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

FORM 10-K

(Mark One)

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

For the fiscal year ended November 30, 2023

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
FOR THE TRANSITION PERIOD FROM TO

Commission File Number 001-39398

NURIX THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**27-0838048**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1700 Owens Street, Suite 205 San Francisco, CA	**94158**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (415) 660-5320

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	NRIX	Nasdaq Global Market

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

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

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

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

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

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

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

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

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 ☒

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. ☐

The aggregate market value of the common stock held by non-affiliates of the Registrant, based on the closing price of the Registrant's common stock on May 31, 2023 (the last business day of the Registrant's most recently completed second fiscal quarter) as reported by the Nasdaq Global Market on such date was approximately $470.8 million. This calculation does not reflect a determination that certain persons are affiliates of the Registrant for any other purpose.

As of February 5, 2024, the Registrant had 48,894,084 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain sections of the Registrant's definitive Proxy Statement to be filed in connection with the Registrant's 2024 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. Such definitive Proxy Statement will be filed with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days of the Registrant's fiscal year ended November 30, 2023.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Annual Report on Form 10-K other than statements of historical fact, including statements concerning our business strategy and plans, future operating results and financial position, as well as our objectives and expectations for our future operations, are forward-looking statements.

In some cases, you can identify forward-looking statements by such terminology as "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect" and similar expressions that convey uncertainty of future events or outcomes, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements about:

- the timing and conduct of our clinical trial programs for our lead drug candidates NX-5948, NX-2127 and NX-1607 and other drug candidates, including statements regarding the timing of data and anticipated announcements, the selection of new development candidates and the initiation of clinical trials;
- the timing of, and our ability to obtain, marketing approvals for our lead drug candidates NX-5948, NX-2127 and NX-1607 and other drug candidates;
- our plans to pursue research and development of other drug candidates;
- the timing of investigational new drug application (IND) submissions for our drug candidates;
- the potential advantages of our DELigase platform, our drug candidates and Degrader-Antibody Conjugates (DACs);
- the extent to which our scientific approach, our DELigase platform, protein degradation, antibody-drug conjugation, and DACs may potentially address a broad range of diseases;
- the potential benefits of our arrangements with Gilead Sciences, Inc., Sanofi S.A. and Seagen Inc. (now a part of Pfizer Inc.);
- the timing of and our ability to obtain and maintain regulatory approvals for our drug candidates;
- the potential receipt of revenue from future sales of our drug candidates;
- the rate and degree of market acceptance and clinical utility of our drug candidates;
- our estimates regarding the potential market opportunity for our drug candidates;
- our sales, marketing and distribution capabilities and strategy;
- our ability to establish and maintain arrangements for the manufacturing of our drug candidates;
- the expected impact of global business, political and macroeconomic conditions, including inflation, increasing interest rates and volatile market conditions, uncertainty with respect to the federal budget and debt ceiling and potential government shutdowns related thereto, cybersecurity events, instability in the global banking system, and global events, including regional conflicts around the world, on our business, clinical trials, financial condition, liquidity and results of operations;
- the potential achievement of milestones and receipt of royalty payments under our collaborations;
- our ability to enter into additional collaborations with third parties;
- our intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the impact of government laws and regulations; and
- our competitive position.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition, results of operations, prospects and financial needs. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. We disclaim any intention or obligation to update publicly or revise any forward-looking statements for any reason or to conform such statements to actual results or revised expectations, except as required by law.

Risk Factors Summary

Our business is subject to a number of risks and uncertainties, including those risks discussed at-length below. These risks include, among others, the following:

- We have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.
- We have never generated revenue from product sales and may never be profitable.
- We will need substantial additional funding. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts.
- Current and future legislation may increase the difficulty and cost for us, and any collaborators, to obtain marketing approval of and commercialize our drug candidates and affect the prices we, or they, may obtain.
- We are early in our development efforts. Our lead drug candidates, NX-5948, NX-2127 and NX-1607, are in the early stages of clinical development. If we are unable to advance our drug candidates through clinical development, develop, obtain regulatory approval for and commercialize our drug candidates or experience significant delays in doing so, our business may be materially harmed.
- Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.
- If serious adverse events, undesirable side effects or unexpected characteristics are identified during the development of any drug candidates we may develop, we may need to abandon or limit our further clinical development of those drug candidates.
- The results of preclinical studies and early-stage clinical trials may not be predictive of future results. Initial success in clinical trials may not be indicative of results obtained when these trials are completed or in later-stage trials.
- If we decide to seek Orphan Drug Designation or other designations from regulators for any of our current or future drug candidates, we may be unsuccessful or may be unable to maintain the benefits associated with these designations, including the potential for supplemental market exclusivity associated with an Orphan Drug Designation.
- If any of our drug candidates are not considered to be a new active substance or are deemed to fall within the "global marketing authorization" of an existing medicinal product or if pediatric studies are not adequately completed, this may result in lack of regulatory data protection or failure to obtain an extension to existing regulatory data protection.
- We face substantial competition in an environment of rapid technological change, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We expect to depend on collaborations with third parties for the research, development and commercialization of certain of the drug candidates we may develop. If any such collaborations are not successful, we may not be able to capitalize on the market potential of those drug candidates.
- We rely on third-party contract manufacturing organizations (CMOs) for the manufacture of both drug substance and finished drug product for our drug candidates for preclinical and clinical testing and expect to continue to do so for any future clinical trials and commercialization. This reliance on third parties may increase the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.
- If we are unable to obtain and maintain patent protection for our technology, our current drug candidates and any future drug candidates that we may develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize technology and drug candidates similar or identical to ours, and our ability to successfully commercialize our technology and drug candidates may be impaired, and we may not be able to compete effectively in our market.
- We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on our business.
- Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations.

- If we fail to attract and retain management and other key personnel, we may be unable to continue to successfully develop our current and any future drug candidates, commercialize our drug candidates or otherwise implement our business plan.
- Even if we are able to commercialize any drug candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

PART I

Item 1. Business

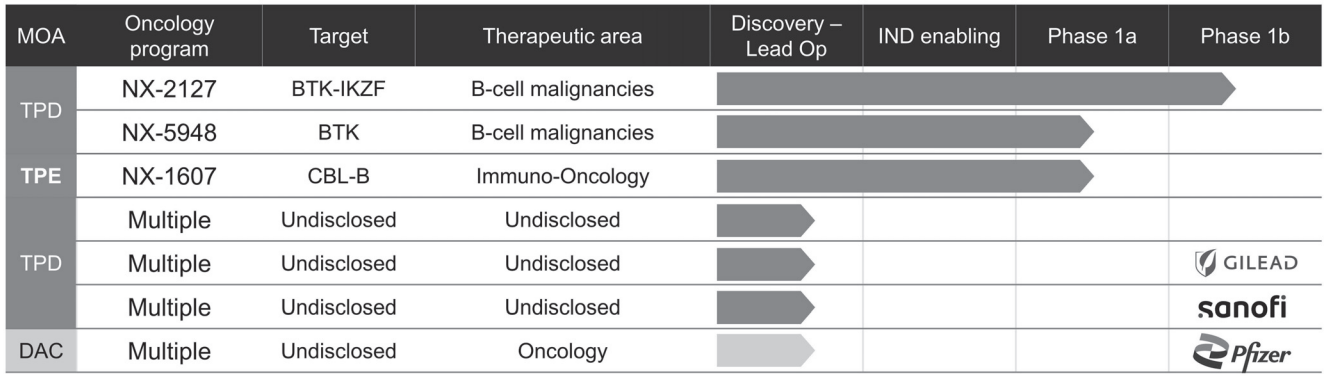
When used in this report, unless otherwise indicated, "Nurix," "Company," "we," "us" and "our" refers to Nurix Therapeutics, Inc. and its wholly owned subsidiaries.

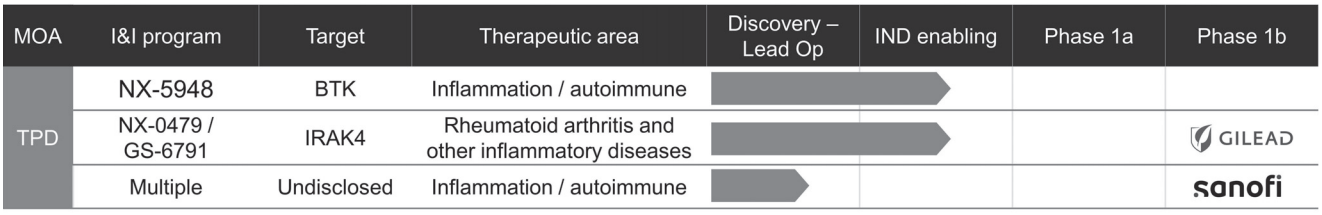
Overview

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative small molecules and antibody therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer, inflammatory conditions and other challenging diseases. Leveraging our extensive expertise in E3 ligases together with our proprietary DNA-encoded libraries, we have built DELigase, an integrated discovery platform to identify and advance novel drug candidates targeting E3 ligases, a broad class of enzymes that can modulate proteins within the cell. Our drug discovery approach is to either harness or inhibit the natural function of E3 ligases within the ubiquitin-proteasome system to selectively decrease or increase cellular protein levels. Our wholly owned, clinical stage pipeline includes targeted protein degraders of Bruton's tyrosine kinase (BTK), a B-cell signaling protein, and inhibitors of Casitas B-lineage lymphoma proto-oncogene B (CBL-B), an E3 ligase that regulates activation of multiple immune cell types including T cells and NK cells. Our partnered drug discovery pipeline consists of multiple programs under collaboration agreements with Gilead Sciences, Inc. (Gilead), Sanofi S.A. (Sanofi) and Seagen Inc. (now a part of Pfizer Inc.) (Pfizer), within which we retain certain options for co-development, co-commercialization and profit sharing in the United States for multiple drug candidates.

Our Clinical Development Pipeline

Our wholly owned pipeline of Targeted Protein Modulation (TPM) drug candidates comprises three clinical stage programs in our Targeted Protein Degradation (TPD) and Targeted Protein Elevation (TPE) portfolios. These two portfolios demonstrate our ability to either decrease or increase protein levels in cells through the modulation of E3 ligases. The following chart summarizes our clinical pipeline and ongoing clinical studies:





MOA, mechanism of action; **IND**, investigational new drug; **DAC**, degrader-antibody conjugates; **I&I**, inflammation and immunology

Targeted Protein Degradation

Our portfolio of targeted protein degraders of BTK, a B-cell signaling protein, comprises NX-5948, an orally bioavailable BTK degrader for the treatment of relapsed or refractory B-cell malignancies and potentially autoimmune diseases, and NX-2127, an orally bioavailable BTK degrader that also degrades cereblon neosubstrates IKZF1 (Ikaros) and IKZF3 (Aiolos) for the treatment of relapsed or refractory B-cell malignancies.

NX-5948: We are currently treating patients in a Phase 1a/1b dose-escalation and cohort expansion study in patients with relapsed or refractory B-cell malignancies. In January 2024, the U.S. Food and Drug Administration (FDA) granted Fast Track designation for NX-5948 for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two lines of therapy, including a BTK inhibitor (BTKi) and a B-cell lymphoma 2 (BCL2) inhibitor.

NX-2127: We are currently treating patients in a Phase 1a/1b dose-escalation and cohort expansion study of NX-2127 in patients with relapsed or refractory B-cell malignancies. We have initiated Phase 1b expansion cohorts for patients with relapsed CLL, diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL). Enrollment of new patients in this clinical trial is paused pending resolution of a partial clinical hold, which was implemented by the FDA in late October 2023. Patients already enrolled who are receiving clinical benefit may continue treatment.

Targeted Protein Elevation

Our targeted protein elevation program includes NX-1607, an orally bioavailable an inhibitor of CBL-B, an E3 ligase that regulates the activation of multiple immune cell types including T cells and NK cells. NX-1607 is targeted for immuno-oncology indications.

We are currently treating patients in a Phase 1a/1b dose-escalation and cohort expansion study of NX-1607 in patients with a range of oncology indications. This study also includes a cohort within the Phase 1a dose escalation study testing NX-1607 in combination with paclitaxel, a taxane chemotherapy commonly used across a range of relapsed and refractory solid tumor indications. NX-1607 was awarded an Innovative Passport from the UK Medicines and Healthcare products Regulatory Agency to accelerate time to market and facilitate patient access to novel drugs to treat serious and life-threatening diseases.

Drug Discovery Pipeline

In addition to our clinical stage drug candidates, we are extending our protein modulation portfolio, both on our own and with partners by developing new targeted protein degraders and ligase inhibitors for a number of targets for which we believe the protein modulation modality can be clinically advantageous over existing therapies. These existing and future programs may have the potential to address diseases with significant unmet need, including cancer, autoimmunity, inflammation, and other challenging diseases.

We have entered into several revenue generating collaborations with large biopharmaceutical companies, including with Gilead, Sanofi and Seagen (now a part of Pfizer), to leverage our DELigase platform for drug discovery. These collaborations allow us to further advance our future pipeline with multiple currently identified targets included in these collaborations. In aggregate, we have received $413.0 million in non-dilutive financing from our collaborators to date, and as of November 30, 2023, we are eligible to receive up to $8.1 billion in potential future fees and milestone payments, as well as royalties on future product sales. We retain certain options for co-development, co-commercialization and profit sharing in the United States for multiple drug candidates pursuant to these collaborations.

Corporate Strategy

Our strategy is to leverage our DELigase platform to discover breakthrough therapies to not only improve upon existing drugs, but also address targets that are thought to be undruggable with current modalities. The key elements of our strategy are to:

- ***Advance our lead programs through clinical development.*** We have three drug candidates in Phase 1 clinical development and anticipate the following advancements in 2024.
    - **NX-5948.** Enrollment is ongoing in our Phase 1a/1b clinical trial of NX-5948 in adults with relapsed or refractory B-cell malignancies, including CLL. In 2024, we seek to define doses for Phase 1b cohort expansion in CLL and NHL and accelerate Phase 1 clinical trial enrollment to enable pivotal trials. We plan to present additional clinical data with higher dose levels and longer treatment duration in mid-2024.

- **NX-2127.** Screening and enrollment of new patients in our Phase 1a/1b clinical trial of NX-2127 in adults with relapsed or refractory B-cell malignancies have been paused due to a partial clinical hold placed on the study by the FDA. Patients currently enrolled in the clinical study who are deriving clinical benefit may continue to receive treatment in accordance with the ongoing study protocol. In 2024, we expect to resolve the partial clinical hold to enable the introduction of newly manufactured drug product into the ongoing Phase 1 clinical trial.
- **NX-1607.** Enrollment is ongoing in our Phase 1 trial for NX-1607 in adults with a range of oncology indications. In 2024, we expect to present data from the Phase 1a dose escalation portion of the trial of NX-1607 and to define dose(s) to enable Phase 1b cohort expansion.

- ***Advance our portfolio of preclinical programs to generate development candidates for our partners and our proprietary pipeline.*** Our research efforts are largely focused on the advancement of multiple programs for our partners Gilead, Sanofi, and Pfizer and for our proprietary pipeline. These partnered and wholly owned programs are at various stages of DNA-encoded library (DEL) screening, lead optimization and preclinical research. We aim to advance at least one program to the development candidate stage in 2024.
- ***Enhance and refine our DELigase platform*.** Targeted Protein Modulation is a rapidly emerging therapeutic modality that can provide significant advantages over existing modalities. Our proprietary DELigase platform enables us to advance an industry-leading approach to either selectively decrease or increase protein levels. We intend to continue to invest resources in our research and development activities to enhance our DELigase platform both in terms of the number of ligases available for drug discovery and the scale of our DEL collection. We plan to continue to leverage our platform capabilities to further enhance our position as a leader in the promising field of protein modulation.
- ***Explore additional strategic collaborations to maximize the commercial potential of our DELigase platform and our drug candidates*.** We have received $413.0 million in non-dilutive funding to date from our collaborations to support our research and development activities and to create new targeted protein modulation drugs with our partners. Under our Gilead, Sanofi and Pfizer collaborations, as of November 30, 2023, we have the opportunity to receive up to $8.1 billion in potential future fees and milestone payments, as well as royalties on future sales while retaining certain commercialization options. We currently retain worldwide development and commercialization rights to our BTK and CBL-B portfolios. While we intend to become a fully integrated biopharmaceutical company and build a targeted sales force in the United States to support the commercialization of our drug candidates, if approved, we intend to selectively evaluate technology collaborations and commercialization partnerships for our drug candidates with partners whose capabilities complement our own while retaining meaningful commercial rights in key geographic territories.

