ended December 31, 2023. This increase was primarily related to an increase in stock-based compensation of $8.2 million.

Other Income (Expense), Net

The decrease in other income (expense), net of $18.9 million is primarily related to $32.6 million in expense due to the change in fair value of our investments in Kyverna Therapeutics, Inc. ("Kyverna") and AvenCell and a $2.0 million decrease in interest income, offset in part by a $15.6 million change related to our equity method loss recorded in the year ended December 31, 2023.

Liquidity and Capital Resources

Since our inception through December 31, 2024, we have funded our operations through our initial public offering and concurrent private placements, follow-on public offerings, our collaboration agreements, at-the-market offerings and the sale of convertible preferred stock.

As of December 31, 2024, we had $861.7 million in cash, cash equivalents and marketable securities.

At-the-Market Offering Programs

2022 Sale Agreement

In 2022, we entered into an Open Market Sale Agreement (the "2022 Sale Agreement") with Jefferies LLC ("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. In February 2024, we entered into an amendment to the 2022 Sale Agreement (the "2022 Sale Agreement, as amended") to increase the size of the at-the-market offering program from $400.0 million to $750.0 million. We agreed to pay cash commissions of up to 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement, as amended. To date through December 31, 2024 we have issued 14,522,533 shares of our common stock under the 2022 Sale Agreement, as amended. During the year ended December 31, 2024, we issued 7,004,370 shares of our common stock, in a series of sales, at an average price of $25.68 per share, in accordance with the 2022 Sale Agreement, as amended, for aggregate net proceeds of $174.8 million, after payment of cash commissions and approximately $0.3 million related to legal, accounting and other fees in connection with the sales. As of December 31, 2024, $249.1 million in shares of common stock remain eligible for sale under the 2022 Sale Agreement, as amended.

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 2025, we expect our expenses to decrease compared to prior periods as a result of our recently announced strategic reorganization in January 2025, as we focus resources on high value programs within our pipeline, such as NTLA-2002 and nex-z, to ensure efficient execution, achieve near-term clinical milestones, and prepare for commercial launch.

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 SAS ("SparingVision"), ONK Therapeutics, Ltd. ("ONK") and ReCode Therapeutics, Inc. ("ReCode"), 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, 2024, 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 the first half of 2027, 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.

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:

	Year Ended December 31,	
	2024	2023
	(In thousands)	
Net cash used in operating activities	$ (348,880)	$ (394,086)
Net cash provided by (used in) investing activities	125,567	(31,347)
Net cash provided by financing activities	185,747	130,323

Net cash used in operating activities

Net cash used in operating activities of $348.9 million during the year ended December 31, 2024 primarily consists of a net loss of $519.0 million, further reduced by the non-cash recognition of $21.0 million of previously eliminated intra-entity profit recorded within "collaboration revenue" and accretion of investment discounts and premiums of $17.8 million. These decreases are offset in part by stock-based compensation of $154.3 million, $32.6 million in net adjustments to the fair value of our investments in Kyverna and AvenCell, net changes in operating assets and liabilities of $11.9 million and depreciation of $10.3 million.

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 provided by (used in) investing activities

During the year ended December 31, 2024, we added $125.6 million of net cash through investing activities. The increase in the year ended December 31, 2024 is primarily due to $131.3 million in marketable securities that matured (net of purchases), offset in part by $5.8 million in cash used for the purchase of property and equipment.

During the year ended December 31, 2023 we used cash of $31.3 million in investing activities. The decrease in the year ended December 31, 2023 is primarily due to $17.4 million in marketable securities purchased (net of maturities) and $14.0 million in cash used for the purchase of property and equipment.

Net cash provided by financing activities

Net cash provided by financing activities of $185.7 million during the year ended December 31, 2024 includes $176.9 million in net proceeds from at-the-market offerings, $5.9 million in cash received from the exercise of stock options and $3.0 million in cash received from the issuance of shares through our employee stock purchase plan.

Net cash provided by financing activities of $130.3 million during the year ended December 31, 2023 includes $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.

Contractual 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

As of December 31, 2024, our total undiscounted future minimum lease payments for our property leases that have commenced were $294.8 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 11 of the consolidated financial statements included in this Annual Report on Form 10-K.

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 Therapeutics, Inc. ("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.

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 U.S. GAAP. 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 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 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, 2024, 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 clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense.

Stock-Based Compensation

Our share-based compensation programs grant awards that have included stock options and restricted stock units. Grants are awarded to employees and non-employees, including directors. 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.

We measure employee stock-based compensation for stock options based on the grant date fair value of the equity awards using the Black-Scholes option pricing model. For awards with service conditions only, we recognize stock-based compensation expense on a straight-line basis over the requisite service period. 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, which requires significant judgment. Our stock price is a key input that will drive the grant date fair value of the equity awards. Forfeitures are recorded as they occur.

The fair value of market-based restricted stock units and performance-based restricted stock units with a Total Shareholder Return ("TSR") multiplier are determined using a Monte Carlo simulation model, which uses multiple input variables to determine the probability of satisfying the market condition requirements.

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, 2024, we had cash equivalents, restricted cash equivalents and marketable securities of $739.4 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 interest 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, 2024.

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, 2024.

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, 2024. 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, 2024, 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, 2024 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, 2024, 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, 2024, 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, 2024, of the Company and our report dated February 27, 2025, 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 27, 2025

Item 9B. Other Information

Rule 10b5-1 Trading Plans

The following table describes for the three months ended December 31, 2024 each trading arrangement under which 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.

Name *(Title)*	Action Taken *(Date of Action)*	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
James E. Basta *(EVP, General Counsel)*	Terminated *(October 31, 2024)*	Rule 10b5-1 trading arrangement	Sale	Until the earlier of (a) November 11, 2024; (b) the first date on which all trades have been executed or all trading orders related to such trades have expired; and (c) the date on which the plan holder gives notice to terminate the plan.	None

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 Securities and Exchange Commission (the "SEC") with respect to our 2025 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 30, 2025.

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 2025 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 2025 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 2025 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 2025 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 2025 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.

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, 2024 and 2023, 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, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, 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, 2024, 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 27, 2025, 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.

Equity-Method Investment — Accounting for the Loss of Significant Influence – Refer to Note 10 to the financial statements.

Critical Audit Matter Description

The Company historically accounted for its investment in AvenCell Therapeutics, Inc. ("AvenCell") (the "AvenCell investment") under the equity method of accounting in accordance with ASC 323, *Investments – Equity Method and Joint Ventures* ("ASC 323"). During the year ended December 31, 2024, the Company determined that they lost the ability to exercise significant influence over AvenCell. This resulted in management having to determine the accounting for the AvenCell investment as part of the transition from ASC 323 to ASC 321*, Investments — Equity Securities* ("ASC 321").

We identified the accounting for the transition of the AvenCell investment from ASC 323 to ASC 321 as a critical audit matter. Auditing the Company's application of the guidance required significant auditor judgment, including the need to involve an internal subject matter expert, due to the complex nature of evaluating the treatment of previously eliminated intra-entity profit and previously recognized accumulated other comprehensive loss associated with the AvenCell investment, under the guidance in ASC 323.