Targeted Protein Modulation

In disease settings where currently available treatments are limited by suboptimal efficacy or safety, or where relevant protein targets are not druggable by conventional means, we believe targeted protein modulation represents a novel treatment paradigm with the potential to improve upon or become the standard of care. Recent advances in the field have highlighted the significant therapeutic potential of harnessing E3 ligases to promote targeted protein degradation. In addition, we believe the largely unexplored area of inhibiting E3 ligases directly to increase protein levels represents an equally promising approach. Using our powerful DELigase platform, we have demonstrated our ability to discover and advance small molecule drug candidates to decrease or increase protein levels by either harnessing or inhibiting the activity of the appropriate E3 ligase, depending on the desired therapeutic effect. We have carefully selected and are advancing over 90 E3 ligases in our DELigase platform, expanding the universe of E3 ligases that can be modulated beyond cereblon and von Hippel-Lindau (VHL), the two predominantly used in the field of targeted protein degradation today. Our DEL collection consists of billions of small molecule compounds used to identify potential binders to ligases and protein targets as critical starting points in our drug discovery process. The differentiation of our protein modulation platform is in its breadth and versatility, enabling us to alter protein levels either upward or downward for both clinically validated targets, such as BTK, and for targets previously thought to be "undruggable;" that is, proteins that could not be addressed by conventional pharmacological means, such as CBL-B.

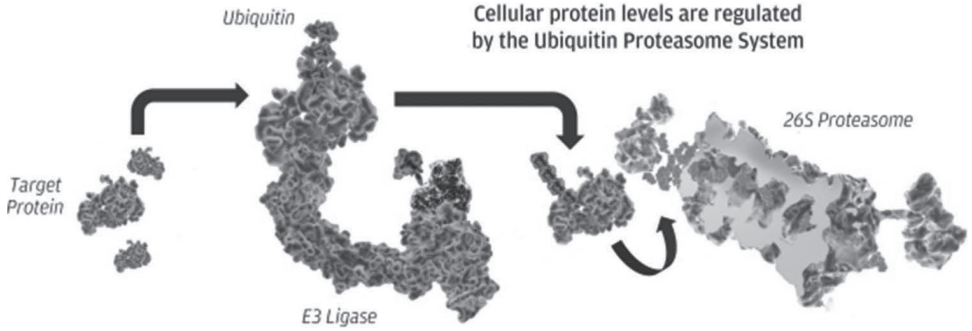
Proteins as targets in treating disease

Each cell type within the body is comprised of proteins that define its biochemistry and biological function. When proteins are expressed and regulated correctly, the health of each individual cell as well as the body as a whole is maintained. However, disease can occur when normal cellular processes are dysregulated as a result of changes in protein structure, function, expression levels or pathway regulation. Factors such as genetic mutations, infection, exposure to toxins, diet and behavior can lead to dysregulation of cellular processes and, if unchecked, a disease process.

The traditional approach to discovering treatments for disease has involved the development of small molecule drugs that bind to a protein's surface and modulate its activity. These "druggable" proteins contain distinct structural features that mediate protein function called active sites which can be exploited when identifying and optimizing compounds that disrupt protein activity. However, the vast majority of the body's proteins do not have distinct active sites that can be targeted using traditional discovery methods. Because dysregulation and disease are not restricted to these "druggable" proteins, a significant number of therapeutically relevant proteins have not been addressed by traditional small molecule drugs. Other modalities, including antibody and protein-based therapies, genetic medicines and cell therapies, have emerged to address these issues but are still limited by their modes of delivery, their scalability and their therapeutic applications.

Leveraging E3 ligases and the ubiquitin proteasome system as a new treatment modality

Normal cellular physiology requires highly orchestrated and regulated processes that operate at the level of individual proteins. The ability of proteins to respond to stimuli quickly and in a coordinated fashion requires protein function to be readily controllable. One of the most exquisitely ordered cellular systems governing cellular proteins is the ubiquitin proteasome system (UPS).



As depicted above, the UPS is responsible for regulating and maintaining normal protein levels in the cell. An important class of enzymes called E3 ligases mediate this process with a high degree of specificity by recognizing individual proteins and catalyzing the attachment of ubiquitin protein tags to their surface. Proteins marked with chains of ubiquitin are then shuttled to the proteasome for degradation and removal from the cell. In addition to protein degradation, E3 ligases also mediate other functions such as protein localization, receptor internalization, protein signaling and protein quality control. There are over 600 E3 ligases encoded within the human genome, representing more than 5% of genes. The prevalence of the E3 ligase class of enzymes reflects the diversity of their physiological roles and biological significance and may allow for the creation of a wide spectrum of ligase-targeted therapeutics.

Modulating protein levels through small molecule therapeutics targeting E3 ligases

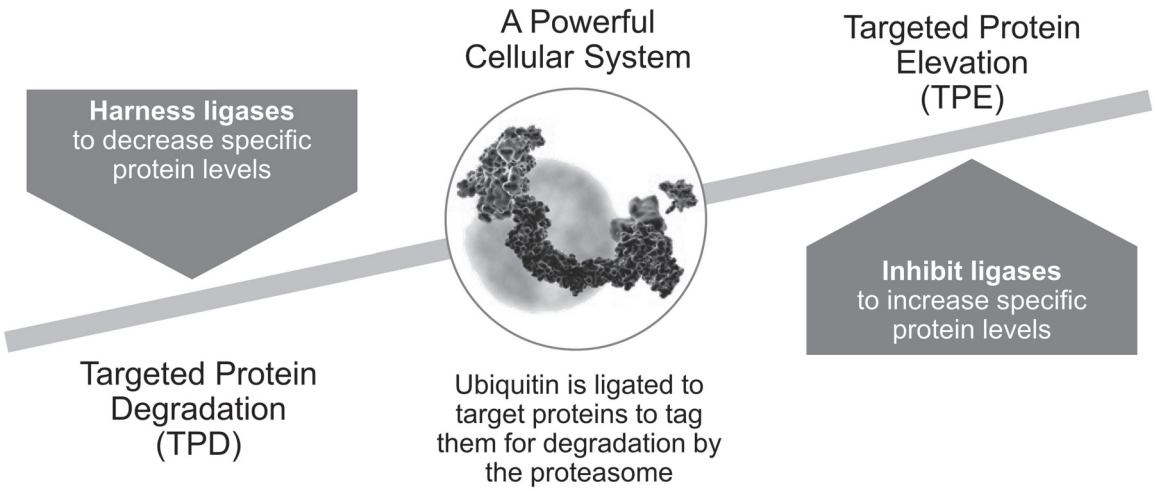
Advances in our understanding of the UPS suggest broad potential for the development of new therapies that modulate E3 ligases in the context of diseases such as cancer and autoimmune disorders. An example are the so-called immunomodulatory drugs, Revlimid (lenalidomide) and Pomalyst (pomalidomide), which are approved cancer drugs. These drugs exert their therapeutic effects by targeting the E3 ligase cereblon and redirecting its activity toward proteins it would not normally degrade such as Ikaros and Aiolos (also known as IKZF1 and IKZF3), transcription factors regulating immune cell function. Elucidation of this mechanism led to the recognition that pharmacological control of E3 ligase activity could more generally represent a promising new paradigm for small molecule drug action. This idea has since translated into the development of targeted protein degraders, which we believe have significant therapeutic potential. In addition, the largely unexplored area of inhibiting E3 ligases directly to increase cellular protein levels, which we call Targeted Protein Elevation, may represent an equally promising approach.

Targeted Protein Modulation is the term we use to describe our ability to either decrease target protein levels by harnessing E3 ligases for targeted protein degradation or increase protein levels through the inhibition of E3 ligases for targeted protein elevation.

- ***Targeted Protein Degradation (Harnessing E3 ligases).*** Targeted protein degradation harnesses the natural activity of ligases to remove specific proteins from the cell. Targeted protein degradation is accomplished by using bifunctional small molecules, which are composed of an E3 ligase binding element, or harness, linked to a target protein binding element. Unlike traditional small molecule inhibition, targeted protein degradation is catalytic whereby one molecule can induce the degradation of multiple copies of the protein target, enabling the efficient elimination of cellular proteins. In addition, since the effect is mediated through the binding of a small molecule drug rather than through functional inhibition, proteins lacking active sites are potentially targetable, greatly expanding the spectrum of both proteins and diseases amenable to small molecule therapeutic intervention.

- ***Targeted Protein Elevation (Inhibiting E3 ligases).*** By inhibiting the function of E3 ligases in targeted protein elevation, it is possible to rapidly increase specific protein levels to control biological pathways. Increasing the levels of distinct sets of proteins could be a powerful approach to blocking pathological processes and restoring normal physiology. While there is enthusiasm in the scientific community around the therapeutic potential of E3 ligase inhibition, the discovery of such inhibitors has been impeded by the limited understanding of this biochemically and structurally complex class of proteins.

Targeted Protein Modulation



We believe that targeting E3 ligases to modulate protein levels represents a new therapeutic frontier that retains the favorable attributes of small molecule treatment modalities while addressing some major limitations. In addition to the points above, we believe other key differentiating attributes of our treatment modality include:

- ***Expansive therapeutic potential.*** The UPS and its associated E3 ligases function across the majority of cell types and organ systems, making it possible to modulate virtually any protein of interest for a wide range of diseases.
- ***Deliverable and tunable.*** Oral delivery of small molecule compounds lends itself to broad medical applicability in a range of patient populations with delivery that may be readily calibrated through dosing schedule and quantity.
- ***Ease of manufacturing***. Development and manufacturing of small molecules utilizes established, cost-efficient processes that are readily scalable.

Our Programs

Our targeted protein degradation portfolio includes two clinical stage drug candidates that catalyze potent degradation of BTK, a well validated target for B-cell malignancies. Our two BTK degrader drug candidates, NX-5948 and NX-2127, are oral drug candidates being evaluated for the treatment of relapsed or refractory B-cell malignancies including CLL and non-Hodgkin's lymphoma (NHL). NX-5948 is designed to solely degrade BTK, and NX-2127 is designed to degrade BTK and the immunomodulatory substrates of Ikaros and Aiolos. NX-5948 has the potential to address B-cell mediated autoimmune indications due to its specificity for BTK, and neurologic autoimmune indications due to its ability to cross the blood brain barrier.

In preclinical studies and in patient-derived samples, we have demonstrated the ability of both NX-5948 and NX-2127 to degrade BTK in cells harboring either wild type BTK or a variety of clinically relevant mutant forms of BTK that are known to confer resistance to both currently marketed BTK inhibitors and next-generation BTK inhibitors in late-stage development. Based on our preclinical and clinical data, we believe that both NX-5948 and NX-2127 have the potential to demonstrate unique and improved clinical benefit over the current standard-of-care in multiple oncology indications.

Our targeted protein elevation portfolio includes our lead ligase inhibitor NX-1607, an oral, clinical stage small molecule drug candidate that inhibits CBL-B, an intracellular orchestrator of the activation of T cells, B cells and NK cells. In preclinical studies, primary human T cells exposed to NX-1607 demonstrated increased T-cell activation in the absence of co-stimulation with CD3 and CD28, a potential advantage in an immune suppressive tumor microenvironment. In addition, NX-1607 has been shown in preclinical models to increase T-cell proliferation and result in increased secretion of interleukin-2 (IL-2), a key cytokine involved in immune activation. We believe that oral delivery of a CBL-B inhibitor has the potential to drive immune cell activation and stimulation of localized IL-2 secretion, leading to enhanced anti-tumor response across a wide range of oncology indications.

Targeted protein degradation portfolio in clinical trials

We have developed two targeted protein degrader drug candidates that are potent degraders of the BTK protein, a clinically validated signaling factor that drives B-cell activation and proliferation. Both of our BTK degraders harness the E3 ligase cereblon. NX-5948 is designed to selectively degrade BTK and has demonstrated the ability to cross the blood brain barrier in animal models and degrade BTK in both brain-resident tumor cells and normal microglia in the brain. NX-2127 was engineered to degrade both BTK and cereblon neosubstrates Ikaros and Aiolos for the treatment of relapsed or refractory B-cell malignancies. In several B-cell malignancy indications, and in particular in certain NHL subtypes, we believe dual activity may provide therapeutic advantages not addressable by pure BTK degraders or inhibitors, that could in turn result in improved outcomes for patients. We are currently treating patients with relapsed or refractory B-cell malignancies in Phase 1 trials for NX-5948 and NX-2127.

BTK's role in B-cell malignancy

BTK is a key component of the B-cell receptor signaling pathway and has been clinically validated as a target in the treatment of B-cell malignancies, most notably in CLL but also in NHL. In 2022, it was estimated that over 20 thousand patients were diagnosed with CLL and over 80 thousand patients were diagnosed with NHLs in the United States. Approximately 85% of NHLs are a result of B-cell malignancies. The natural progression of NHL varies widely and takes multiple forms, ranging from aggressive subtypes such as DLBCL, to more indolent forms such as follicular lymphoma (FL).

Background on BTK inhibitors and immunomodulatory drugs for B-cell malignancies

The first generation BTK inhibitor Imbruvica, or ibrutinib, is approved for the treatment of CLL, Waldenstrom's macroglobulinemia (WM), and chronic graft versus host disease (GVHD). Second generation BTK inhibitors include Calquence, or acalabrutinib, which is approved for use in CLL and MCL, and Brukinsa, or zanubrutinib, which is approved for use in CLL, MCL, WM and marginal zone lymphoma (MZL). Based on reported sales to date, we estimate that 2023 BTK sales were approximately $8.7 billion. These BTK inhibitors bind covalently to cysteine C481 of the BTK protein and irreversibly inhibit BTK; however, all have some off-target binding to other kinases, which leads to unwanted side effects. In addition, acquired resistance, most commonly through mutations in C481, may limit long term efficacy of these first and second generation BTK inhibitors. A number of noncovalent BTK inhibitors are currently being investigated in clinical trials as potential therapies for patients with relapsed and refractory disease, including Jaypirca, or pirtobrutinib, which was recently approved for use in CLL and MCL. However, the noncovalent inhibitors are also subject to acquired resistance, and treatment with these agents has led to the discovery of a broad range of new resistance mutations.

BTK degraders possess several unique properties that offer potential advantages over inhibitors:

- **Addresses scaffold function of BTK.** Removal of the BTK protein rather than just inactivating the kinase domain addresses the scaffolding activity of BTK, more completely blocking the signaling activity of both wild type and mutant forms of BTK.
- **Event-driven pharmacology.** BTK degraders do not require strong and prolonged binding to BTK to trigger degradation, which increases the ability our degraders to act on mutated BTK and may decrease the probability of forming new resistance mutations.
- **Catalytic activity.** A single degrader molecule is able to affect multiple target BTK molecules sequentially without the need to be constantly bound to the target.

We believe that targeted protein degradation of BTK may be a superior approach to existing covalent or noncovalent BTK inhibitors, particularly in the relapsed and refractory setting, and in the setting of resistance mutations to both covalent and noncovalent inhibitors.

The immunomodulatory drugs including Revlimid, or lenalidomide, and Pomalyst, or pomalidomide, are analogs of Thalomid, or thalidomide. These drugs possess several anti-tumor properties, including anti-angiogenic and anti-proliferative effects. They also have multiple effects on the immune system, including enhancement of T-cell mediated and NK-cell mediated immunity. Revlimid, the market leader in this class by global sales, was first approved in 2006 for the treatment of multiple myeloma. In May of 2019, Revlimid in combination with Rituxan received a supplemental indication approval for previously treated FL, MZL and MCL, and in August of 2020, Revlimid in combination with Monjuvi received a supplemental indication in DLBCL, thus validating the importance of this drug class in these indications. In 2022, global sales of this drug class including Revlimid and Pomalyst were approximately $13.5 billion. Subsequent to their approval and successful commercialization, studies demonstrated that these immunomodulatory drugs exert their therapeutic effect by triggering the degradation of specific proteins including Aiolos and Ikaros through the E3 ligase activity of cereblon and hence were identified retrospectively as the first approved drugs to target an E3 ligase.