How the Critical Audit Matter Was Addressed in the Audit

Our principal audit procedures related to the Company's accounting for the AvenCell investment upon the transition from ASC 323 to ASC 321 included the following:

- We tested the effectiveness of controls over the Company's processes for assessing the accounting treatment of the AvenCell investment upon the transition from ASC 323 to ASC 321.
- With the assistance of professionals in our firm having expertise in equity-method accounting, we evaluated the Company's application of relevant accounting guidance regarding the treatment of previously eliminated intra-entity profit and accumulated other comprehensive loss associated with the AvenCell investment upon the transition from ASC 323 to ASC 321.
- We obtained and read the Company's accounting position paper assessing the accounting treatment of the AvenCell investment upon the transition from ASC 323 to ASC 321.
- We tested the mathematical accuracy of management's calculations of the accounting associated with the AvenCell investment upon the transition from ASC 323 to ASC 321.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 27, 2025

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

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

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

	December 31, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents	$ 189,182	$ 226,748
Marketable securities	412,333	685,475
Accounts receivable	8,517	36,456
Prepaid expenses and other current assets	29,831	49,651
Total current assets	639,863	998,330
Marketable securities - noncurrent	260,215	99,864
Property and equipment, net	27,381	32,760
Operating lease right-of-use assets	219,292	115,375
Equity method investment	-	11,765
Investments and other assets	44,264	42,883
Total assets	$ 1,191,015	$ 1,300,977
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 14,589	$ 7,452
Accrued expenses	55,355	67,017
Current portion of operating lease liability	20,246	18,599
Current portion of deferred revenue	20,661	22,140
Total current liabilities	110,851	115,208
Deferred revenue, net of current portion	18,256	38,853
Long-term operating lease liability	189,952	96,747
Total liabilities	319,059	250,808
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Common stock, $0.0001 par value; 240,000,000 shares authorized at December 31, 2024 and December 31, 2023; 102,029,594 and 92,997,158 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	10	9
Additional paid-in capital	3,048,741	2,710,797
Accumulated other comprehensive income (loss)	605	(2,258)
Accumulated deficit	(2,177,400)	(1,658,379)
Total stockholders' equity	871,956	1,050,169
Total liabilities and stockholders' equity	$ 1,191,015	$ 1,300,977

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,		
	2024	2023	2022
Collaboration revenue	$ 57,877	$ 36,275	$ 52,121
Operating expenses:			
Research and development	466,311	435,069	419,979
General and administrative	125,829	116,497	90,306
Total operating expenses	592,140	551,566	510,285
Operating loss	(534,263)	(515,291)	(458,164)
Other income (expense), net:			
Interest income	47,807	49,832	8,542
Change in fair value of investments, net	(32,565)	-	-
Loss from equity method investment	-	(15,633)	(11,079)
Change in fair value of contingent consideration	-	(100)	(13,485)
Total other income (expense), net	15,242	34,099	(16,022)
Net loss	$ (519,021)	$ (481,192)	$ (474,186)
Net loss per share, basic and diluted	$ (5.25)	$ (5.42)	$ (6.16)
Weighted average shares outstanding, basic and diluted	98,849	88,770	76,972
Other comprehensive loss:			
Unrealized gain (loss) on marketable securities	731	3,635	(1,637)
Other comprehensive gain (loss) from equity method investment	-	1,568	(3,192)
Comprehensive loss	$ (518,290)	$ (475,989)	$ (479,015)

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, 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 income (loss) - unrealized loss on marketable securities	-	-	-	(1,637)	-	(1,637)
Other comprehensive income (loss) - unrealized loss on 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 income (loss) - unrealized gain on marketable securities	-	-	-	3,635	-	3,635
Other comprehensive income (loss) - unrealized gain on 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
Issuance of common stock through at-the-market offerings, net of issuance costs of $254 - 2022 Sale Agreement	7,004,370	1	174,823	-	-	174,824
Exercise of stock options	373,807	-	5,862	-	-	5,862
Vesting of restricted stock units	1,433,669	-	-	-	-	-
Issuance of shares under employee stock purchase plan	220,590	-	2,986	-	-	2,986
Stock-based compensation	-	-	154,273	-	-	154,273
Other comprehensive income (loss) - unrealized gain on marketable securities	-	-	-	731	-	731
Reclassification of other comprehensive income (loss) - equity method investment	-	-	-	2,132	-	2,132
Net loss	-	-	-	-	(519,021)	(519,021)
Balance at December 31, 2024	102,029,594	$ 10	$3,048,741	$ 605	$ (2,177,400)	$ 871,956

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,		
	2024	**2023**	**2022**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (519,021)	$ (481,192)	$ (474,186)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	10,285	8,976	7,572
(Gain) loss on disposal of property and equipment	(76)	72	(162)
Stock-based compensation	154,273	134,050	91,400
(Accretion) amortization of investment discounts and premiums	(17,817)	(25,897)	4,003
(Recognition) deferral of equity method investment intra-entity profit on sales	(20,967)	6,624	11,405
Change in fair value of investments, net	32,565	-	-
Loss from equity method investment	-	15,633	11,079
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	27,939	(32,688)	(1,737)
Prepaid expenses and other current assets	5,184	(27,168)	(2,160)
Operating lease right-of-use assets	21,466	19,011	13,121
Other assets	917	(707)	(1,091)
Accounts payable	6,800	2,522	(4,584)
Accrued expenses	(10,383)	6,024	15,924
Deferred revenue	(22,076)	(2,778)	(63,464)
Operating lease liabilities	(17,969)	(16,668)	(9,882)
Net cash used in operating activities	(348,880)	(394,086)	(333,287)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(5,778)	(13,985)	(13,558)
Purchases of marketable securities	(935,573)	(904,464)	(429,032)
Sales and maturities of marketable securities	1,066,918	887,102	647,581
Proceeds from sale of property and equipment	-	-	150
Acquired in-process research and development, net of cash acquired of $287	-	-	(44,832)
Net cash provided by (used in) investing activities	125,567	(31,347)	160,309
CASH FLOWS FROM FINANCING ACTIVITIES:			
Net proceeds from issuance of common stock through follow-on offerings, net of issuance costs	-	-	337,892
Net proceeds from issuance of common stock through at-the-market offerings	176,899	119,795	227,897
Proceeds from options exercised	5,862	6,599	14,517
Issuance of shares through employee stock purchase plan	2,986	3,929	2,649
Net cash provided by financing activities	185,747	130,323	582,955
Net (decrease) increase in cash, cash equivalents and restricted cash equivalents	(37,566)	(295,110)	409,977
Cash, cash equivalents and restricted cash equivalents, beginning of period	240,353	535,463	125,486
Cash, cash equivalents and restricted cash equivalents, end of period	$ 202,787	$ 240,353	$ 535,463
Reconciliation of cash, cash equivalents and restricted cash equivalents to consolidated balance sheet:			
Cash and cash equivalents	$ 189,182	$ 226,748	$ 523,506
Restricted cash equivalents, included in investments and other assets	13,605	13,605	11,957
Total cash, cash equivalents and restricted cash equivalents	$ 202,787	$ 240,353	$ 535,463
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Purchases of property and equipment unpaid at period end	$ 577	$ 1,525	$ 1,623
Operating lease liability arising from obtaining right-of-use assets	112,821	1,311	67,053
Non-cash trade-in of property and equipment	99	-	200
Proceeds from at-the-market offerings unpaid at period end	-	2,075	-
Shares issued for Rewrite contingent consideration	-	24,126	-
Contingent consideration liability assumed in asset acquisition	-	-	10,541

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 revolutionizing medicine with CRISPR-based therapies. CRISPR is a gene editing technology which is also sometimes referred to as CRISPR/Cas or CRISPR/Cas9 when referring to the use of CRISPR technology with the Cas9 enzyme. Since its inception, Intellia has focused on leveraging gene editing technology to develop novel, first-in-class medicines that address important unmet medical needs and advance the treatment paradigm for patients. Intellia's deep scientific, technical and clinical development experience, along with its people, is helping set the standard for a new class of medicine. To harness the full potential of gene editing, Intellia continues to expand the capabilities of its CRISPR-based platform with novel editing and delivery technologies. To fully realize the transformative potential of CRISPR-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 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 as the tool to create the engineered cell therapy. For its *ex vivo* programs, CRISPR 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 and related technologies to create new classes of genetic medicine.