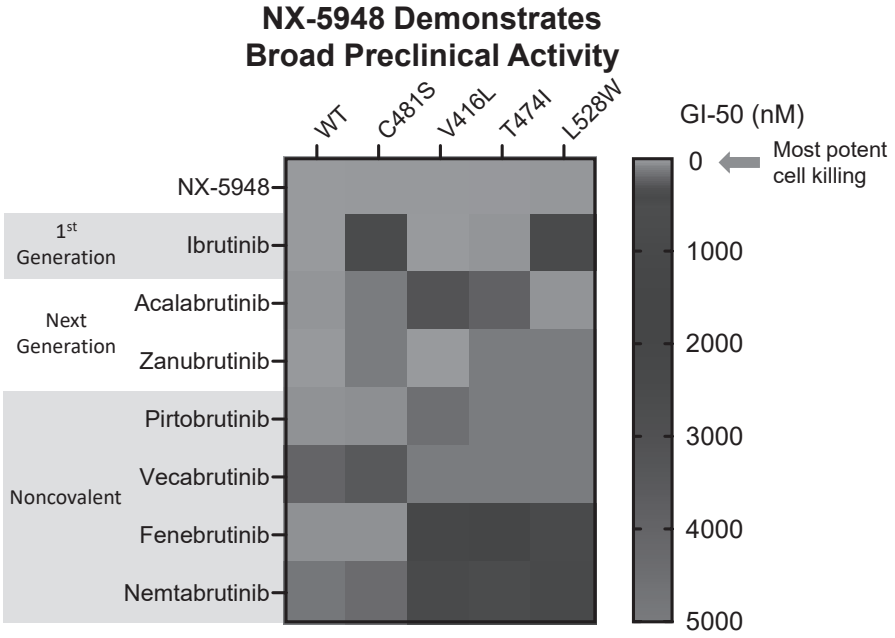
Published studies have recently reported early clinical data showing that combining a BTK inhibitor with an immunomodulatory drug may have the potential to augment clinical activity of certain standard of care agents in some hematologic malignancies such as non-germinal center B-cell like (non-GCB) DLBCL. Further, scientific publications have previously described synthetic lethality in a DLBCL cell line treated with both ibrutinib and lenalidomide. By targeting both BTK and cereblon-mediated immunomodulatory pathways simultaneously, it is believed that the survival mechanisms driven by accumulated mutations within certain cancers can be overcome, thereby preventing escape and disease relapse. This may be especially effective if each pathway has not only different functions but also if they share certain critical components. One possible intersection pathway is the suppression of interferon regulatory factor 4 (IRF4), a member of a family of transcription factors leading to a cell lethal increase in interferon production. The early clinical study cited above was particularly noteworthy since few combinations have previously produced promising results in DLBCL. This may suggest that simultaneous degradation of BTK combined with cereblon-mediated immunomodulatory activity by a single agent could produce an additive or synergistic effect in certain B-cell malignancies.

Potential advantages of BTK degraders

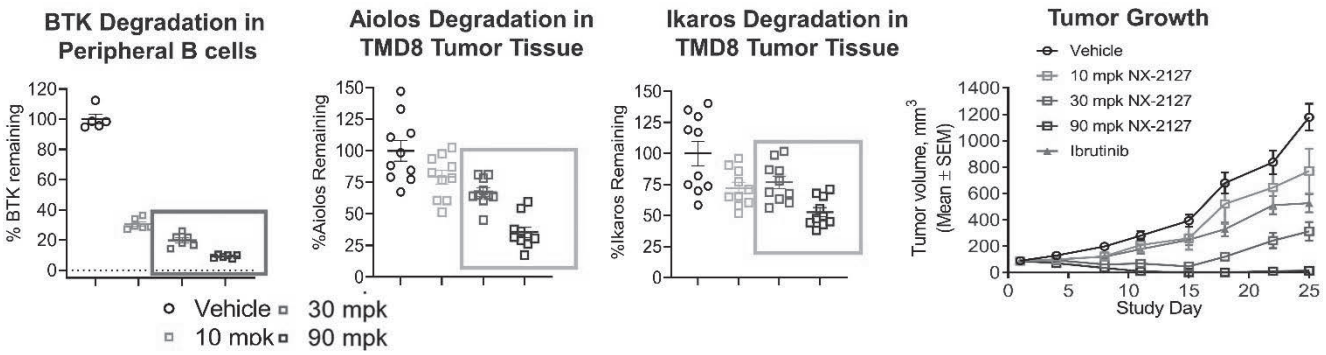
We have conducted extensive preclinical studies of our two clinical stage BTK degraders. We have demonstrated that both NX-5948 and NX-2127 can induce BTK degradation and inhibit tumor growth with oral administration in xenograft mouse models implanted with both wild type and ibrutinib-resistant lymphoma cell lines. We have also demonstrated the ability of both NX-5948 and NX-2127 to degrade BTK in circulating B-cells of non-human primates and in B-cell lymphoma patients following once daily oral dosing in ongoing Phase 1 trials. We have specifically designed NX-5948 to degrade BTK with limited or no degradation of cereblon neosubstrates, and we have designed NX-2127 as a dual degrader of BTK as well as the cereblon neosubstrates Aiolos and Ikaros, for potential applications in indications where adding immunomodulatory activity may be beneficial.

We have optimized NX-5948 and NX-2127 to be able to degrade both wild type BTK and the C481S variant of BTK that has been identified as the most common mutation in patients who have become resistant to ibrutinib therapy over time. Both agents have subsequently demonstrated the ability to degrade additional mutant variants of BTK associated with resistance to BTK inhibitors including L528W, T474I, M437R and V416L.

In our model of DLBCL cell line (TM8) harboring the most common resistance mutations, both NX-5948 and NX-2127 retained activity while all tested inhibitors demonstrated a major decrease in activity against at least one resistance mutation. The figure below shows a heat map of the relative activity of NX-5948 compared to a panel of first and second generation covalent BTK inhibitors and non-covalent BTK inhibitors.

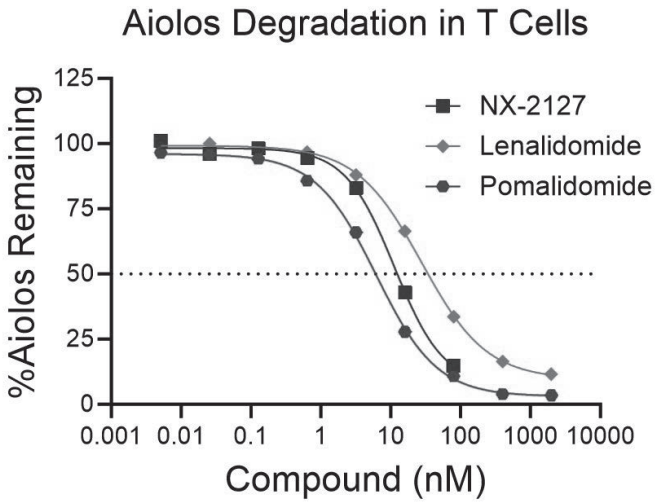


Potent tumor growth inhibition was achieved at varying doses of orally administered NX-2127 in mouse xenograft tumor models with a wild type BTK protein, as shown in the figure below on the top right. In this same model, NX-2127 demonstrated potent degradation of BTK in both circulating B cells (below on the top left) and in lymphoma tumors (below top middle). In this model system, 80% BTK degradation in circulating B cells correlated with 74% tumor growth inhibition, and 90% BTK degradation in circulating B cells correlated with 100% tumor growth inhibition. These target levels of inhibition suggest a potential therapeutic range correlating BTK degradation to tumor growth inhibition.



Oral dose of NX-2127 (mg/kg)	10	30	90
% BTK degradation in peripheral B cells	69%	80%	91%
% Aiolos degradation in tumor tissue	21%	33%	64%
% Ikaros degradation in tumor tissue	28%	23%	47%
% Tumor growth inhibition vs Vehicle(Day 24)	58%	74%	100%

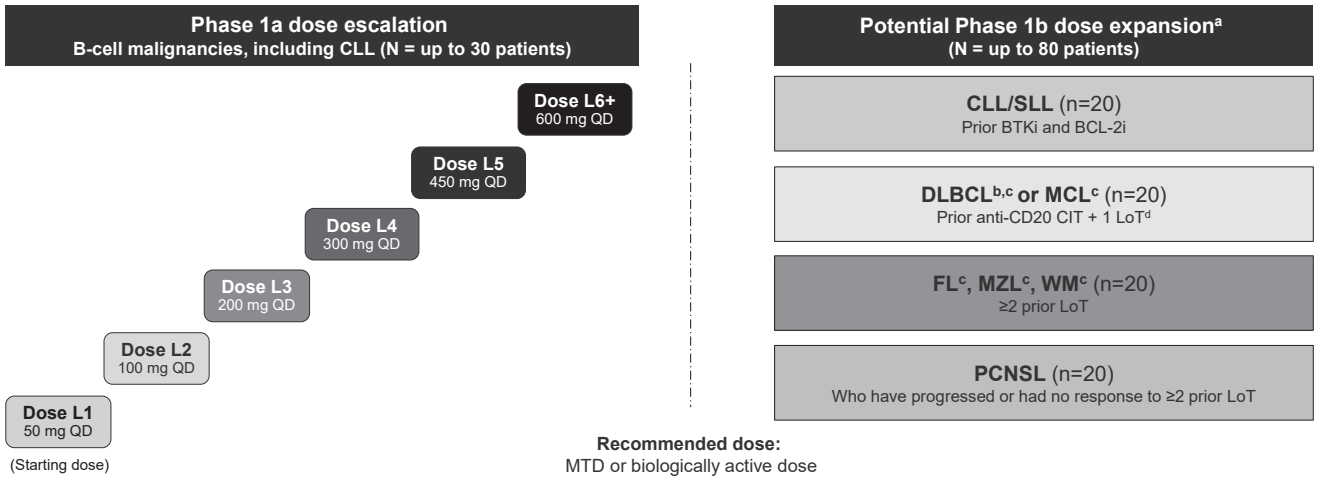
In addition to BTK degradation, we have also demonstrated the ability of NX-2127 to degrade both Aiolos (as shown in the figure below) and Ikaros (not shown), proteins targeted by immunomodulatory drugs Revlimid (lenalidomide) and Pomalyst (pomalidomide). Studies in human T cells comparing NX-2127 to lenalidomide and pomalidomide have shown comparable Aiolos degradation and resultant T-cell activation, as shown in the figure below. Based on the clinical data of both ibrutinib and the immunomodulatory drug in B-cell malignancies, we believe that this strategy of targeting both BTK and Aiolos/Ikaros in a single oral treatment may improve anti-tumor activity.



Clinical development studies for NX-5948

We are studying the pharmacology, safety, and clinical activity of NX-5948 in multiple subtypes of relapsed and refractory B-cell malignancies, including those in which ibrutinib has shown only modest effects or is ineffective, as in the case of CLL patients with BTK inhibitor resistance mutations.

As illustrated in the diagram below, we are conducting a Phase 1a/1b dose-escalation and cohort expansion study of NX-5948 in patients with relapsed or refractory CLL and NHL. The Phase 1a portion is designed as a monotherapy dose escalation trial to investigate the safety and tolerability of NX-5948 and to identify a biologically active dose for cohort expansion and potentially a maximum tolerated dose. The Phase 1b portion of the trial is designed as a monotherapy expansion trial in up to five potential cohorts. The patients in the study represent a heavily pre-treated population with a variety of previous treatment options. Some patients also have resistance mutations and other high risk molecular features. The study is currently enrolling in the United States, the United Kingdom (UK) and the Netherlands.

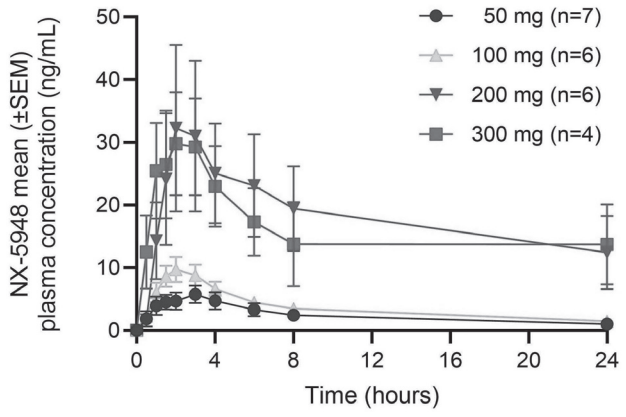


[a]Subtypes include: transformed indolent lymphoma (e.g., grade 3b/transformed FL), Richter-transformed DLBCL, high-grade B-cell lymphoma with MYC and BCL-2 and/or BCL-6 rearrangements, high-grade B-cell lymphomas NOS; [b]Includes patients with secondary CNS involvement; [c]Additional lines of therapy include anthracycline for non-GCB DLBCL and BTKi for MCL
Abbreviations: **BCL-2i**, B-cell lymphoma-2 inhibitor; **BTKi**, Bruton's tyrosine kinase inhibitor; **CIT**, chemo-immunotherapy; **CLL**, chronic lymphocytic leukemia; **CNS**, central nervous system; **DLBCL**, diffuse large B-cell lymphoma; **FL**, follicular lymphoma; **GCB**, germinal center B-cell; **L**, level; **MCL**, mantle cell lymphoma; **LoT**, line of therapy; **MZL**, marginal zone lymphoma; **NOS**, not otherwise specified; **PCNSL**, primary central nervous system lymphoma; **SLL**, small lymphocytic lymphoma; **WM**, Waldenströms macroglobulinemia

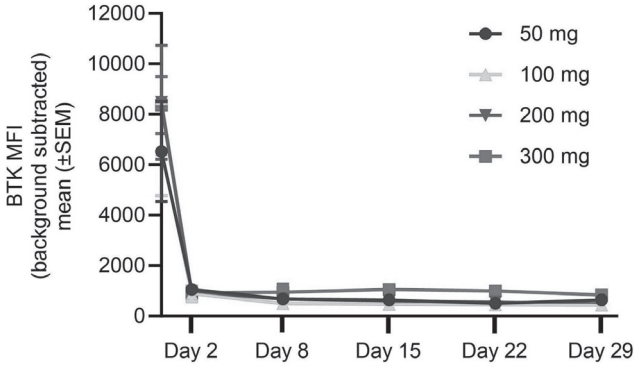
Initial clinical findings

Initial clinical findings from the NX-5948 clinical trial were presented at the 65th American Society of Hematology (ASH) annual meeting in December 2023. Pharmacokinetics (PK) and pharmacodynamics data from the ongoing Phase 1a trial shown below demonstrate dose-dependent PK and rapid, robust, and sustained BTK degradation in all patients with once daily oral dosing of NX-5948, confirming the findings and projections from previous preclinical research.

NX-5948 C1D1 pharmacokinetics



BTK degradation in patients receiving NX-5948



BTK, Bruton's tyrosine kinase; **MFI**, mean fluorescence intensity; **SEM**, standard error of the mean

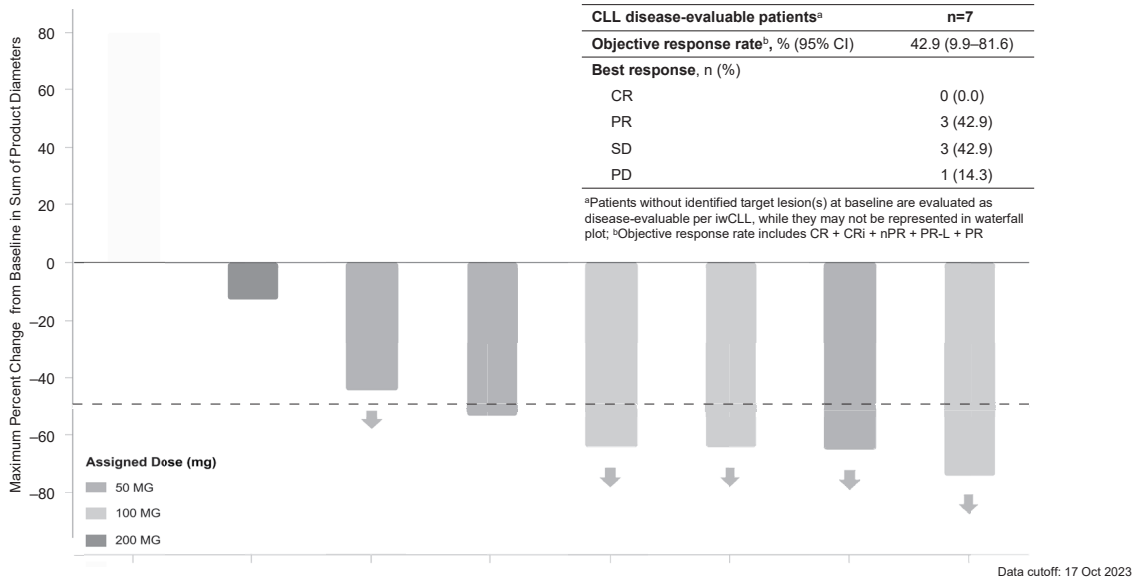
Source: Searle et al., ASH 2023, Poster #4473

Results from the first data disclosure of the NX-5948 Phase 1a trial showed that NX-5948 is well tolerated and demonstrates clinical benefit.

Out of 26 patients dosed, there were no dose limiting toxicities and no treatment emergent adverse events (TEAEs) resulting in drug discontinuation. There were four NX-5948-related grade ≥3 TEAEs and no related serious adverse events (SAEs).

As of the October 17, 2023 data cutoff, in the CLL patient population six out of seven dosed patients showed clinical benefit, including three partial responses (one ongoing over nine months) and three stable disease outcomes (two still on treatment). In the NHL patient population (19 dosed), durable responses were noted across indications, with eight patients, or almost half of the patient population, continuing treatment. An expanded data set from a larger number of patients treated at higher doses and for a longer duration of time is expected in 2024.

NX-5948 CLL efficacy

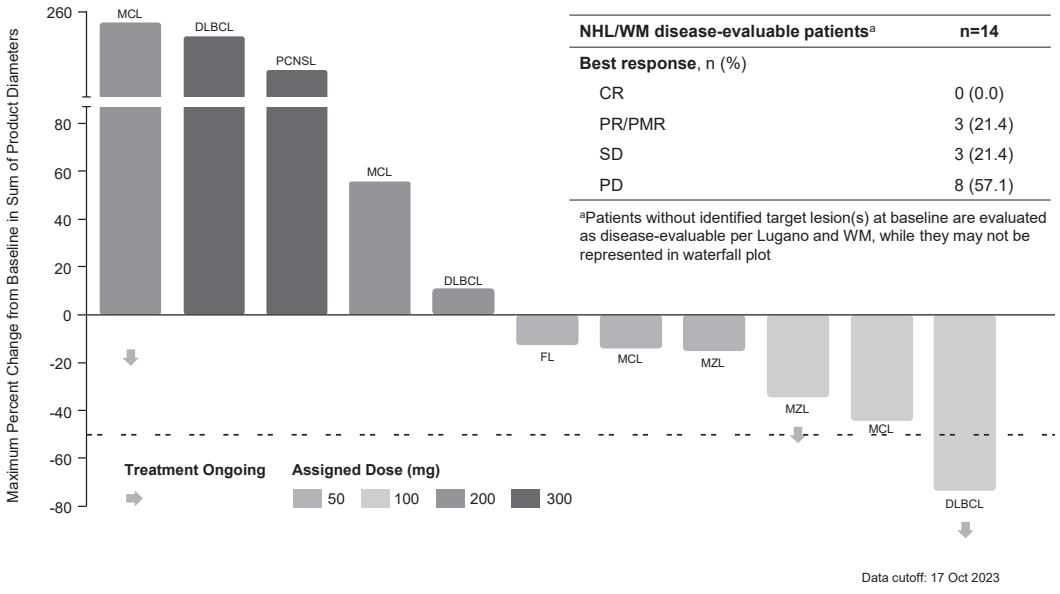


CLL disease-evaluable patients[a]	n=7
Objective response rate[b], % (95% CI)	42.9 (9.9–81.6)
Best response, n (%)	
CR	0 (0.0)
PR	3 (42.9)
SD	3 (42.9)
PD	1 (14.3)

[a]Patients without identified target lesion(s) at baseline are evaluated as disease-evaluable per iwCLL, while they may not be represented in waterfall plot; [b]Objective response rate includes CR + CRi + nPR + PR-L + PR

CI, confidence interval; **CLL**, chronic lymphocytic leukemia; **CR**, complete response; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease

NX-5948 NHL efficacy



NHL/WM disease-evaluable patients[a]	n=14
Best response, n (%)	
CR	0 (0.0)
PR/PMR	3 (21.4)
SD	3 (21.4)
PD	8 (57.1)

[a]Patients without identified target lesion(s) at baseline are evaluated as disease-evaluable per Lugano and WM, while they may not be represented in waterfall plot

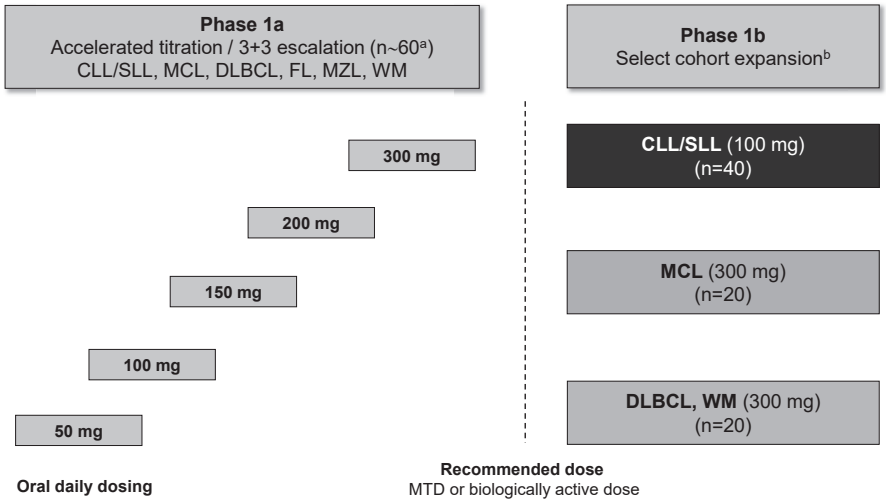
CR, complete response; **DLBCL**, diffuse large B-cell lymphoma; **FL**, follicular lymphoma; **MCL**, mantle cell lymphoma; **MZL**, marginal zone lymphoma; **NHL**, non-Hodgkin's lymphoma; **PCNSL**, primary CNS lymphoma; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease; **WM**, Waldenstrom's macroglobulinemia

Source: Searle et al., ASH 2023, Poster #4473

Clinical development of NX-2127

We are studying the pharmacology, safety and clinical activity of NX-2127 in multiple subtypes of relapsed and refractory B-cell malignancies, including CLL, DLBCL, MCL, MZL and FL. We plan to focus development in indications where NX-2127 shows evidence of compelling clinical activity and where there is high unmet need.

As illustrated in the diagram below, the Phase 1a/1b dose-escalation and cohort expansion trial is evaluating doses ranging from 50 mg to 300 mg, and currently includes expansion cohorts for patients with CLL, DLBCL and MCL. The Phase 1a portion is designed as a monotherapy dose escalation trial to investigate the safety and tolerability of NX-2127 and to identify a maximum tolerated dose for further evaluation. The Phase 1b portion of the trial is designed as a monotherapy expansion trial in defined cohorts. We selected a 100 mg dose for a Phase 1b expansion in CLL patients and selected a 300 mg dose for Phase 1b expansion in MCL and DLBCL patients. The patient population in the trial was heavily pre-treated and included a sizeable proportion of patients with resistance mutations. Enrollment of new patients in this clinical trial is currently paused pending resolution of a partial clinical hold.

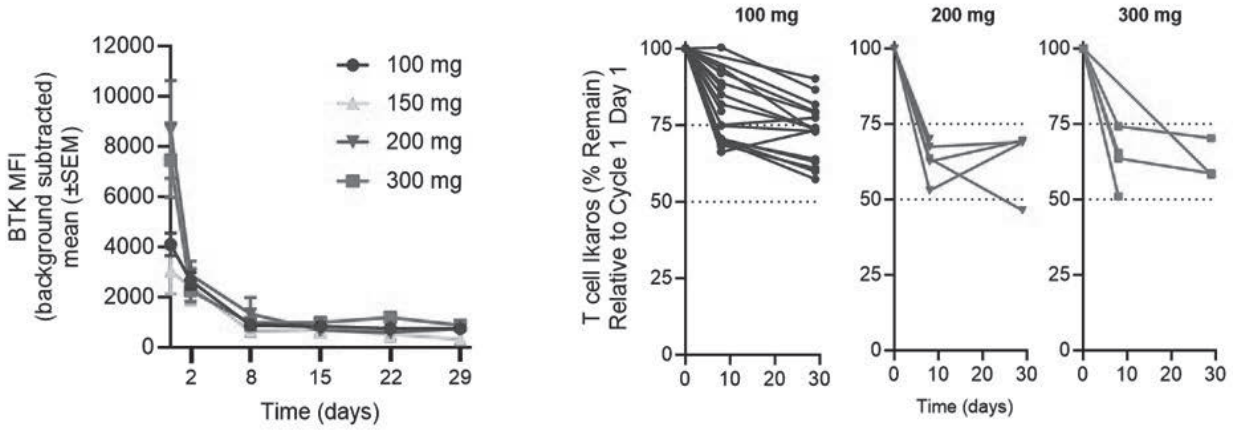


[a]Planned number of evaluable patients (i.e., meeting DLT evaluability criteria); [b]Planned number of evaluable patients (i.e., meeting efficacy evaluability criteria)
CLL, chronic lymphocytic leukemia; **DLBCL**, diffuse large B-cell lymphoma; **DLT**, dose-limiting toxicity; **FL**, follicular lymphoma; **MCL**, mantle cell lymphoma; **MTD**, maximum tolerated dose; **MZL**, marginal zone lymphoma; **PD**, pharmacodynamics; **PK**, pharmacokinetics; **PCNSL**, primary central nervous system lymphoma; **SLL**, small lymphocytic lymphoma; **WM**, Waldenstrom's macroglobulinemia

Clinical findings

Updated data from the NX-2127 clinical study presented at the 65th ASH annual meeting in December 2023 described positive data for NX-2127 in patients with NHL and CLL, confirming a manageable safety profile that is consistent with previous reports for BTK-targeted and immunomodulatory therapies.

BTK and Ikaros degradation was demonstrated at all dose levels in patient samples, as shown in the figure below.

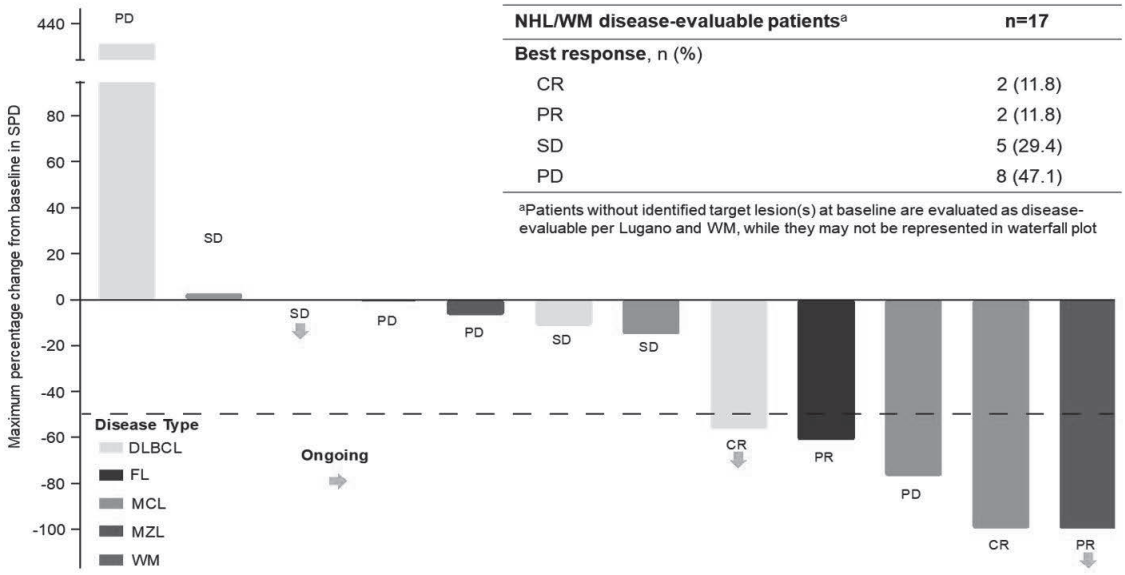


Source: Danilov et al., ASH 2023, Poster #4463

The safety findings from the study confirmed the manageable and predictable safety profile. The most common TEAEs (any grade) were fatigue, neutropenia, hypertension, bruising/contusion, and diarrhea. The most common grade ≥3 TEAEs were neutropenia, hypertension and anemia. Atrial fibrillation was observed in six patients (11.1%; down from 17% reported previously), with three patients (5.6%) having grade ≥3 events. Twenty-one patients (38.9%) had serious TEAEs, of whom eight (14.8%) had SAEs considered related to NX-2127 treatment. Two patients experienced dose limiting toxicities (cognitive disturbance, neutropenia; both at the 300 mg dose).

Efficacy findings showed promising clinical activity: For patients with NHL encouraging and durable responses were observed, including two complete responses at week eight and two partial responses at week eight. For patients with CLL despite a median of five prior lines of treatment and BTK mutations present in 36% of patients, NX-2127 treatment resulted in an objective overall response rate of 40.7%, including partial responses in 11 patients, with treatment ongoing in 13 patients. Tumor shrinkage and clinical responses were observed in patients regardless of prior lines of therapy or baseline BTK mutations.