The Company was founded and commenced operations in 2014. 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, 2024, the Company has funded 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, 2024 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, unrealized gain (loss) on marketable securities and other comprehensive gain (loss) from equity method investment.

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, 2024 and 2023, cash equivalents consisted of interest-bearing money market accounts, U.S. Treasury bills and other government securities.

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, 2024 and 2023, these restricted cash equivalents amounted to $13.6 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.

Investments in Equity Securities

Investments in equity securities, other than equity method investments, are recorded at fair market value if fair value is readily determinable and any gains and losses are included in "Change in fair value of investments, net," on the consolidated statement of operations and comprehensive loss. In the absence of a readily determinable fair value, the Company measures the investment at cost less impairment, plus or minus observable changes, if any. 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 equity 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.

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, 2024, the Company's accounts receivable were related to its collaborations with Regeneron Pharmaceuticals, Inc. ("Regeneron"), SparingVision SAS ("SparingVision"), AvenCell Therapeutics, Inc. ("AvenCell") and ReCode Therapeutics, Inc. ("ReCode"). As of December 31, 2023, the Company's accounts receivable were related to its collaborations with Regeneron, SparingVision, AvenCell and Kyverna Therapeutics, Inc. ("Kyverna").

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.

Leases

The Company accounts for its leases in accordance with Financial Accounting Standards Board ("FASB") Accounting Standard Codification ("ASC") 842, *Leases (Topic 842)* ("ASC 842"). At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company has elected not to recognize leases with an original term of one year or less on the balance sheet. The Company does not have any financing leases.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received and prepaid lease payments. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Lease expense for operating lease payments is recognized on a straight-line basis over the lease term.

The Company is required to pay fees for operating expenses in addition to monthly base rent for certain operating leases. The Company has elected the practical expedient which allows non-lease components to be combined with lease components for all asset classes. Variable lease payments are not included within the lease right-of-use asset and lease liability on the consolidated balance sheet, and instead are reflected as expense in the period they are incurred.

The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew or terminate a lease are not included in the Company's assessment unless there is reasonable certainty of execution. The lease commencement date is the date on which a lessor makes the underlying asset available for use by the Company. Lease payments (including payments pertaining to lessor-owned leasehold improvements) made to the lessor prior to lease commencement are recorded as prepaid rent and included in "Prepaid expenses and other current assets" on the Company's consolidated balance sheets. The prepaid rent balance is reclassified to the right-of-use asset at lease commencement.

The Company's real estate operating leases provide for scheduled annual rent increases throughout the lease terms. The Company recognizes the effects of the scheduled rent increases on a straight-line basis over the full terms of the lease. Tenant improvement allowances, if any, provided by a landlord are recorded as a reduction of the right-of-use asset related to that lease at lease commencement.

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 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 income (expense) 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 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, 2024 or 2023 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, 2024, 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 both the Company and the co-party to the arrangement 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, accounting for the Company's co-development agreements with Regeneron and AvenCell is 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 share-based compensation programs grant awards that have included stock options and restricted stock units. Grants are awarded to employees and non-employees, including directors. 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 and performance-based restricted stock units with a Total Shareholder Return ("TSR") multiplier are 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 performance or 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.

Net Loss per Share

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

Segment Information

The Company has identified one operating and reportable segment: the development of gene editing-based therapies. All of the Company's material assets are held in the United States ("U.S.") and all of the Company's collaboration revenue has been generated in the U.S. The operating segment's revenue is primarily generated through collaboration arrangements with third parties. The Company does not have any intra-entity sales or transfers.

The Company manages all business activities on a consolidated basis. The Company's chief operating decision maker ("CODM") is the chief executive officer ("CEO").

The accounting policies for the segment are the same as described those described in Note 2, "Summary of Significant Accounting Policies." The CODM evaluates the performance of the operating segment and allocates resources based on net loss that also is reported on the consolidated statements of operations and comprehensive loss. The CODM uses net loss to monitor budget versus actual results and to analyze cash flows in assessing performance of the segment and allocating resources. The measure of the operating segment assets is reported on the consolidated balance sheets as total assets.

The following table summarizes the reportable segment's financial information:

	Year Ended December 31,		
	2024	2023	2022
Collaboration revenue	$ 57,877	$ 36,275	$ 52,121
Less:			
Research and development:			
External development expenses - Nex-z	69,793	54,454	37,849
External development expenses - NTLA-2002	42,173	24,560	11,611
External development expenses - NTLA-3001	8,709	17,312	11,506
Other research and development (1)	345,636	338,743	359,013
Total research and development	466,311	435,069	419,979
General and administrative (2)	125,829	116,497	90,306
Interest income	(47,807)	(49,832)	(8,542)
Loss from equity method investment	-	15,633	11,079
Other segment information (3)	32,565	100	13,485
Segment and consolidated net loss	$ (519,021)	$ (481,192)	$ (474,186)

(1) Includes unallocated research and development expenses including stock-based compensation of $94.2 million, $82.2 million and $56.3 million for the years ended December 31, 2024, 2023 and 2022, respectively, as disclosed within Note 12, "Stock-Based Compensation."

(2) Includes stock-based compensation of $60.0 million, $51.8 million and $35.1 million for the years ended December 31, 2024, 2023 and 2022, respectively, as disclosed within Note 12, "Stock-Based Compensation."

(3) Includes change in fair value of investments and change in fair value of contingent consideration, as disclosed on the Company's consolidated statements of operations and comprehensive loss.

Depreciation and amortization expense totaled $10.3 million, $9.0 million, and $7.6 million for the years ended December 31, 2024, 2023 and 2022, respectively, as disclosed within Note 5, "Property and Equipment, Net."

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, 2024, the Company did not account for any of its investments under the equity method of accounting. At December 31, 2023, the Company accounted for its investment in AvenCell under the equity method of accounting. Refer to Note 10 for further details regarding the transition out of the equity method of accounting.

Recently Adopted Accounting Pronouncements

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting - Improvements to Reportable Segment Disclosures* ("ASU 2023-07"). 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 Company adopted ASU 2023-07 in the fourth quarter of 2024 through enhanced disclosures related to its reportable segment. See "Segment Information" above for details.

Recently Issued Accounting Pronouncements Not Yet Effective

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.

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses.* This ASU requires disclosure of specified information about certain costs and expenses in the footnotes to the financial statements. This ASU is effective for annual periods beginning after December 15, 2026 and is applicable to the Company's fiscal year beginning January 1, 2027, 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, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	(In thousands)			
Marketable securities:				
U.S. Treasury and other government-backed securities	$ 352,309	$ 580	$ (273)	$ 352,616
Financial institution debt securities	217,544	528	(245)	217,827
Corporate debt securities	94,924	163	(160)	94,927
Other asset-backed securities	7,168	10	-	7,178
Total	$ 671,945	$ 1,281	$ (678)	$ 672,548

	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

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. There were no material realized gains or losses in the years ended December 31, 2024 or 2023. 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 losses as temporary in nature.

The Company's available-for-sale securities that are classified as short-term marketable securities in the consolidated balance sheets mature within one year or less as of the balance sheet date. Available-for-sale securities that are classified as noncurrent in the consolidated balance sheets 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, 2024 and 2023, the Company did not hold any marketable securities 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 (unadjusted) 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 recognized at fair value on a recurring basis consisted of the following:

	December 31, 2024			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Assets				
Cash equivalents and restricted cash equivalents	$ 66,898	$ 66,898	$ -	$ -
Marketable securities:				
U.S. Treasury and other government-backed securities	352,616	169,735	182,881	-
Financial institution debt securities	217,827	-	217,827	-
Corporate debt securities	94,927	-	94,927	-
Other asset-backed securities	7,178	-	7,178	-
Total marketable securities	672,548	169,735	502,813	-
Investment in Kyverna Therapeutics, Inc.	4,390	4,390	-	-
Total assets	$ 743,836	$ 241,023	$ 502,813	$ -

	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 assets	$ 921,593	$ 256,810	$ 664,783	$ -

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.

The Company has determined that the estimated fair value of its investment in Kyverna, a publicly traded company, is reported as Level 1 as it is valued at a quoted market price in an active market. The investment in Kyverna is classified within "Investments and other assets" in the consolidated balance sheets. Refer to Note 10 for further details.

Other Investments

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, 2024 or 2023. The carrying value of the SparingVision investment was $14.6 million and $14.8 million as of December 31, 2024 and 2023, respectively. Refer to Note 10 for further details.

The Company's investment in AvenCell was initially recorded at fair value, determined according to Level 3 inputs in the fair value hierarchy described above. The AvenCell investment is included in "Investments and other assets" on the consolidated balance sheet as of December 31, 2024. This investment is accounted for using the measurement alternative at cost minus impairment, adjusted for changes in observable prices. The Company previously accounted for the AvenCell investment under the equity method; refer to Note 10 for further details including the change in fair value.

In the fourth quarter of 2024, AvenCell completed a Series B financing, which represented an observable price change in the investment in AvenCell. The Company determined the fair value of the AvenCell investment using an option pricing model which requires the input of certain subjective assumptions. The key assumptions used in the option pricing model, which are Level 3 inputs, include the anticipated holding period to an exit and liquidity event, the indicated equity volatility (95%), and the risk free rate (3.9%). The carrying value of the Company's investment in AvenCell was $7.9 million and $11.8 million as of December 31, 2024 and December 31, 2023, respectively.

Contingent Consideration

As part of its acquisition of Rewrite Therapeutics, Inc. ("Rewrite") in 2022, 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 (in thousands):

Balance at December 31, 2022	$	24,026
Change in fair value		100
Payment of contingent consideration		(24,126)
Balance at December 31, 2023	$	-

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
	2024	2023
	(In thousands)	
Laboratory equipment	$ 68,354	$ 63,970
Office furniture and equipment	2,632	2,633
Computer software	1,902	1,902
Computer equipment	985	982
Leasehold improvements	3,199	3,134
Total property and equipment	77,072	72,621
Less: accumulated depreciation and amortization	(49,691)	(39,861)
Property and equipment, net	$ 27,381	$ 32,760

Depreciation and amortization expense was $10.3 million, $9.0 million and $7.6 million for the years ended December 31, 2024, 2023 and 2022, respectively.

6. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2024	2023
	(In thousands)	
Accrued research and development	$ 26,362	$ 27,411
Employee compensation and benefits	24,075	26,615
Accrued legal and professional expenses	2,845	2,063
Accrued construction costs	-	6,891
Accrued other	2,073	4,037
Total accrued expenses	$ 55,355	$ 67,017

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,		
	2024	2023	2022
Federal statutory income tax rate	(21.0)%	(21.0)%	(21.0)%
State income taxes	(7.9)	(8.6)	(8.3)
Research and development tax credits	(7.4)	(6.9)	(5.3)
Stock-based compensation	2.0	1.6	(0.1)
Non-deductible officers' compensation	0.1	-	0.1
In-process research and development	-	-	2.5
Change in valuation allowance	34.2	34.9	32.1
Effective income tax rate	—%	—%	—%

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

	December 31,	
	2024	2023
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 296,766	$ 258,664
Research and development credit carryforwards	200,816	151,333
Section 174 capitalized research	216,469	150,993
Operating lease liability	57,438	31,183
Deferred revenue	10,634	9,633
Stock-based compensation	34,827	30,408
Accruals and allowances	5,468	6,244
Prepaid rent	4,410	1,190
Equity investment adjustments	16,560	7,580
Intangibles, including in-process research and development	920	1,017
Capitalized start-up costs	211	249
Gross deferred tax assets	844,519	648,494
Deferred tax asset valuation allowance	(783,211)	(616,082)
Total deferred tax assets	61,308	32,412
Deferred tax liabilities:		
Fixed assets	(1,385)	(1,221)
Operating lease right-of-use assets	(59,923)	(31,191)
Total deferred tax liabilities	(61,308)	(32,412)
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 $405.3 million and $365.8 million for the years ended December 31, 2024 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, 2024 and 2023, the Company had federal net operating loss carryforwards of $1,088.4 million and $954.0 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 $1,051.5 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, 2024 and 2023, the Company also had state net operating loss carryforwards of $1,079.2 million and $922.8 million, respectively, which may be available to offset future income tax liabilities and begin to expire in 2034.

As of December 31, 2024 and 2023, the Company had federal tax credit carryforwards of approximately $139.3 million and $100.7 million, respectively, which begin to expire in 2034. As of December 31, 2024 and 2023, the Company had state research and development and other credit carryforwards of $77.9 million and $64.1 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, 2024 and 2023. The valuation allowance increased by $167.1 million in 2024, $161.3 million in 2023, and $150.0 million in 2022.

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, 2024. To the extent there was a change in control during 2023 and 2024, 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, 2024, 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 2021 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.

8. Commitments and Contingencies

Litigation

From time to time, the Company may be 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.

BlueAllele Corp. v. Intellia Therapeutics, Inc.

On July 8, 2024, BlueAllele Corp. ("BlueAllele") filed a complaint alleging infringement by the Company of various patents in the U.S. District Court for the District of Delaware. Specifically, BlueAllele alleges that the Company's experimentation, basic

research, identification, optimization, manufacturing and/or use of bi-directional insertion template technology infringes the asserted patents and seeks unspecified compensatory damages and an injunction against the alleged infringing activities. On September 12, 2024, the Company filed a motion to dismiss the complaint, and on December 9, 2024, the court denied the Company's motion to dismiss and discovery began. On January 6, 2025, the Company filed its answer and counterclaims, and BlueAllele filed a motion to dismiss the Company's counterclaims on January 27, 2025. On February 21, 2025, the court substantially denied BlueAllele's motion to dismiss, and granted the motion with respect to one counterclaim. At this stage, the Company is unable to determine the likelihood of an unfavorable outcome or estimate the amount or range of potential loss, if any.

Gonzalez v. Intellia Therapeutics, Inc.

On February 11, 2025, a purported stockholder of the Company filed a lawsuit, captioned *Gonzalez v. Intellia Therapeutics, Inc.*, No. 1:25-cv-01353 (D. Mass.), in the U.S. District Court for the District of Massachusetts against the Company and certain of our officers on behalf of a putative class of stockholders who purchased Company shares from July 30, 2024 through January 8, 2025. The complaint alleges claims under Sections 10(b) and 20(a) and Rule 10b-5 of the Securities Exchange Act of 1934 (the "Exchange Act") premised upon statements relating to the Company's NTLA-3001 program and the demand for viral-based editing. The complaint seeks unspecified damages, interest, reasonable attorneys' fees and other costs. The Company intends to defend vigorously against the claims. At this stage, the Company is unable to determine the likelihood of an unfavorable outcome or estimate the amount or range of potential loss, if any.