NX-2127 NHL efficacy



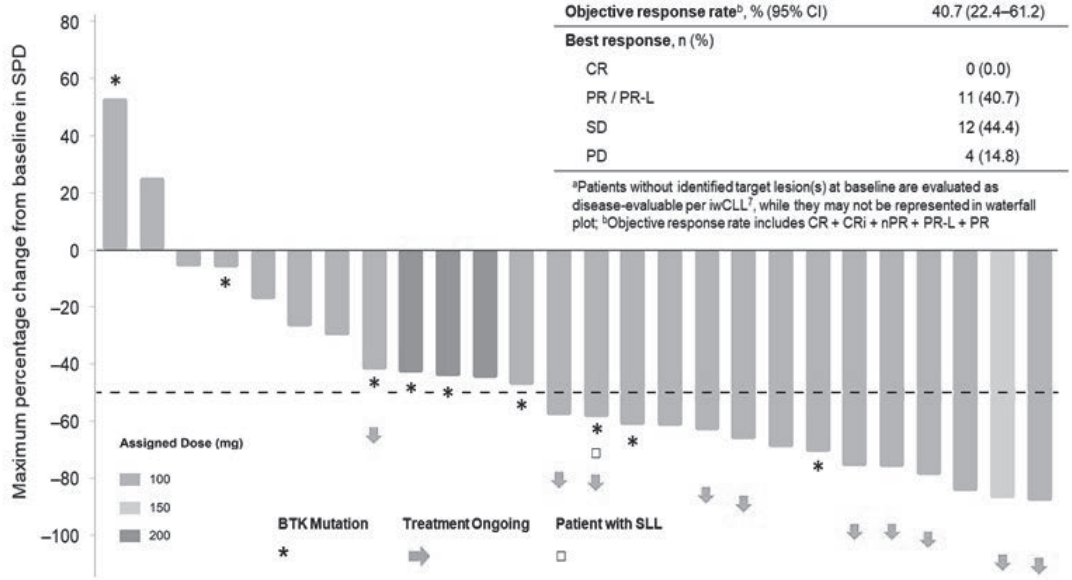
NHL/WM disease-evaluable patients[a]	n=17
Best response, n (%)	
CR	2 (11.8)
PR	2 (11.8)
SD	5 (29.4)
PD	8 (47.1)

[a]Patients without identified target lesion(s) at baseline are evaluated as disease-evaluable per Lugano and WM, while they may not be represented in waterfall plot

CR, complete response; **DLBCL,** diffuse large B-cell lymphoma; **FL**, follicular lymphoma; **MCL,** mantle cell lymphoma; **MZL,** marginal zone lymphoma; **NHL**, non-Hodgkin's lymphoma; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease; **WM,** Waldenstrom's macroglobulinemia

Data cutoff: 15 Sep 2023
Danilov A, et al. Blood 2023;142(Suppl 1):4463

NX-2127 CLL efficacy



CLL/SLL disease-evaluable patients[a]	n=27
Objective response rate[b], % (95% CI)	40.7 (22.4–61.2)
Best response, n (%)	
CR	0 (0.0)
PR / PR-L	11 (40.7)
SD	12 (44.4)
PD	4 (14.8)

[a]Patients without identified target lesion(s) at baseline are evaluated as disease-evaluable per iwCLL[7], while they may not be represented in waterfall plot; [b]Objective response rate includes CR + CRi + nPR + PR-L + PR

CI, confidence interval; **CR**, complete response; **DLBCL,** diffuse large B-cell lymphoma; **FL**, follicular lymphoma; **MCL,** mantle cell lymphoma; **MZL,** marginal zone lymphoma; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease; **SPD**, sum of product diameters; **WM,** Waldenstrom's macroglobulinemia

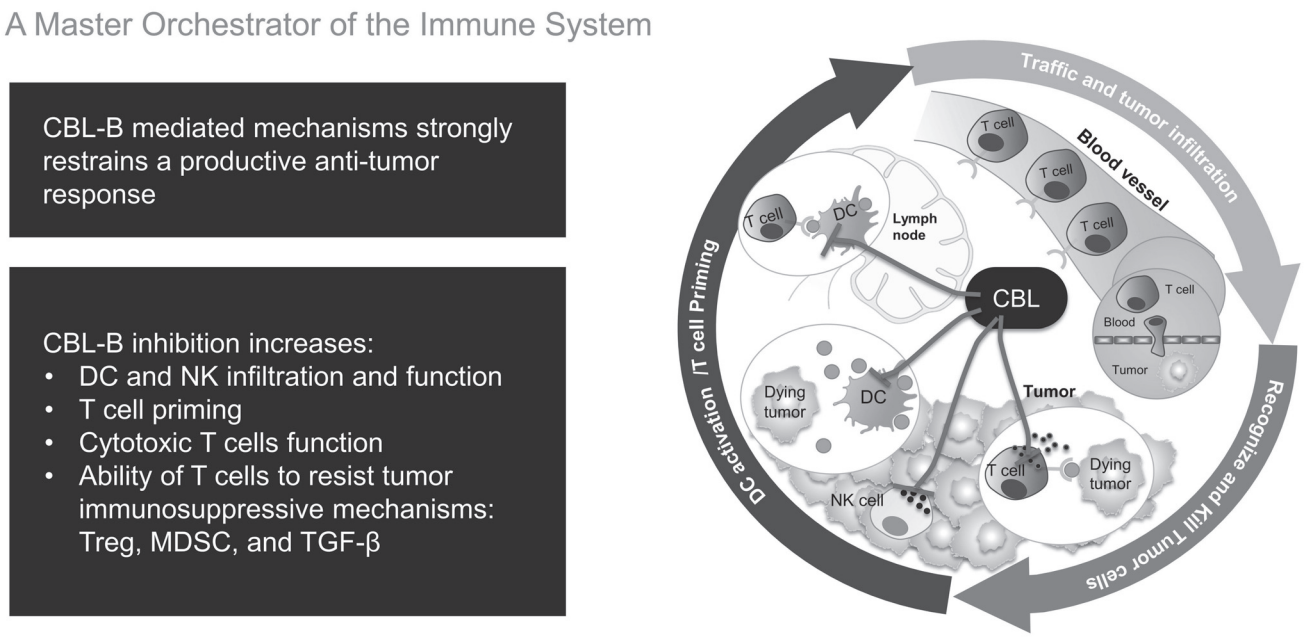
Data cutoff: 15 Sep 2023
Danilov A, et al. Blood 2023;142(Suppl 1):4463

Source: Danilov et al., ASH 2023, Poster #4463

Targeted protein elevation portfolio in clinical trials

Background on CBL-B

T cells play a key role in cell-mediated adaptive immune response. Activation, expansion and function of antigen-specific T cells is a multistep process and its outcome depends on the balance of positive and negative feedback mechanisms controlling each step. Many factors can hamper the development of an efficient anti-tumor immune response, such as insufficient expression of tumor antigens, defective antigen presentation, inhibitory molecular interactions including those effected by immune checkpoints, immune suppressive factors or suppressor cells and T-cell exhaustion.



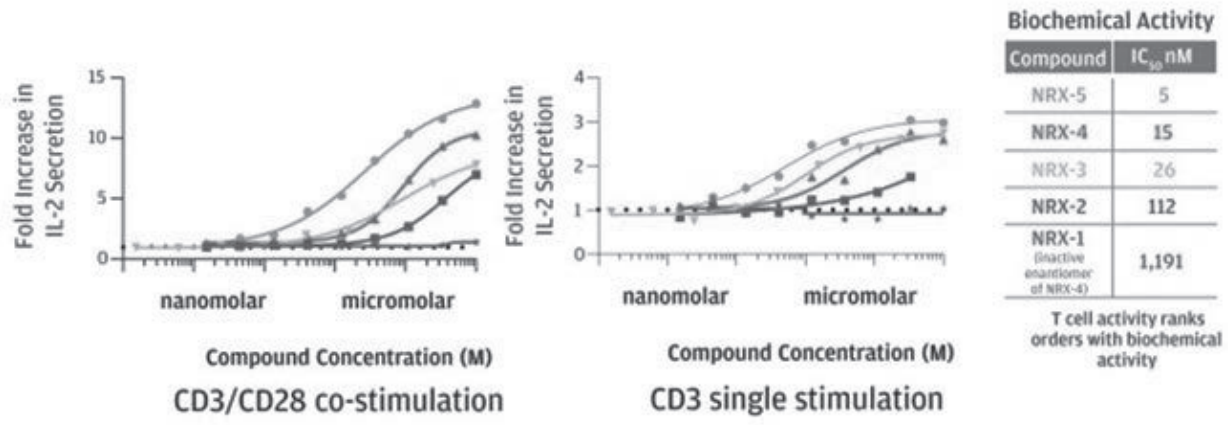
CBL-B, an E3 ligase expressed in immune cell lineages, functions as an intracellular orchestrator of the immune response by negatively regulating T-cell activation, as illustrated above. CBL-B also limits function and survival of NK cells, B cells and dendritic cells as well as promotes T-cell exhaustion, anergy, and cell death. As such CBL-B represents a pivotal pathway negatively regulating immunity. CBL-B deficient animal models demonstrate enhanced signal dependent T-cell activation and robust T-cell dependent anti-tumor immunity.

CBL-B is highly expressed in human CD4+ and CD8+ T cells, with expression tightly regulated by CD28 and CTLA-4 and other co-stimulatory and inhibitory signals. T cells typically require two signals for activation, the first provided by interaction of the T-cell receptor (TCR) with a peptide presented by an MHC molecule, and the second through co-stimulatory molecules on antigen-presenting cells. CBL-B plays an essential role in the negative regulation of T-cell activation by regulating the activity of the TCR through substrate proteins that require a costimulatory signal to mount a productive immune response upon TCR engagement. Studies have found that CBL-B deficient T cells display lower thresholds for activation by antigen recognition receptors and co-stimulatory molecules such as CD28. For example, loss of CBL-B in T cells results in T cells that can be activated upon TCR engagement without co-stimulation by CD28. Importantly, our CBL-B inhibitors do not appear to activate T cells in the absence of TCR engagement. Such CBL-B deficient T cells are resistant to T-cell anergy, a tolerance mechanism in which T cells are functionally inactivated and T-cell proliferation is greatly impaired. Notably, CBL-B deficient T cells show increased rates of proliferation as well as elevated cytokine secretion including IL-2. The increased secretion of IL-2 is of particular importance in the optimization and development of our CBL-B inhibitors, serves as a key cellular biomarker for measuring successful T-cell activation and is a known therapeutic cytokine in oncology.

We believe that our oral, small molecule CBL-B inhibitor, NX-1607, has several potential immunotherapy applications through enhancing T-cell mediated anti-tumor activity by lowering the activation threshold of T cells in a suppressive tumor microenvironment where CBL-B plays a key role in the downregulation of T cells. Importantly, NX-1607 does not appear to activate T cells in the absence of TCR engagement. We are studying NX-1607 in a Phase 1a dose escalation trial in multiple solid tumors and lymphoma. Solid tumors represent the vast majority of human cancers. Various immunotherapy strategies have been developed in order to increase the efficiency of anti-tumor immune response, including the use of antibody checkpoint inhibitors such as anti-PD-1, anti-PD-L1 and anti-CTLA-4, which block the "brakes" of immune response. These immune-stimulating antibodies have a more favorable clinical outcome than traditional treatment modalities on a growing list of tumor types. However, most patients fail to respond or experience only transient responses.

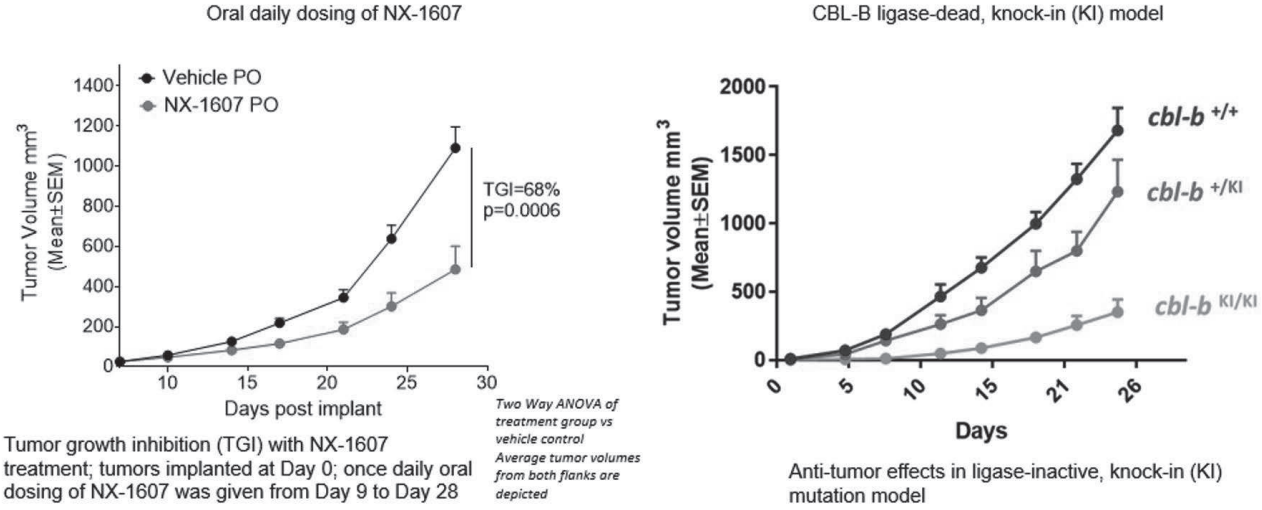
Preclinical development of CBL-B inhibitors

We have developed a series of potent small molecule inhibitors of CBL-B activity that have demonstrated biochemical activity and effects *in vitro* on human immune cells as well as in mouse tumor models. Consistent with studies cited above, CBL-B inhibitors enhanced *ex vivo* T-cell activation as measured by induction of IL-2, a key cytokine required for immune cell activation and proliferation. Induction of IL-2 secretion occurs at low nanomolar concentrations in primary human and mouse T cells stimulated with anti-CD3/anti-CD28 antibodies or anti-CD3 antibodies alone. As illustrated below, we demonstrated several fold increases in IL-2 production in tandem with increasing biochemical activity of our CBL-B inhibitors. In addition, certain of our CBL-B inhibitors reduced anergy and exhaustion in an *ex vivo* model of T-cell exhaustion using human donor T cells and further, this effect was additive to that achieved with an anti-PD-1 antibody. Based on our findings to date, we believe that CBL-B inhibitors may induce an immune cell localized IL-2 secretion that in combination with other immune activation effects will enhance anti-tumor responses. The precursor compounds shown in the graphs below led to the optimization and selection of NX-1607 as a development candidate.

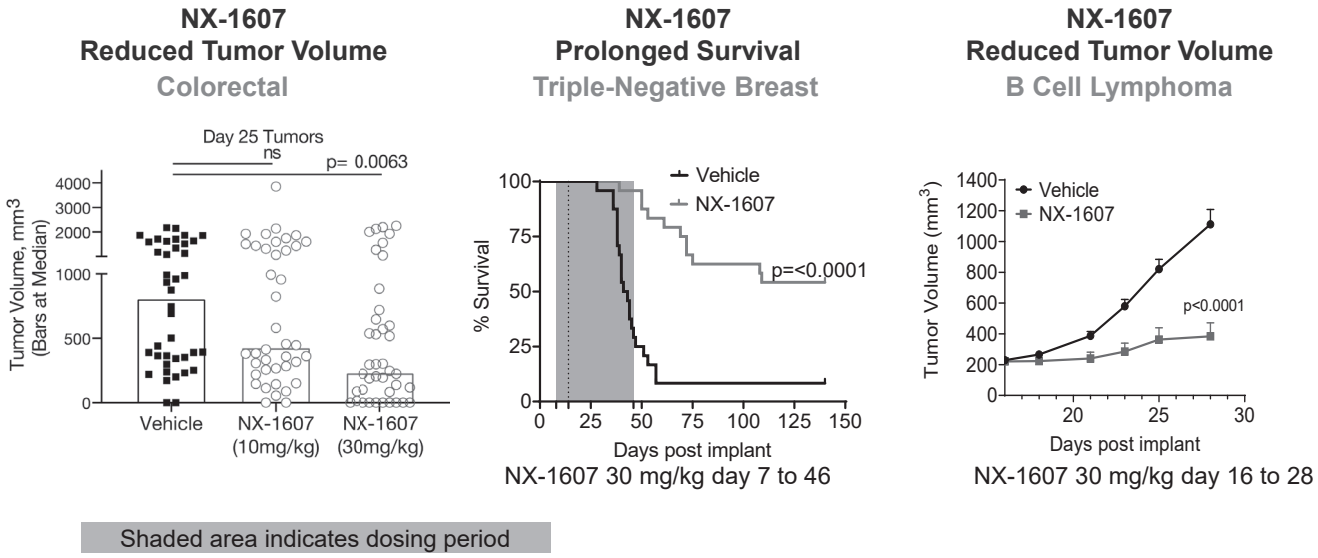


NX-1607, an oral CBL-B inhibitor for immuno-oncology

NX-1607 is an investigational, orally bioavailable, potent inhibitor of CBL-B. *In vitro* studies demonstrated that NX-1607 treatment resulted in a dose-dependent increase in T cell activation in TCR stimulated primary human T cells in the presence and, to a lesser extent, in the absence of CD28 co-stimulation, a potential advantage in a suppressive tumor microenvironment. *In vitro*, NX-1607 has been demonstrated to increase T-cell activation in primary human T cells in the absence of co-stimulation with CD3 and CD28, a potential advantage in a suppressive tumor microenvironment. *In vivo*, oral administration of NX-1607 in mice has demonstrated notable tumor growth inhibition in a tumor model as illustrated in the figure below on the left. The tumor growth inhibition with oral administration of NX-1607 recapitulates the genetic experiment in mice with a ligase-inactive version of CBL-B which also shows tumor growth inhibition as illustrated in the figure below on the right.