During the year ended December 31, 2024, except as noted above, there have been no material changes to any outstanding litigation, nor is the Company a party to any material new litigation.

License and Other Agreements

The Company is party to license and other agreements, which may include contingent payments. These payments could include up to $130.0 million related to Rewrite, including $100.0 million upon achievement of a regulatory approval milestone and $30.0 million upon achievement of pre-specified research milestones. As of December 31, 2024, 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 gene editing 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, 2024, the Company's accounts receivable were related to its collaborations with Regeneron, AvenCell, SparingVision and ReCode, and the Company's contract liabilities were related to its collaborations with Regeneron and SparingVision. 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.

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, 2024				
Accounts receivable	$ 36,456	$ 26,524	$ (54,463)	$ 8,517
Contract liabilities - deferred revenue	$ 60,993	$ -	$ (22,076)	$ 38,917

	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

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

	Year Ended December 31,		
Revenue recognized in the period from:	**2024**	**2023**	**2022**
Amounts included in the contract liability at the beginning of the period	$ 22,076	$ 23,462	$ 52,060

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 that was paid 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.

The Company recognized $20.7 million, $11.7 million and $22.5 million of collaboration revenue in the years ended December 31, 2024, 2023 and 2022, respectively, in the consolidated statements of operations and comprehensive loss related to the 2016 Regeneron Agreement, the 2020 Regeneron Amendment and the 2024 Technology Collaboration Extension.

As of December 31, 2024, there was approximately $26.4 million of the aggregate transaction price remaining to be recognized that will be recognized through April 2026, the remaining period of the collaboration.

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; 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.

The Company recognized $2.3 million and $0.4 million of collaboration revenue in the years ended December 31, 2024 and 2023, respectively, in the consolidated statement of operations and comprehensive loss related to the 2023 Regeneron Amendment.

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. The Company terminated the hemophilia B Co/Co agreement in September 2024. The Company will continue to support Regeneron with the development of gene editing products directed to hemophilia B, as applicable, under the 2016 Regeneron Agreement.

The Company recognized $21.9 million, $19.6 million, and $11.9 million, respectively, primarily representing payments due from Regeneron pursuant to the ATTR Co/Co agreement, in the years ended December 31, 2024, 2023 and 2022. The Company recognized contra-revenue related to the Hemophilia Co/Co agreements amounting to approximately $11.7 million in the year ended December 31, 2024, $10.7 million in the year ended December 31, 2023 and $10.4 million in the year ended December 31, 2022.

As of December 31, 2024 and December 31, 2023, the Company had accounts receivable of $7.2 million and $35.7 million, respectively, and deferred revenue of $26.4 million and $47.1 million, respectively, related to the Regeneron 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.

The Company granted SparingVision exclusive rights to its 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 will research and develop novel self-inactivating adeno-associated virus ("AAV") vectors and lipid nanoparticle ("LNP")-based approaches 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.

The Company will have an option to obtain exclusive U.S. commercialization rights for product candidates arising from two of three collaboration targets. For product candidates the Company chooses to option, it will pay an opt-in fee between $10.0 million and $20.0 million depending on the stage of development of the target, reimburse certain costs, share in 50% of development costs and pay royalties to SparingVision on U.S. sales.

In exchange for the license, the Company received 83,316 shares of SparingVision's 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. The Company will also be eligible to receive certain research, development and commercial milestone payments (up to approximately $200.0 million per product) as well as royalties on potential future sales of products arising from the collaboration.

SparingVision LCA: Accounting Analysis. The Company determined that the accounting for the SparingVision LCA is within the scope of ASC 606. The Company evaluated the promised goods and services and determined that it included one performance obligation: a combined performance obligation including the license to the CRISPR technology as well as ongoing research and support services, including participation in a joint steering committee ("JSC").

The transaction price was determined to be $14.8 million, which represents the fair value of the Company's equity interest in SparingVision at the time of closing. The Company allocated the full transaction price to the combined performance obligation, which was recorded as deferred revenue upon execution of the agreement. The Company will use a costs-incurred input method to recognize revenue, measuring the progress of the programs based on the costs incurred against budget, which in management's judgment is the best measure of progress towards satisfying the performance obligation.

Effective November 2024, SparingVision provided notice to the Company to terminate one of their three ocular targets due to a reprioritization strategy.

The Company recognized $2.5 million, $1.8 million and $0.2 million in revenue related to the SparingVision LCA for the years ended December 31, 2024, 2023 and 2022, respectively. As of December 31, 2024 and December 31, 2023, the Company had $0.6 million and $0.5 million in accounts receivable, respectively, related to the SparingVision LCA. As of December 31, 2024 and December 31, 2023, the Company had deferred revenue of $12.5 million and $13.9 million, respectively, related to the SparingVision LCA, which is expected to be recognized over a six to nine year period from the signing of the agreement.

ReCode Therapeutics, Inc. ("ReCode")

On February 14, 2024, the Company entered into a license, collaboration and option agreement with ReCode (the "ReCode LCA"), a clinical-stage genetic medicines company, to develop novel genomic medicines for the treatment of cystic fibrosis ("CF"). The ReCode LCA leverages the Company's proprietary CRISPR-based gene editing platform, including its deoxyribonucleic acid ("DNA") writing technology, and ReCode's proprietary Selective Organ Targeting ("SORT") LNP 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 and worldwide commercialization for certain programs arising from the collaboration. The Company also has an option to lead commercialization in the U.S. for certain programs (the "Co/Co option").

The ReCode LCA did not include an exchange of upfront consideration between the parties. The Company will be eligible to receive pre-specified development and commercial milestone payments, up to $262.0 million per product, as well as single digit

royalties on potential sales. Certain milestone and royalty payments may be removed or reduced for a product if the Company exercises the Co/Co option. The Company is entitled to cost reimbursements for certain research activities, which will be recorded as revenue. The Company did not recognize material revenue from the ReCode LCA during the year ended December 31, 2024.

Other Agreements

The Company has existing license and collaboration agreements with AvenCell, Kyverna, and ONK Therapeutics, Ltd. ("ONK"). Since December 31, 2023, there have been no material changes to the key terms of the AvenCell, Kyverna and ONK license and collaboration agreements. 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, 2023.

During the year ended December 31, 2024, the Company recognized $21.0 million of previously eliminated intra-entity profit related to its license and collaboration agreement with AvenCell (the "AvenCell LCA") in the consolidated statements of operations and comprehensive loss. During the years ended December 31, 2023 and 2022, the Company recognized $13.2 million and $22.8 million in revenue related to the AvenCell LCA, after eliminating $6.6 million and $11.4 million in intra-entity profits during those respective periods. The eliminated revenue was deferred and excluded from the results of operations of the Company until the first quarter of 2024. The Company did not recognize material revenue related to materials shipments under the AvenCell LCA during the years ended December 31, 2024, 2023 and 2022 and did not recognize material contra-revenue under the AvenCell Co/Co agreement during the years ended December 31, 2024 and 2023. The Company recognized $2.0 million of contra-revenue during the year ended December 31, 2022. The Company had no material accounts receivable from AvenCell or accrued expenses related to AvenCell agreements as of December 31, 2024 and 2023.

The Company did not recognize material revenue from Kyverna during the years ended December 31, 2024 and 2023 and recognized $6.6 million during the year ended December 31, 2022. The Company did not recognize material revenue from ONK during the years ended December 31, 2024, 2023 and 2022.

10. Investments and Other Assets

Investments and other assets consisted of the following:

	December 31,	
	2024	2023
	(In thousands)	
Investment in Kyverna	$ 4,390	$ 10,000
Other investments	22,481	14,760
Restricted cash equivalents, long-term	13,605	13,605
Prepaid expenses and other assets, long-term	3,788	4,518
Total investments and other assets	$ 44,264	$ 42,883

Kyverna Therapeutics, Inc.

In February 2024, Kyverna completed an initial public offering of its common stock (the "Kyverna IPO"). Prior to the Kyverna IPO, the Company accounted for its investment in Kyverna using the measurement alternative as Kyverna was a private company with no readily observable transaction price, and the investment was valued at $10.0 million as of December 31, 2023 and 2022. As of December 31, 2024, the Company's investment in Kyverna is valued at $4.4 million. The Company recognized an unrealized loss of $5.6 million, recorded within "change in fair value of investments, net" in the consolidated statement of operations and comprehensive loss during the year ended December 31, 2024, associated with changes in the fair value of Kyverna's common stock.

AvenCell Therapeutics, Inc.

As of December 31, 2023, the Company held a 33.33% equity interest in AvenCell and accounted for its investment using the equity method of accounting, as the Company had significant influence, but not control, over AvenCell, and the investment was valued at $11.8 million. During the first quarter of 2024, in conjunction with the completion of a debt financing, AvenCell increased the size of their board, with a single investor having control over AvenCell's operational and financial decisions. From that point forward, the Company no longer had the ability to exercise significant influence over AvenCell, and therefore the Company's investment in AvenCell has been accounted for in accordance with ASC 321, *Investments in Equity Securities* ("ASC 321") and AvenCell is no longer considered to be a related party.

The transition from equity method accounting to ASC 321 required the Company to reclassify $2.1 million from accumulated other comprehensive loss amounts and recognize $21.0 million of previously eliminated intra-entity profit, both of which resulted in an increase in the carrying value of the investment in AvenCell. In the fourth quarter of 2024, AvenCell completed a Series B

financing, which represented an observable price change in the investment in AvenCell. As a result of this observable price change, the carrying value of the Company's investment in AvenCell was reduced to $7.9 million. The Company recognized an unrealized loss of $27.0 million, recorded within "Change in fair value of investments, net" in the consolidated statement of operations and comprehensive loss during the year ended December 31, 2024, associated with changes in the fair value of its investment in AvenCell.

SparingVision SAS

As of December 31, 2024 and December 31, 2023, the carrying value of the Company's investment in SparingVision, included within "Other investments" in the table above, was $14.6 million.

11. Leases

Property Leases

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 approximately one to twelve 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.

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.

In February 2022 and subsequently amended in June 2023, the Company entered into an agreement to lease approximately 140,000 square feet of office, general laboratory and manufacturing space at 840 Winter Street in Waltham, Massachusetts (the "840 Winter Lease"). In November 2024 the Company determined, in accordance with ASC 842, that the criteria for commencement of the lease had been met as the lessor had made the space available for the Company's use. The Company recorded a right of use asset of $125.7 million and a lease liability of $113.1 million related to the 840 Winter Lease. The difference between the right-of-use asset and the lease liability of $12.6 million relates to prepaid rent. The initial term of the 840 Winter Lease was twelve years, ending in September 2036. The Company had options to extend the lease for two five-year terms, which were not reasonably certain of exercise as of the commencement date. The 840 Winter Lease is subject to 3% fixed rate rent escalations and requires the Company to make monthly payments for operating costs such as real estate taxes, maintenance costs, and utilities. These costs are variable in nature and have therefore been excluded from consideration in the contract. Refer to Note 16 for further information regarding the 840 Winter Lease.

In January 2023, the Company executed a sublease for approximately 13,000 square feet 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.

The following table contains a summary of the lease costs recognized and other information pertaining to the Company's operating leases:

	Year Ended December 31,	
	2024	2023
	(In thousands)	
Lease cost		
Operating lease cost	$ 30,648	$ 27,849
Variable lease cost	8,535	6,991
Sublease income	(1,674)	(1,439)
Net lease cost	$ 37,509	$ 33,401

	Year Ended December 31,	
	2024	2023
	(In thousands)	
Other information		
Operating cash flows used for operating leases	$ 27,152	$ 25,456
Operating lease liabilities arising from obtaining right-of-use assets	112,821	1,311

	As Of December 31,	
	2024	2023
Lease term and discount rate		
Weighted average remaining lease term	8.9 years	6.2 years
Weighted average discount rate	7.45%	7.37%

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, 2024:

	Future Operating Lease Payments
Year Ending December 31,	(in thousands)
2025	$ 35,105
2026	37,874
2027	31,610
2028	26,702
2029	27,418
Thereafter	136,126
Total lease payments	$ 294,835
Less: imputed interest	(84,637)
Total operating lease liabilities at December 31, 2024	$ 210,198

12. Stock-Based Compensation

Stock-based compensation expense is classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Ended December 31,		
	2024	2023	2022
		(In thousands)	
Research and development	$ 94,230	$ 82,211	$ 56,279
General and administrative	60,043	51,839	35,121
Total	$ 154,273	$ 134,050	$ 91,400

Stock Option and Incentive Plans

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. As of December 31, 2024, there were 4,809,483 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.

In June 2024, the Company adopted the 2024 Inducement Plan (the "Inducement Plan"). The Inducement Plan provides for the grant of non-qualified stock options, stock appreciation rights, RSAs, RSUs, unrestricted stock awards and dividend equivalent rights to individuals who are not employed by the Company. Recipients of 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. In accordance with the Inducement Plan, 850,000 shares of common stock were reserved for future issuance; there were 368,902 shares available for future issuance under the Inducement Plan as of December 31, 2024.

Restricted Stock Units

The following table summarizes the Company's RSU activity for the year ended December 31, 2024:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Unvested restricted stock units as of December 31, 2023	4,041,753	$ 50.40
Granted	3,601,376	32.43
Vested	(1,433,669)	52.08
Cancelled	(661,930)	43.43
Unvested restricted stock units as of December 31, 2024	5,547,530	$ 39.13

Restricted Stock Units - Service Awards

The Company awards RSUs with a service condition to new employees upon hire, non-employee directors upon appointment, and to existing employees and non-employee directors as part of their annual grant. RSUs with a service condition granted to new and existing employees, and to non-employee directors upon appointment, under the 2015 Plan in 2024 and 2023 and the Inducement Plan in 2024 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. RSUs granted to non-employee directors with a service condition as part of their annual grant generally vest on the first anniversary of the original vesting date.

In the year ended December 31, 2024, the Company granted 2,828,675 RSUs with a service condition to new and existing employees and non-employee directors, which have the potential to vest over a period of one to three years. The weighted average grant date fair value of these RSUs was $29.90.

Unvested restricted stock units as of December 31, 2024 in the table above includes 4,596,901 RSUs that are service-based.

Restricted Stock Units - Market Awards

In 2024, 2023 and 2022, market-based RSUs were granted to senior executives. These RSUs have the potential to vest after a period of three years, with a vesting start date of January 1, 2024, 2023 and 2022, respectively, 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 number of market-based RSUs granted in the year ended December 31, 2024, 2023 and 2022 was 286,084, 181,743 and 55,144, respectively. The grant date fair value for the market-based RSUs, calculated using a Monte Carlo valuation model, was $51.12, $68.55 and $126.49, respectively. The following assumptions were used to determine the grant date fair value for the three years, respectively: risk free interest rate: 4.28%, 4.60% and 1.44%; expected volatility: 77.2%, 84.34% and 82.53%. The expected term for all grants was approximately 3.0 years; the expected dividend yield was 0.0%.