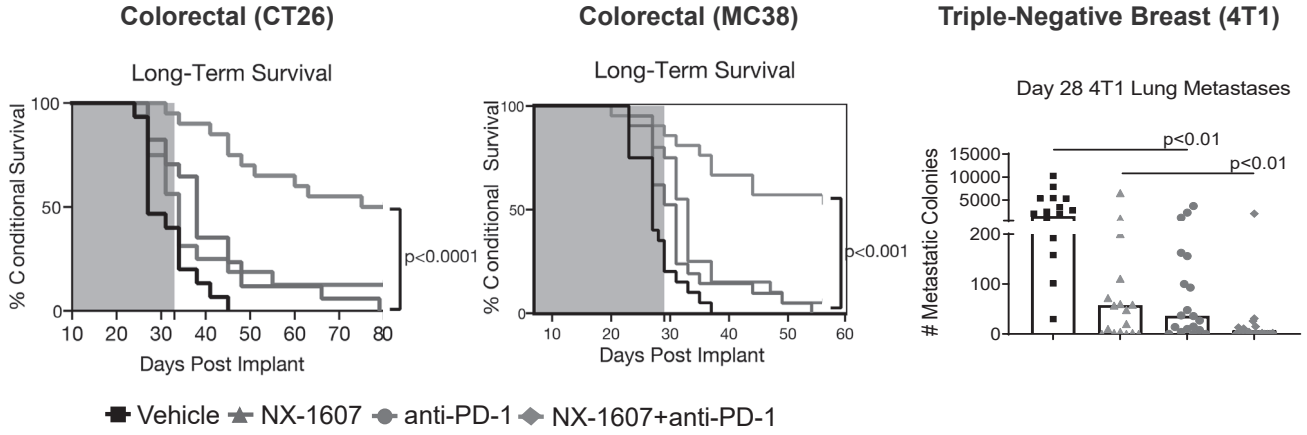


The *in vivo* effects of orally administered NX-1607 were further evaluated as a single agent in several mouse models of cancer. In the experiments shown in the figure below on the left, oral treatment with NX-1607 at a dose of 30 mg/kg (blue circles) significantly reduced the size of tumors measured at day 25 compared to vehicle treated animals (black squares) in this colorectal cancer model. In the figure below in the middle, oral treatment with NX-1607 significantly increased survival in this neoadjuvant model of metastatic triple-negative breast cancer in which treatment was initiated just prior to surgical primary tumor resection. Without further treatment, all mice in the vehicle group (black line) died by day 60 as a result of disseminated tumor metastases in the lung, liver and brain. By contrast, animals treated with NX-1607 (blue line) administered as a daily oral dose starting at day seven and continuing through day 46 demonstrated a highly significant prolongation of survival. In the figure below on the right, oral treatment with NX-1607 (blue squares) significantly reduced the size of tumors and the rate of tumor growth compared to the vehicle group (black circles) in a B-cell lymphoma model.



Shaded area indicates dosing period

The *in vivo* effects of orally administered NX-1607 were evaluated in combination with an antibody to PD-1 in several mouse models of cancer as shown in the figure below. In the left and middle panels, the combination of oral NX-1607 plus anti-PD-1 (light blue lines) demonstrated increased survival in two separate colorectal cancer models compared with animals treated with either NX-1607 alone (blue line), anti-PD-1 alone (red line) or vehicle (black line). In the panel on the right, the activity of oral NX-1607, anti-PD-1 and the combination of NX-1607 and anti-PD-1 were tested in a model of metastatic triple-negative breast cancer. Both single agent NX-1607 (blue triangles) and single agent anti-PD-1 (red circles) reduced the number of lung metastases at day 28 compared with the vehicle group (black squares), but the combination of NX-1607 and anti-PD-1 (light blue diamonds) was superior to either single agent.

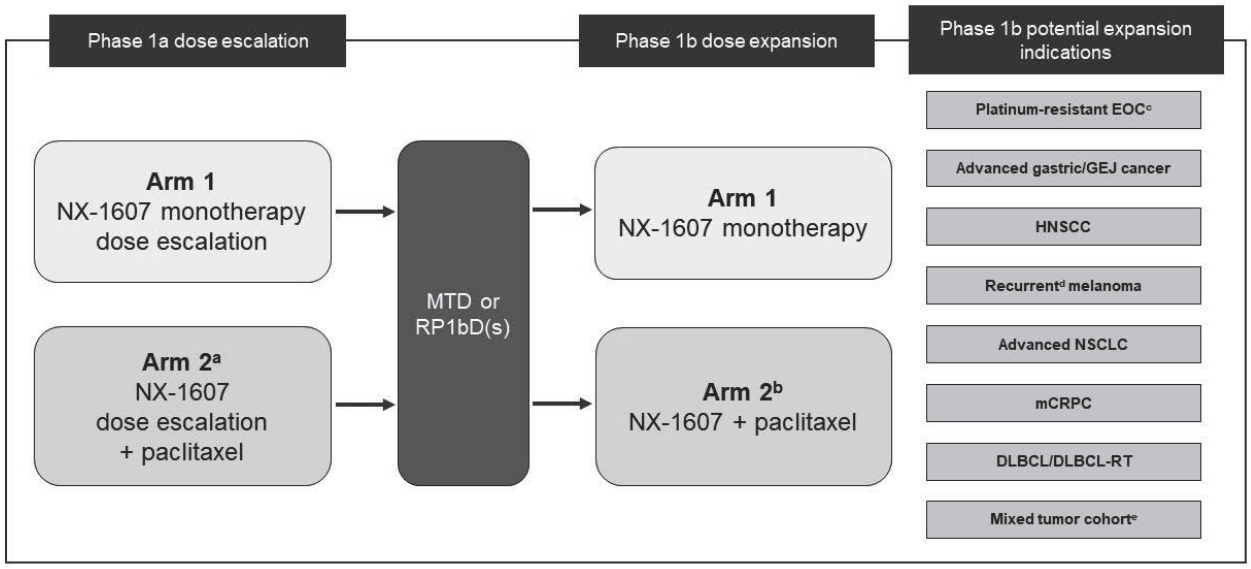


Shaded area indicates dosing period: NX-1607 (30 mg/kg, PO daily) and anti-PD-1 twice a week at 10 mg/kg dosing period

Clinical development of NX-1607

We are studying the pharmacology, safety and clinical activity of single-agent NX-1607 and the combination of NX-1607 with taxane chemotherapy in multiple solid tumor indications and lymphoma. The solid tumors selected for this initial assessment include three different immune phenotypes: checkpoint-resistant tumors, tumors with an immunosuppressive microenvironment and tumors that are poorly immunogenic. We believe that there is a scientific rationale for the role of CBL-B inhibition in each of these immune phenotypes.

As illustrated in the diagram below, we are conducting a Phase 1a/1b dose-escalation and cohort expansion study of NX-1607 in patients with relapsed or refractory solid tumors and lymphoma. We are currently enrolling patients in the Phase 1a dose escalation portion of the monotherapy trial.



[a]Starting dose for NX-1607 in Arm 2 will be ≥1 dose level below the highest previously cleared monotherapy dose level and dosing regimen. [b]Combination indications for Arm 2 may include platinum-resistant EOC, gastric cancer, HNSCC, NSCLC, TNBC, urothelial cancer, cervical cancer. [c]Including primary peritoneal and fallopian tube carcinoma. [d]Includes metastatic or unresectable disease. [e]Includes MPM, TNBC, locally advanced/metastatic urothelial cancer, cervical cancer, MSS CRC- or DLBCL/DLBCL-RT

Our DELigase platform

Our approach leverages the specificity of E3 ligases and the natural function of the UPS to regulate the cellular proteome for therapeutic effect. Development of therapies that modulate E3 ligases has been historically limited by the inherent difficulties in building biochemical and cellular assays relevant for measuring E3 ligase function, as well as by the relative lack of mechanistic understanding of this critical class of proteins. Through our focused efforts and investment over the past several years, we have developed proprietary tools, in-depth knowledge and expertise relating to E3 ligases as targets for drug discovery. In addition, we have assembled a team that has extensive experience applying DEL discovery technologies to a wide variety of proteins including targets previously considered undruggable. Together, these capabilities and insights have allowed us to develop a powerful platform technology called DELigase to identify and advance novel drug candidates that either selectively increase or decrease protein levels within the cell.

Our DELigase platform combines our proprietary DELs and E3 ligase expertise to empower efficient drug discovery. DEL technology is well suited to finding new binders for targets thought to be undruggable, which include the vast majority of proteins encoded in the human genome including E3 ligases.

DEL technology taps enormous chemical space to overcome "druggability" limits

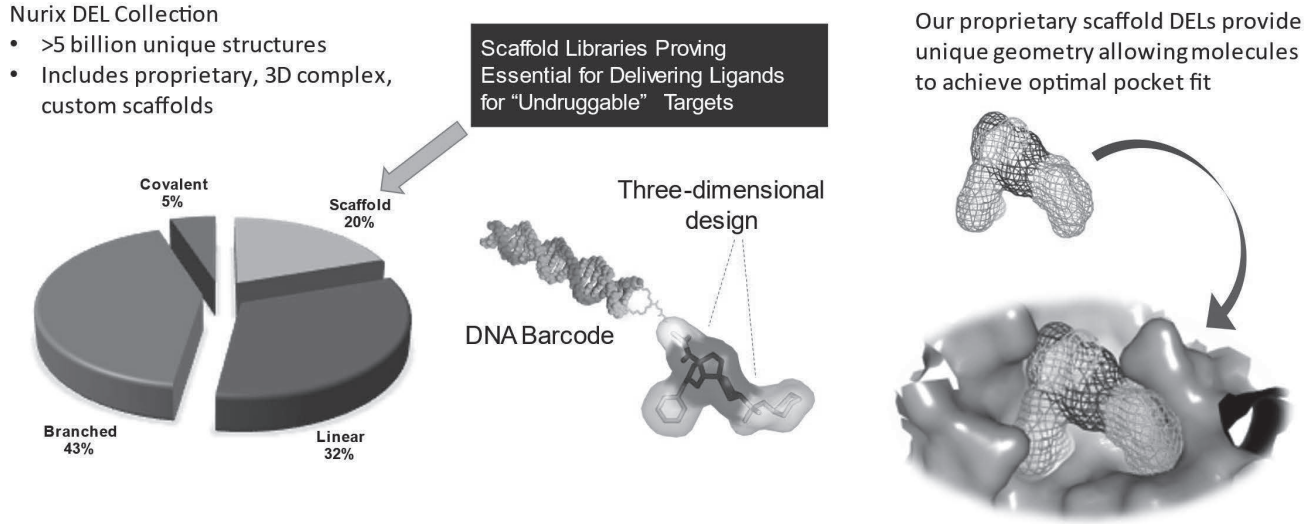
Our DEL collection comprises several billion compounds whereas typical screening collections contain less than a few million. This increased scale provides the necessary chemical diversity to identify chemical starting points for more challenging protein targets that have been considered undruggable by other approaches. DEL technology evaluates each library compound simultaneously in a single experiment, enabling a more accurate assessment of compound function. In addition, because DEL drug discovery is performed by measuring compound binding rather than biochemical activity it allows inclusion of proteins for which biochemical assays are lacking or not feasible. Further, the relative ease with which binding screens can be performed and interpreted provides sufficient flexibility to allow evaluation of structurally complicated proteins like E3 ligases, which display distinct conformations and activity states and are often part of large multi-protein complexes. Lastly, a chemical linker attaches each DEL compound to a strand of DNA, which functions as a structure barcode allowing screening hits to be easily identified. DEL's built in chemical linker is also an advantage in the context of identifying bifunctional degraders, as it allows the discovery of compounds that can effectively bind proteins when linked to a partner molecule.

Our DELigase platform was designed for E3 ligase discovery

Our integrated DELigase platform relies on proprietary DELs we have specifically engineered to identify and select binders against a diverse group of target protein classes, including some considered to be undruggable, as well as binders to E3 ligases. Key features of our DELigase platform include:

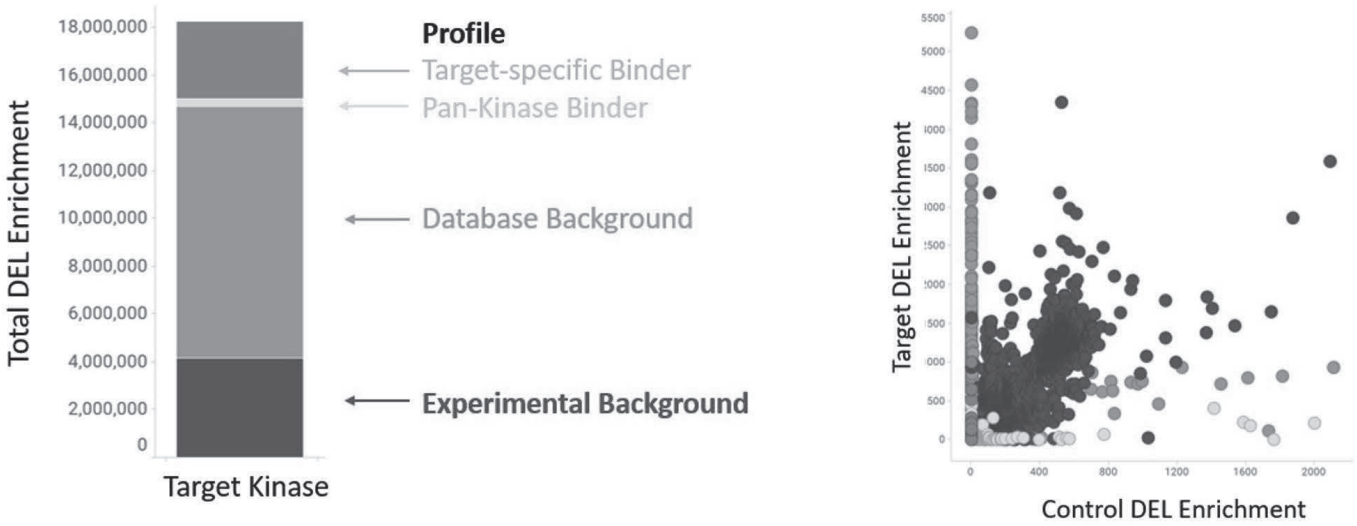
- ***Custom-synthesized DELs.*** Our custom-synthesized chemical scaffolds impart desirable, drug-like chemical properties, like solubility, into each library compound in a manner that cannot be achieved when building DEL collections solely from commercial inputs. The three-dimensional design of the proprietary scaffolds allows our library compounds to complement the surface of the target proteins, making them ideal for binding targets classically considered undruggable, such as E3 ligases. For 75% of the undruggable targets screened by us, the scaffold libraries have been the sole source of hits from our collection. Our collection of over 5 billion compounds also enables us to find diverse hits for classical targets and contains a sizable subset of covalent compounds, which have been shown as another effective way to bind E3 ligases. Covalent compounds have begun to show promise in augmenting performance of targeted protein degraders, suggesting that our covalent DELs may have additional utility for Targeted Protein Modulation.