Unvested restricted stock units as of December 31, 2024 in the table above includes 468,277 RSUs that are market-based.

Restricted Stock Units - Performance-Based Awards with TSR Multiplier

Also in 2024, performance-based RSUs ("PSUs") with a relative TSR modifier were granted to senior executives. The number of PSUs with a relative TSR modifier granted in the year ended December 31, 2024 was 486,617. These PSUs, to the extent earned, shall vest on January 1, 2027, and the number of shares to be delivered will be determined based upon the achievement of certain performance goals, which can range from 0% to 200%. Following the determination of the achievement of performance criteria, the amount of shares awarded will be subject to adjustment based on the application of a TSR modifier, which can range from 75% to 125%. The grant date fair value for these PSUs, calculated using a Monte Carlo valuation model, was $36.16. The following assumptions were used to determine the grant date fair value: risk free interest rate: 4.28%; expected volatility: 77.2%; expected term: approximately 3.0 years; expected dividend yield: 0.0%. The Company recognizes compensation expense ratably over the required service period based on its estimate of the number of shares that will vest based upon the probability of achieving the performance goals.

Unvested restricted stock units as of December 31, 2024 in the table above includes 437,934 PSUs with a TSR multiplier.

Restricted Stock Units - Performance-Based Awards

In 2022, the Company granted 66,296 performance-based RSUs 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, 2024 and, therefore, no related stock-based compensation expense was recorded during the period then ending.

Unvested restricted stock units as of December 31, 2024 in the table above includes 44,418 performance-based RSUs.

The weighted-average grant date fair value of all RSUs granted during the year ended December 31, 2024, 2023 and 2022 was $32.43, $41.30 and $70.90, respectively. The total fair value of RSUs vested (measured on the date of vesting) for the year ended December 31, 2024, 2023 and 2022 was $40.0 million, $24.9 million and $10.4 million, respectively.

As of December 31, 2024, there was $106.5 million of unrecognized stock-based compensation expense related to all RSUs that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 1.6 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 $21.21, $28.92 and $57.23 per option for those options granted during the year ended December 31, 2024, 2023 and 2022, respectively. Weighted average assumptions used to apply this pricing model were as follows:

	Year Ended December 31,		
	2024	2023	2022
Risk-free interest rate	4.2%	4.4%	1.9%
Expected term of options	6.0 years	6.0 years	5.9 years
Expected volatility of underlying stock	76.3%	78.7%	76.2%
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. 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.

Expected Dividend Yield. The Company has not paid cash dividends and has no intention to pay cash dividends in the future.

Stock options 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 vesting provisions. The maximum term of stock options granted under the 2015 Plan and the Inducement Plan is ten years.

The following is a summary of stock option activity for the year ended December 31, 2024:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In years)	(In thousands)
Outstanding at December 31, 2023	5,458,999	$ 50.38	6.65	$ 35,922
Granted	918,161	30.72		
Exercised	(373,807)	15.68		
Forfeited	(590,567)	70.25		
Outstanding at December 31, 2024	5,412,786	$ 47.27	6.18	$ 350
Exercisable at December 31, 2024	4,246,614	$ 48.40	5.47	$ 350

The total intrinsic value (the amount by which the fair market value exceeded the exercise price) of stock options exercised during the year ended December 31, 2024, 2023 and 2022 was $3.1 million, $7.6 million, and $42.8 million, respectively.

As of December 31, 2024, there was $22.2 million of unrecognized compensation cost related to stock options that have not yet vested, which are expected to be recognized over a weighted average remaining vesting period of 1.1 years.

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, 2024, there were 856,897 shares available for future issuance under the 2016 Plan. The number of shares reserved for issuance under the 2016 Plan will be cumulatively increased on each January 1st by the lesser of a) one percent of the number of shares of common stock issued and outstanding on the immediately preceding December 31st, 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 year ended December 31, 2024, 2023 and 2022, the Company issued 220,590, 142,079 and 77,618 shares of common stock under the 2016 Plan, respectively. The weighted-average purchase prices of shares issued under the 2016 Plan were $13.54, $27.65 and $34.15 per share for the year ended December 31, 2024, 2023 and 2022, respectively.

The fair value of shares under the 2016 Plan was estimated at the beginning of the offering period using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2024	2023	2022
Risk-free interest rate	5.24%-5.37%	4.7%-5.53%	0.22%-2.52%
Expected term (in years)	0.5 years	0.5 years	0.5 years
Expected volatility of underlying stock	56.7%-59.0%	60.4%-69.2%	63.6%-95.3%
Expected dividend yield	0.0%	0.0%	0.0%

13. Loss Per Share

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

Basic and diluted loss per share was calculated as follows:

	Year Ended December 31,		
	2024	2023	2022
		(In thousands)	
Net loss	$ (519,021)	$ (481,192)	$ (474,186)
Weighted average shares outstanding, basic and diluted	98,849	88,770	76,972
Net loss per share, basic and diluted	$ (5.25)	$ (5.42)	$ (6.16)

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,		
	2024	2023	2022
		(In thousands)	
Unvested restricted stock units	5,547	4,042	1,941
Stock options	5,413	5,459	5,472
	10,960	9,501	7,413

14. Stockholders' Equity

At-the-Market Offering Programs

2022 Sale Agreement

In 2022, the Company entered into an Open Market Sale Agreement (the "2022 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 the Company's common stock having aggregate gross proceeds of up to $400.0 million. In February 2024, the Company entered into an amendment to the 2022 Sale Agreement (the "2022 Sale Agreement, as amended") to increase the size of the at-the-market offering program from $400.0 million to $750.0 million. The Company agreed to pay cash commissions of up to 3.0% of the gross proceeds of sales of common stock under the 2022 Sale Agreement, as amended. Through December 31, 2024, the Company issued 14,522,533 shares of its common stock under the 2022 Sale Agreement, as amended. During the year ended December 31, 2024, the Company issued 7,004,370 shares of its common stock, in a series of sales, at an average price of $25.68 per share, in accordance with the 2022 Sale Agreement, as amended, for aggregate net proceeds of $174.8 million, after payment of cash commissions and approximately $0.3 million related to legal, accounting and other fees in connection with the sales. 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. 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. 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, 2024, $249.1 million in shares of common stock remain eligible for sale under the 2022 Sale Agreement, as amended.

15. 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 $3.2 million, $3.3 million and $2.7 million for the years ended December 31, 2024, 2023 and 2022, respectively.

16. Subsequent Events

Strategic Reorganization

In January 2025, the Company announced the prioritization of its current and near-term clinical programs and a strategic restructuring to streamline its operations. The pipeline prioritization is intended to focus resources on high value programs, NTLA-2002 and nex-z, to ensure efficient execution, achieve near-term clinical milestones, and prepare Intellia for commercial launch. As part of this prioritization, the Company discontinued development of NTLA-3001 for the treatment of alpha-1 antitrypsin deficiency-associated lung disease and select research-stage programs.

In connection with this portfolio prioritization and strategic restructuring, the Company implemented a net reduction of its employee headcount by approximately 27%, which will take place over 2025. The Company estimates that it will incur charges of approximately $8.0 million for severance and other employee termination-related costs, primarily in the first quarter of 2025. These costs consist primarily of cash expenditures related to severance payments. The Company estimates that the workforce reduction will be substantially completed in the first quarter of 2025. The estimate of costs that the Company expects to incur, and the timing thereof, are subject to a number of assumptions and actual results may differ. The Company may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the actions described above.