Design of the Nurix DEL Collection



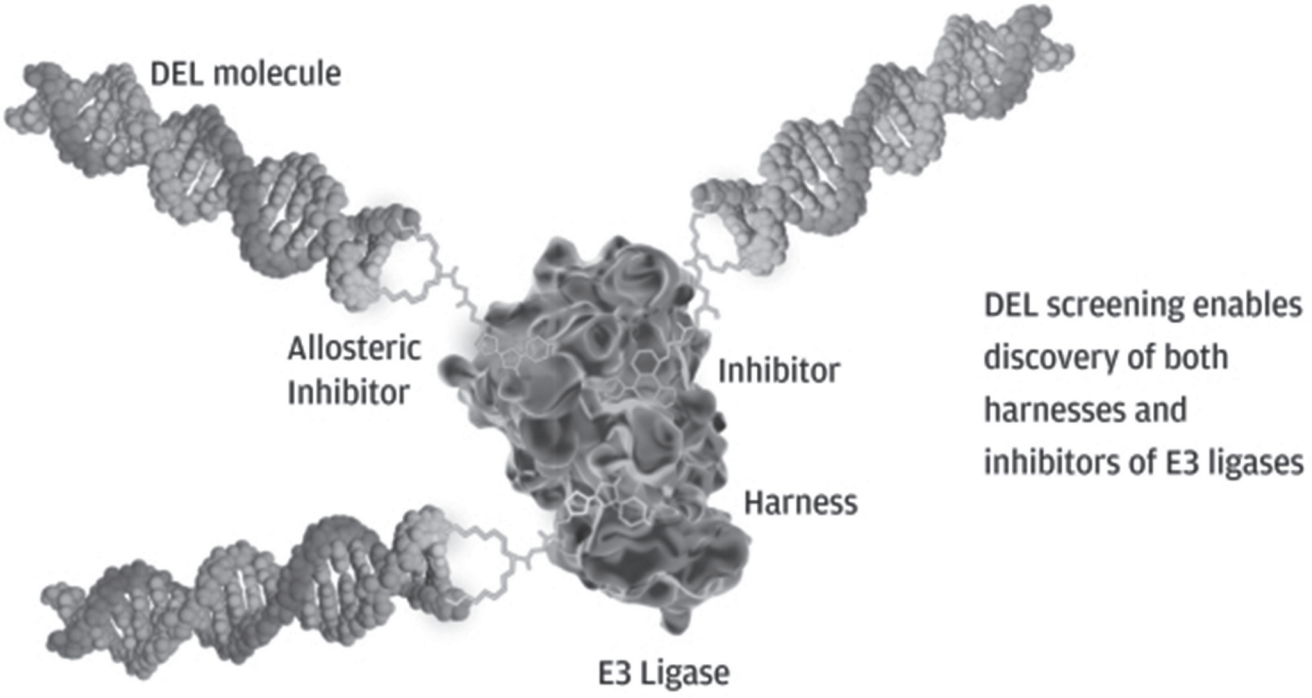
- ***Proprietary data analysis and hit confirmation technologies.*** We have built a suite of custom analytical tools for interpretation and prioritization of our DEL binder outputs, which routinely contain thousands of productive hits. By leveraging data collected from hundreds of DEL screens, we are able to rapidly eliminate background signal and reveal the most promising target-specific ligands. We have also developed machine learning and high throughput methods for nanoscale hit resynthesis and affinity selection mass spectroscopy that allow a more comprehensive and industrialized process for finding the best chemical starting points for future pipeline programs.

Leveraging the Nurix DEL Database for clear classification of enriched DEL ligands

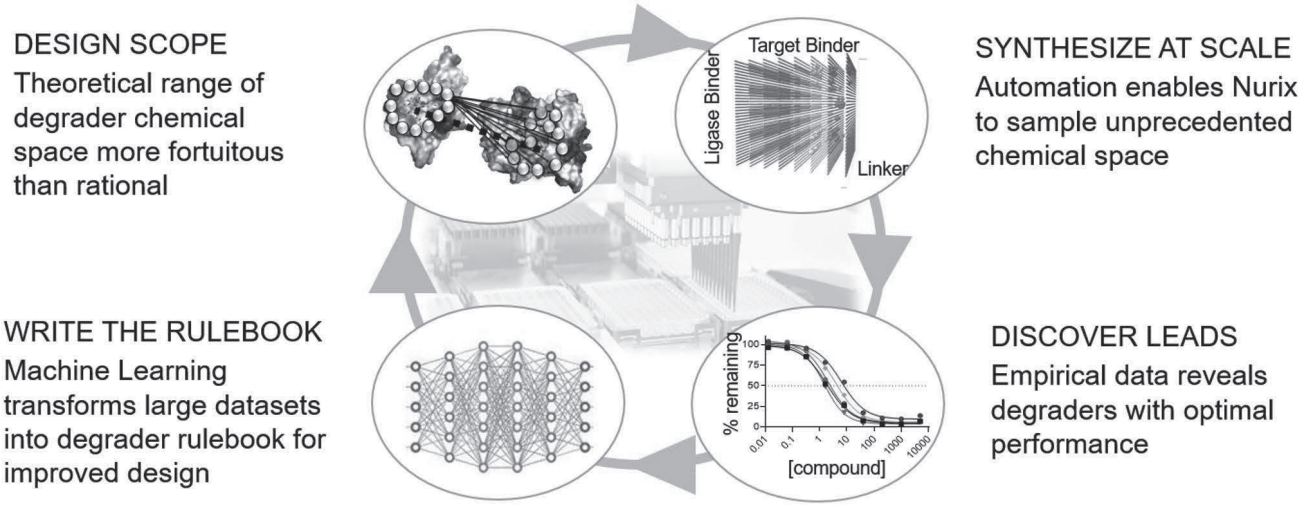


- ***Many screens, one protein target.*** E3 ligases can exist in multiple potential conformation states. Our approach uses comprehensive parallel screening campaigns to interrogate numerous states and surfaces of the target protein. An illustration of how we probe the surface of an E3 ligase by DEL screening is depicted in the graphic below.

DELs allow access to a spectrum of binders across the protein surface, some of which inhibit protein function.



- ***Rapid automated chemistry.*** Our state-of-the-art automated chemistry robotic suite allows for rapid synthesis of both binders and fully assembled degrader molecules. This automation enables us to sample unprecedented chemical space and allows for faster design test cycles which accelerates drug discovery projects.



- **Harnessing our data generation pipelines with Machine Learning.** Our investment in scalable science has created large data streams stemming from our DEL, automated chemistry, and high-throughput experimental platforms. Our internal machine learning team leverages these data in developing models to enable property prediction of our targeted degraders, to support small molecule and TPD lead optimization efforts and to enhance the data analysis and lead ID workflows of our DEL platform.

Our DELigase discovery platform enables us to address multiple therapeutic applications

We have expanded the universe of E3 ligases available for therapeutic manipulation from the two predominantly used in the field, cereblon and VHL, by screening over 60 additional E3 ligases to date. We have carefully selected these E3 ligases for use in drug discovery across our three core areas of therapeutic expertise: oncology, immuno-oncology and immune disorders. We consider the unique biological function of each ligase and the therapeutic requirements of the disease state for inhibitor programs. For ligases that direct targeted protein degradation, we take into account the biochemical specificity of the E3 ligase as well as tissue specificity of action and cellular localization of the target protein. E3 ligases that are required for cancer cell survival are also of high interest for cancer indications to reduce the risk of intrinsic resistance to degrader action. We are growing our set of E3 ligases for use in our DELigase platform tailored to our core therapeutic areas.

DELigase for E3 ligase harnesses

We apply our platform to utilize the ubiquitination function of E3 ligases for targeted protein degradation. Our DELigase platform enables us to identify binders to E3 ligases, which we refer to as harnesses, as well as binders to degradation targets. We use these molecular starting points to design compounds using a modular approach that connects an E3 ligase harness to a target protein binder with a linker. We refer to these bifunctional molecules as targeted protein degraders, which function by bringing the E3 ligase into proximity of the target protein to catalyzing its ubiquitination and degradation.

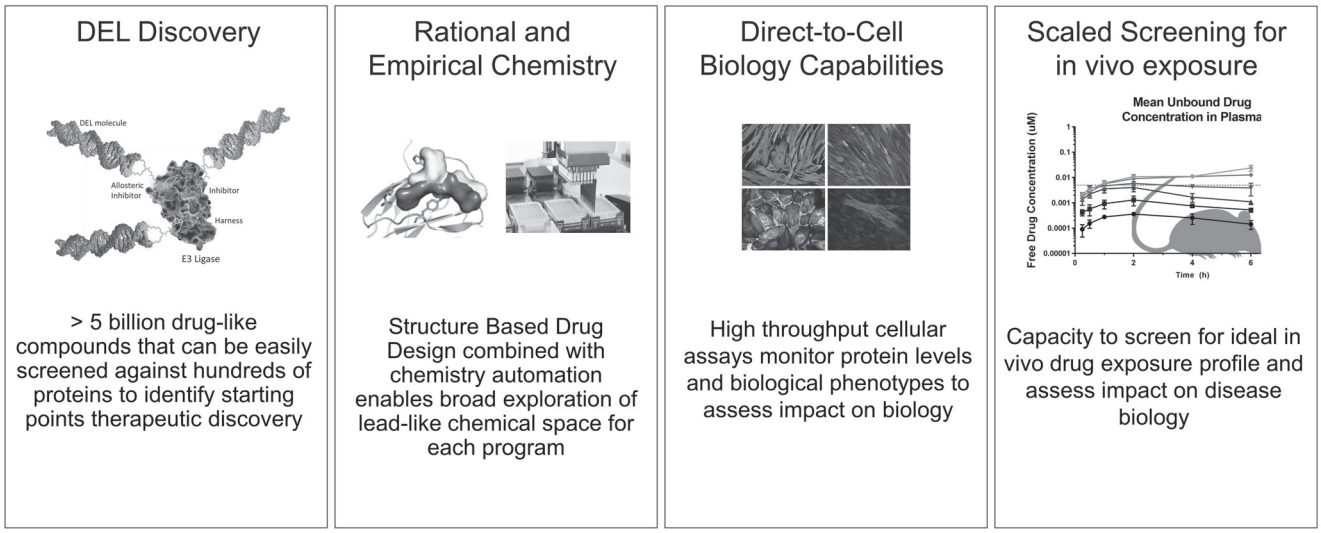
DELigase for E3 ligase inhibitors

By inhibiting the function of E3 ligases, it is possible to rapidly increase specific protein levels to control biological pathways. Increasing the levels of distinct sets of proteins could be a powerful approach to blocking pathological processes and restoring normal physiology. Our DELigase platform enables the identification of inhibitors through parallel screening of distinct E3 ligase activity states using chemical matter tailored specifically for binding to E3 ligases. Our substantial expertise in E3 ligase biochemistry and biology has allowed us to identify and develop potent inhibitors of E3 ligases that play pivotal roles in T-cell signaling and immune cell function.

Drug candidate identification and selection process

We employ a series of processes and studies from target validation to preclinical development for selection of the appropriate candidate for further development. We have invested in an integrated drug development infrastructure that enables us to perform every step of the drug discovery and early preclinical development process within our research facility. Each of our primary areas of core expertise and technology are highlighted in the below illustration.

Our integrated drug discovery and development system and core technical expertise



Collaborations and License Agreements

Gilead

In June 2019, we entered into a global strategic collaboration agreement with Gilead (as subsequently amended, the Gilead Agreement) to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with cancer and other challenging diseases using our DELigase platform to identify novel agents that utilize E3 ligases to induce degradation of five specified drug targets. In August 2019 and September 2022, we entered into the First Amendment and the Second Amendment, respectively, to the Gilead Agreement to clarify certain language of the Gilead Agreement.

Under the Gilead Agreement, Gilead has the option to license drug candidates directed to up to five targets resulting from the collaboration and is responsible for the clinical development and commercialization of drug candidates resulting from the collaboration. We retain the option to co-develop and co-promote, under a profit share structure, up to two drug candidates in the United States, provided that we may only exercise such option once per licensed product and Gilead retains the right to veto our option selection for any one drug candidate of its choice. The collaboration excludes our current internal protein degradation programs for which we retain all rights, and also excludes our future internal programs, provided that we have distinguished future programs as excluded from the scope of the collaboration. In March 2023, Gilead exercised the option to exclusively license one target (Gilead License Option Exercise), the first development candidate resulting from the Gilead Agreement. Pursuant to the Gilead Agreement, we received a license option exercise payment of $20.0 million in April 2023 for the Gilead License Option Exercise.

Over time, Gilead may elect to replace the initial drug targets with other drug targets. For drug targets that are subject to the collaboration, we are obligated to use commercially reasonable efforts to undertake a research program in accordance with a research plan agreed to by the parties and established on a target-by-target basis. We have primary responsibility under the Gilead Agreement for performing preclinical research activities (including target validation, drug discovery, identification or synthesis) pursuant to a research plan. Each party will bear its own costs in the conduct of research activities. Gilead will be responsible for any development, commercialization and manufacturing activities, unless we exercise our co-development and co-promotion option. For those programs that we exercise our option to co-develop and co-promote, we and Gilead will split U.S. development costs as well as U.S. profits and losses evenly, and we will be eligible to receive royalties on net ex-U.S. sales and reduced milestone payments.

Upon signing the Gilead Agreement, Gilead paid us an upfront payment of $45.0 million, plus $3.0 million in additional fees. In addition, from the signing of the Gilead Agreement to November 30, 2023, we received payments of $47.0 million for research milestones and additional payments and $20.0 million for a license option exercise payment. As of November 30, 2023, we are eligible to receive up to approximately $2.3 billion in total additional payments based on certain additional fees, payments and the successful completion of certain preclinical, clinical, development and sales milestones. We also are eligible to receive mid-single digit to low tens percentage tiered royalties on annual net sales from any commercial products directed to the optioned collaboration targets, subject to certain reductions and excluding sales in the United States of any products for which we exercise our option to co-develop and co-promote, for which the parties share profits and losses evenly.

Subject to earlier expiration in certain circumstances, the Gilead Agreement expires on a licensed product-by-licensed product and country-by-country basis upon the later of (1) the expiration of the last to expire patent with a valid claim covering the applicable licensed product in the applicable country, (2) the expiration of any regulatory exclusivity for the applicable licensed product in the applicable country or (3) ten years after the first commercial sale of the applicable licensed product in the applicable country covered by the Gilead Agreement, provided that the term for any profit-shared licensed product in the United States will expire upon the expiration or termination of the applicable profit-share term as set forth in an applicable profit-share agreement to be negotiated upon our exercise of our option to co-develop and co-promote such licensed product. If Gilead does not exercise an option to license a drug candidate, then the Gilead Agreement will terminate at the end of the last to expire option period.

Sanofi

In December 2019, we entered into a strategic collaboration with Genzyme Corporation, a subsidiary of Sanofi, which became effective in January 2020 (as subsequently expanded and amended, the Sanofi Agreement), to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with challenging diseases in multiple therapeutic areas using our DELigase platform to identify small molecules designed to induce degradation of three specified initial drug targets. In January 2021, as part of the existing Sanofi Agreement, Sanofi paid us $22.0 million to exercise its option to expand the number of targets in the Sanofi Agreement from three to a total of five targets.

In January 2021, we entered into the First Amendment to the Sanofi Agreement to modify the research term on all targets. In December 2021, we entered into the Second Amendment to the Sanofi Agreement to extend the substitution deadline on certain targets. In July 2022, we entered into the Third Amendment to the Sanofi Agreement to further extend the substitution deadline on certain targets. Also in July 2022, Sanofi elected to replace certain drug targets, and the substitution extended the research term of those targets by one year to 5.25 years. In August 2022 and November 2023, we entered into the Fourth Amendment and Fifth Amendment, respectively, to the Sanofi Agreement to modify the research plan for certain targets.

Under the Sanofi Agreement, Sanofi has exclusive rights and is responsible for the clinical development, commercialization and manufacture of drug candidates resulting from the collaboration while we retain the option to co-develop, co-promote and co-commercialize all drug candidates in the United States directed to up to two targets, one of which must be selected from a list of targets designated at the execution of the Sanofi Agreement or any replacement of such targets, and one of which must be selected from targets identified by Sanofi as part of their January 2021 expansion. Our right to exercise our option to co-develop, co-promote and co-commercialize a given target is dependent on our ability to demonstrate, within a given timeframe, that we have sufficient cash resources and personnel to commercialize the product. The collaboration excludes our current internal protein degradation programs for which we retain all rights, and also excludes our future internal programs, provided that we distinguished future programs as excluded from the scope of the collaboration.

For drug targets that are subject to the collaboration, we have primary responsibility for conducting preclinical research activities (including target validation, drug discovery, identification or synthesis) in accordance with the applicable research plan agreed to by the parties and established on a target-by-target basis. We are obligated to use commercially reasonable efforts to identify relevant target binders and targeted protein degraders in order to identify development candidates. Subject to certain exceptions, each party will bear its own costs in the conduct of such research. Sanofi will be responsible for any development and commercialization activities unless we exercise our co-development and co-promotion option. For those programs that we exercise our option to co-develop, co-promote and co-commercialize, we will be responsible for a portion of the U.S. development costs, and the parties will split U.S. profits and losses evenly, and we will be eligible to receive royalties on ex-U.S. net sales and reduced milestone payments on such optioned products.

Upon signing the Sanofi Agreement, Sanofi paid us an upfront payment of $55.0 million. Subsequently in January 2021, Sanofi paid us an additional $22.0 million to exercise its option to expand the number of targets beyond the initial targets included in the collaboration. In addition, from the signing of the Sanofi Agreement to November 30, 2023, we received payments of $7.0 million for research milestones. Additionally, we achieved two research milestones in November 2023 and received payments totaling $4.0 million in January 2024 as a result. As of November 30, 2023, we are eligible to receive up to approximately $2.5 billion in total additional payments based on certain additional fees, payments and the successful completion of certain research development, regulatory and sales milestones, as well as mid-single digit to low teen percentage tiered royalties on annual net sales of any commercial products that may result from the collaboration, subject to certain reductions and excluding sales in the United States of any products for which we exercise our option to co-develop and co-promote, for which the parties share profits and losses evenly.