Real Estate Transactions

Tech Square Lease

On February 18, 2025, the Company entered into a Lease Agreement (the "Tech Square Lease") with ARE-Tech Square, LLC, an affiliate of Alexandria Real Estate Equities, Inc. (the "Tech Square Landlord") for office and laboratory space located at 400 Technology Square, Cambridge, Massachusetts ("400 Tech Square"). Under the terms of the Tech Square Lease, the Company will initially lease approximately 101,000 square feet at 400 Tech Square (the "Initial Tech Square Premises"), which will supplement, and eventually replace certain parts of, the Company's current leased premises in Cambridge, Massachusetts. In addition, the Tech Square Lease will expand, in two tranches, to include approximately 46,000 square feet of additional office and laboratory space at 400 Tech Square (the "Additional Tech Square Premises") when each such space becomes available. The Tech Square Lease is expected to commence on July 1, 2025 (the "Commencement Date") with respect to the Initial Tech Square Premises, and the Company's obligation to pay rent will start on the date that is approximately 14 months after the Commencement Date (the "Rent Commencement Date"). In addition, the lease of the Additional Tech Square Premises will commence when the Tech Square Landlord delivers such space to the Company, which is anticipated to occur in December 2027 and January 2028 (in each case, an "Additional Premises Commencement Date"), and the Company's obligation to pay rent for such Additional Tech Square Premises will start on the date that is approximately 14 months after each Additional Premises Commencement Date (in each case, an "Additional Premises Rent Commencement Date"). The Company shall not be obligated to pay the base rent for the applicable premises for three months after the Rent Commencement Date and each Additional Premises Rent Commencement Date, as applicable. The initial term of the Tech Square Lease is twelve years and three months following the Rent Commencement Date, and the Company has an option to extend the Tech Square Lease for an additional term of five years. As of the Rent Commencement Date, the base rent under the Tech Square Lease is expected to be $108.00 per square foot per year, plus certain operating expenses and taxes; provided that the initial base rent may adjust based on certain criteria set forth in the lease. The base rent is subject to scheduled annual increases of 3% on the anniversary of the Commencement Date. In addition, the Tech Square Landlord will contribute up to $41.5 million toward the cost of construction and tenant improvements for the Initial Tech Square Premises, and an additional amount toward the cost of construction and tenant improvements for the Additional Tech Square Premises.

Winter Street Amendment

On February 18, 2025, the Company entered into a Second Amendment to Lease (the "Winter Street Amendment") that amends the 840 Winter Lease. Pursuant to the Winter Street Amendment, the 840 Winter Lease will terminate on or before June 30, 2028. The Company will pay to the landlord lease modification payments totaling $78.0 million in three installments in February 2025, April 2025, and January 2026, and the Company will not pay any base rent, operating expenses or other costs pursuant to the 840 Winter Lease after January 2025.

EXHIBIT INDEX

Exhibit No.	Exhibit Index
3.1*	Second Amended and Restated Certificate of Incorporation of the Registrant, as amended
3.2	Second Amended and Restated By-laws of the Registrant (1)
4.1*	Description of Certain Registrant's Securities
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 (14)
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 (12)
10.15#	Form of Amended and Restated Employment Agreement (6)
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. (7)
10.17	First Amendment to Lease, dated as of April 5, 2019, by and between the Company and MIT 130 Brookline Leasehold LLC (8)
10.18#	Seventh Amended and Restated Non-Employee Director Compensation Policy (14)
10.19	Lease, dated as of March 12, 2020, by and between the Company and 281-295 Albany Street Leasehold LLC (1)
10.20	Second Amendment to Lease, dated as of March 12, 2020, by and between the Company and MIT 130 Brookline Leasehold LLC (1)

10.21†	Amendment No. 1, dated May 30, 2020, to the License and Collaboration Agreement, dated April 11, 2016, by and between the Company and Regeneron Pharmaceuticals, Inc. (10)
10.22	Stock Purchase Agreement, dated May 30, 2020, by and between Intellia Therapeutics, Inc. and Regeneron Pharmaceuticals, Inc. (10)
10.23#	Second Amended and Restated Corporate Bonus Plan, effective November 30, 2023 (16)
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 (12)
10.25	Lease Agreement by and between the Registrant and Are-Winter Street Property, LLC, dated as of February 22, 2022 (12)
10.26#	Amended and Restated Retirement Policy for Equity Awards, effective December 6, 2022 (9)
10.27	Amendment to Lease Agreement by and between the Registrant and Are-Winter Street Property, LLC, dated as of June 20, 2023 (11)
10.28	Letter Agreement (Second Amendment) to License and Collaboration Agreement by and between Registrant and Regeneron Pharmaceuticals, Inc., dated November 22, 2022 (13)
10.29	Third Amendment to License and Collaboration Agreement by and between Registrant and Regeneron Pharmaceuticals, Inc., dated September 29, 2023 (13)
10.30#	Intellia Therapeutics, Inc. 2024 Inducement Plan and forms of award agreements thereunder (15)
10.31†*	Lease Agreement by and between the Registrant and ARE-Tech Square, LLC, dated as of February 18, 2025
10.32†*	Second Amendment to Lease Agreement by and between the Registrant and ARE-Winter Street Property, LLC, dated as of February 18, 2025
10.33#	Employment Agreement between Intellia Therapeutics, Inc. and Edward Dulac (15)
19.1†*	Fourth Amended and Restated Insider Trading Policy
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 Edward J. Dulac III, Executive Vice President, Chief Financial Officer of the Company (17)
97.1#	Intellia Therapeutics, Inc. Compensation Recovery Policy (16)
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 Form S-1 (File No. 333-210689) filed with the Securities and Exchange Commission on April 19, 2016
(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 Registrant's Current Report on Form 8-K (File No. 001-37766) filed with the Securities and Exchange Commission on April 17, 2018
(7) 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
(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 May 2, 2019
(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 23, 2023
(10) 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
(11) 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
(12) 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
(13) 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
(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 8, 2024
(15) 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 26, 2024
(16) 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 22, 2024
(17) 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 27, 2025

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 27, 2025
/s/ Edward J. Dulac III Edward J. Dulac III	Executive Vice President, Chief Financial Officer *(Principal Financial Officer)*	February 27, 2025
/s/ Michael P. Dube Michael P. Dube	Vice President, Chief Accounting Officer *(Principal Accounting Officer)*	February 27, 2025
/s/ Muna Bhanji Muna Bhanji	Director	February 27, 2025
/s/ Bill Chase Bill Chase	Director	February 27, 2025
/s/ Fred Cohen Fred Cohen, M.D.	Director	February 27, 2025
/s/ Brian Goff Brian Goff	Director	February 27, 2025
/s/ Jesse Goodman Jesse Goodman, M.D.	Director	February 27, 2025
/s/ Georgia Keresty Georgia Keresty	Director	February 27, 2025
/s/ Frank Verwiel Frank Verwiel, M.D.	Director	February 27, 2025

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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.
Chair 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

Brian Goff
Chief Executive Officer, Agios Pharmaceuticals, Inc.

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

Edward J. Dulac III
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

Michael P. Dube
Vice President, Chief Accounting Officer

David Lebwohl, M.D.
Executive Vice President, Chief Medical Officer

Birgit Schultes, 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 2025 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, 2024, 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
Toll Free: (800) 736-3001
International: +1 (781) 575-3100
https://www.computershare.com/us

Investor Relations

intelliatx@precisionaq.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