Subject to earlier expiration in certain circumstances, the Sanofi Agreement expires on a licensed product-by-licensed product or profit-shared licensed product-by-profit-shared licensed product basis and country-by-country basis upon on the later of (1) the expiration of the last-to-expire patent with a valid claim covering the applicable licensed product in the applicable country, (2) the expiration of any regulatory exclusivity for the applicable licensed product in the applicable country or (3) ten years after the first commercial sale of the applicable licensed product in the applicable country covered by the Sanofi Agreement.

Pfizer

In September 2023, we entered into a strategic collaboration with Seagen Inc. (now a part of Pfizer Inc.) (the Pfizer Agreement) to develop a suite of targeted protein degraders against multiple targets nominated by Pfizer that are suitable for antibody conjugation. Pfizer will be responsible for conjugating these degraders to antibodies to make Degrader-Antibody Conjugates (DACs), a new class of medicines for use in cancer treatment, and advancing these DAC drug candidates through preclinical and clinical development and commercialization.

Under the Pfizer Agreement, Pfizer has the option to obtain exclusive licenses to develop and commercialize certain degraders, while we retain an option for U.S. profit sharing and co-promotion on two products arising from the collaboration. The collaboration excludes our current internal protein degradation programs for which we retain all rights, and also excludes our future internal programs, provided that we have distinguished future programs as excluded from the scope of the collaboration.

For the targets nominated by Pfizer under the collaboration, we shall use commercially reasonable efforts to identify, synthesize, characterize and deliver targeted protein degraders that selectively bind to and degrade such targets. Development of licensed degraders, with the exception of licensed products for which we exercised our profit-share options, will be at Pfizer's sole cost and expense. For the profit-share products, the parties will share net profits and net losses and global development costs, and we will be eligible to receive royalty and milestone payments on such optioned products.

Under the terms of the Pfizer Agreement, we received an upfront payment of $60.0 million. We are eligible to receive up to approximately $3.4 billion in contingent payments based on specified research, development, regulatory and commercial milestones across multiple programs, and are eligible for mid-single to low double digit percentage tiered royalties on future sales.

Subject to the exceptions described in the Pfizer Agreement, the Pfizer Agreement expires upon the first to occur of (1) the expiration of the last-to-expire option exercise period under the Pfizer Agreement if no such option has been exercised prior to such expiration and (2) the expiration of the last-to-expire royalty term under the Pfizer Agreement.

Manufacturing and Supply

We do not own or operate, and currently have no plans to establish, any facilities for product manufacturing, packaging, storage and distribution, or testing. We rely on and expect to continue to rely on contract manufacturing organizations (CMOs) for both drug substance and finished drug product. We have personnel or engaged consultants with extensive technical, manufacturing, analytical and quality experience and good project management to oversee contract manufacturing and testing activities. We have engaged third-party manufacturers to supply the drug substances for NX-5948, NX-2127 and NX-1607 and to develop and manufacture finished drug products for use in our clinical trials. Should any of these manufacturers become unavailable to us for any reason, we believe that there are a number of potential replacements, although we may incur some delay in identifying and qualifying such replacements.

All of our drug candidates are organic compounds of low molecular weight, generally called small molecules, but which are larger than traditional small molecule therapeutics. We have selected these compounds not only on the basis that they could have potentially favorable efficacy and safety profiles, but also for their ease of synthesis and the reasonable cost of their starting materials. In particular, our lead drug candidates are manufactured using reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities.

Competition

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, development experience, scientific knowledge and intellectual property portfolio provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing, and commercialization. Not only must we compete with other companies that are focused on protein modulation, but any drug candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Moreover, our industry is characterized by the existence of large numbers of patents and frequent allegations of patent infringement.

Our focus is the discovery and development of innovative small molecules and antibody therapies designed to modulate protein levels, including targeted protein degraders. Other companies that primarily focus on developing small molecules that degrade target proteins include, but are not limited to, Arvinas, Inc., BioTheryX, Inc., C4 Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics Inc., Kymera Therapeutics, Inc. and Monte Rosa Therapeutics. Drug candidates from our BTK degrader and CBL-B inhibitor programs may face competition from drugs with similar mechanisms of action. We are aware of clinical-staged BTK degraders currently in development by AbbVie Inc., Accutar Biotechnology, Inc., BeiGene, Ltd, Haisco Pharmaceutical Group Co., Ltd. and Ubix Therapeutics, Inc. In addition, we are aware of a clinical-staged CBL-B inhibitor currently in development by HotSpot Therapeutics, Inc.

Our lead drug candidates target hematologic cancers and immune-mediated diseases. The most common methods of treating patients in oncologic indications are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy. There are a variety of available drug therapies marketed for cancer, including hematologic cancers. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed drugs, there are also several drug candidates in late-stage clinical development for the treatment of oncologic indications and immune-mediated diseases. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our drug candidates for which we obtain market approval.

If any of our drug candidates are approved for the indications for which we currently are conducting clinical trials or for which we expect to conduct clinical trials, they will compete with the foregoing therapies and the currently marketed drugs and potentially any drugs in development. It is also possible that we will face competition from other biologic or pharmaceutical approaches as well as from other types of therapies.

Many of our current or potential competitors, either alone or with strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our drug candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

The key competitive factors affecting the success of all our programs, if approved, are likely to be their efficacy, safety, convenience, price, level of generic competition and availability of reimbursement.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, platforms, drug candidates and improvements thereof that are commercially important to our business, including obtaining, maintaining and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among, other methods, pursuing patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and drug candidates that are important to the development and implementation of our business. Our patent portfolio is intended to cover, but is not limited to, our technology platforms, drug candidates and components thereof and their methods of use, and any other inventions that are commercially important to our business.

We also rely on trade secret protection of our confidential information and know-how relating to our proprietary technology, platforms and drug candidates and continuing innovation to develop, strengthen and maintain our position in our DELigase platform and drug candidates. Trade secrets are difficult to protect and provide us with only limited protection. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned or controlled by third parties; to defend and enforce our proprietary rights, including our patent applications; to defend against challenges and assertions by third parties of their purported intellectual property rights; and to operate without infringement of valid and enforceable patents and other proprietary rights of third parties. For risks related to our intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property.”

We believe that we have a strong global intellectual property position and substantial know how and trade secrets relating to our DELigase platform and drug candidates. As of December 31, 2023, we have five U.S. patents, 22 U.S. patent applications, one foreign patent and 103 foreign applications that we own, and one U.S. patent, four pending U.S. patent applications and 26 foreign patent applications that we co-own with Gilead. The expected expirations for issued patents and patents that may issue from pending applications covering our clinical candidates are between the years 2039 and 2042 for NX-5948 and NX-2127; and between 2040 and 2043 for NX-1607.

The term of individual patents depends upon the laws of the countries in which they are obtained. In most countries in which we file, including the United States, the patent term is 20 years from the earliest date of filing of a non-provisional patent application in the applicable country. However, the patent term of U.S. patents may, in certain cases, be adjusted for administrative delays by the United States Patent and Trademark Office (USPTO) in examining and granting a patent or may be shortened if a patent is terminally disclaimed over an earlier filed patent. In addition, the term of a patent may be extended as compensation for the patent term lost during the FDA regulatory review process. For example, for drugs that are regulated by the FDA under the Hatch-Waxman Act, it is permitted to extend the term of a patent that covers such drug for up to five years beyond the normal expiration date of the patent. For more information on patent term extensions, see “Business—Government Regulation—The Hatch-Waxman Act—Patent term extension.” In the future, if and when our pharmaceutical drug candidates receive FDA approval, we expect to apply for patent term extensions on patents, if issued, covering those drug candidates. We intend to seek patent term extensions to any of our patents, if issued, in any jurisdiction where these are available; however, there is no guarantee that the applicable authorities, including the USPTO and FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

The actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

We also rely on trade secret protection for our know-how, confidential and proprietary information and continuing technological innovation to develop and maintain our competitive position. We seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our confidential and proprietary information as trade secrets, including through contractual means with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors, competitors or other third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements under the commencement of employment or consulting relationships with us. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. To the extent that our employees, contractors, consultants, collaborators and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in relation to the resulting know-how or inventions. For more information, please see the sections titled "Risk Factors—Risks Related to Our Intellectual Property" and "Risk Factors—Risks Related to Regulatory Approval and Marketing of Our Drug Candidates."

Government Regulation

The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

FDA approval process

In the United States, biological and pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act (FDCA), Public Health Service Act (PHSA), and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, quality control, packaging, storage, recordkeeping, approval, labeling, promotion, advertising and marketing, distribution, post-approval monitoring and reporting, sampling, tracking and tracing and import and export of biological and pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications (NDAs) or biologics licensure applications (BLAs), withdrawal of an approval, imposition of a clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal investigations and penalties brought by the FDA and the Department of Justice (DOJ) or other governmental entities.

Biological or pharmaceutical product development for a new product or certain changes to an approved or licensed product in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an investigational new drug application (IND) which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of a drug, or the safety, purity, or potency of a biological product, for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval and licensure requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as *in vitro* and animal trials to assess the characteristics and potential safety and efficacy of the product for initial testing in humans and to establish a rationale for therapeutic use. The conduct of the preclinical tests must comply with federal regulations and requirements, including Good Laboratory Practices (GLPs). The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

An IND is an exemption from the FDCA that allows an unapproved new drug or biological product to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biological product that is not the subject of an approved NDA or BLA. In support of a request for an IND, a sponsor must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. The sponsor may be a company seeking to develop the drug or biological product or, as in the case of an investigator-initiated trial, the sponsor may be an investigator who is conducting the trial. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational new drug or biological product to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice (GCP), which is an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time, as a clinical hold or partial clinical hold, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol, or part of a protocol, is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval or licensure. Specifically, the FDA has promulgated regulations governing the acceptance of data from foreign clinical trials not conducted under an IND, establishing that such data from studies will be accepted as support for an IND or application for marketing approval if the study was conducted in accordance with GCP, including review and approval by an independent ethics committee and use of proper procedures for obtaining informed consent from subjects, and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems such inspection necessary. The GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies. If a marketing application is based solely on foreign clinical data, the FDA requires that the foreign data be applicable to the U.S. population and U.S. medical practice; the studies must have been performed by clinical investigators of recognized competence; and the FDA must be able to validate the data through an onsite inspection or other appropriate means, if the FDA deems such an inspection to be necessary.

The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board (IRB) representing each institution participating in the clinical trial. The IRB must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health (NIH) for public dissemination on its ClinicalTrials.gov website. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial.

Clinical trials to support NDAs or BLAs for marketing approval or licensure are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the drug or biological product is introduced into healthy human subjects or in certain indications such as cancer, into patients with the target disease or condition. The drug is tested in Phase 1 to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence of effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness or potency of the drug or biological product for a particular indication, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a product candidate demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are conducted. In a Phase 3 trial, the drug or biological product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy or potency and purity, and safety, of the product for approval or licensure, to establish the overall risk benefit profile of the product, and to provide adequate information for the labeling of the product.

In most cases the FDA requires at least two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy or potency of the drug. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances, such as where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible. Post-approval studies, or Phase 4 trials, are often required following initial approval and are intended to gain additional experience and data from treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials conducted under an IND must be submitted at least annually to the FDA and more frequently if serious adverse effects occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug or biological product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biological product has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted in an NDA or BLA.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug or biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with current good manufacturing practices (cGMP) requirements. The manufacturing process must be capable of consistently producing quality batches of the drug or biological product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final drug. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug or biological product candidate does not undergo unacceptable deterioration over its shelf life.

After completion of the required clinical testing, an NDA or BLA is prepared and submitted to the FDA. FDA approval of the NDA or BLA is required before marketing of the product may begin in the United States. The application must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an application is substantial. The submission of most NDAs or BLAs is additionally subject to a substantial application user fee, currently set for fiscal year 2023 at $3,242,026 for applications requiring clinical data, and $1,621,013 for applications not requiring clinical data, and the manufacturer and sponsor under an approved NDA or BLA are also subject to annual program fees, currently set for fiscal year 2023 at $393,933 for each prescription product. These fees are typically increased annually. Sponsors of applications for drugs granted Orphan Drug Designation are exempt from these user fees.

The FDA has 60 days from its receipt of an NDA or BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs and BLAs to encourage timeliness. The FDA intends to review applications for standard review product candidates within ten months of the 60-day filing date; and applications for priority review product candidates within six months. Priority review can be applied to drugs or biological products that the FDA determines treat a serious condition, and if approved, would offer a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA is required to refer an application for a novel drug or biological product to an advisory committee for review, evaluation and a recommendation as to whether the application should be approved, or otherwise explain why such referral was not made. An advisory committee is typically a panel that includes clinicians and other experts. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug or biological product is manufactured. The FDA will not approve the application unless compliance with cGMPs is satisfactory and the application contains data that provide substantial evidence that the drug is safe and effective, or the biological product is safe, pure and potent, in the indication studied.

After the FDA evaluates the NDA or BLA and accompanying information and the manufacturing facilities, it issues either an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA or BLA, the FDA will issue an approval letter. The FDA intends to review such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval or licensure.

An approval letter authorizes commercial marketing of the drug or biological product with specific prescribing information for specific indications. As a condition of approval or licensure, the FDA may require a risk evaluation and mitigation strategy (REMS) to help ensure that the benefits of the drug or biological product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug or biological product. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

If the FDA approves or licenses a drug or biological product, it may limit the approved indications for use of the product; require that contraindications, warnings or precautions be included in the product labeling; require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval or licensure; require testing and surveillance programs to monitor the product after commercialization; or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or BLA, or an NDA or BLA supplement before the change can be implemented. An NDA or BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA and BLA supplements as it does in reviewing NDAs and BLAs.

Approval of medicines in the European Union (EU)

In the EU, companies can apply for marketing authorizations under the centralized procedure to the European Medicines Agency (EMA) or they can submit their application to the competent authorities in the European Economic Area (EEA) Member States via the decentralized procedure, the national procedure, or the mutual recognition procedure. The centralized procedure is mandatory for certain medicines, such as those produced by biotechnology, orphan medicinal products, advanced therapy medicinal products and those containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, autoimmune and other immune dysfunctions, viral diseases, or diabetes. The centralized procedure remains optional for medicines containing a new active substance, or which are a significant therapeutic, scientific, or technical innovation or whose authorization would be in the interest of public health. Therefore the centralized procedure remains mandatory for the majority of biological medicinal products.

The marketing authorization granted under the centralized procedure by the EMA will be valid in all EEA Member States. The maximum timeframe for the evaluation of a marketing authorization application by the EMA is 210 days but can be extended should additional information be required by the EMA's Committee for Medicinal Products for Human Use (CHMP). The European Commission makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's positive opinion. An accelerated assessment procedure of 150 days may be implemented for drugs considered to be of major public health interest.

Under the mutual recognition procedure, the national marketing authorization holder may submit an application to other EEA Member States. The Member States involved must decide whether to recognize the approval within 90 days of receiving the application. If a Member State does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding.

Since the UK has left the EU, Great Britain is no longer covered by centralized marketing authorizations. This is not the case for Northern Ireland as under the Northern Ireland Protocol, centralized marketing authorizations continue to be recognized in Northern Ireland. Medicines with existing centralized marketing authorizations were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare Products Regulatory Agency (MHRA), the UK medicines regulator, can rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application is, however, still required. The UK government reached a new agreement with the EU, the "Windsor Framework," which aims to replace the Northern Ireland protocol. According to the Windsor Framework, medicinal products intended for the UK market including Northern Ireland will be authorized by the MHRA and will bear a "UK only" label. This means that medicinal products placed on the market in Northern Ireland will no longer need to be compliant with EU law. These new measures will be implemented beginning January 1, 2025. The MHRA has ceased to participate in the assessment of any centralized procedures since January 1, 2021. Since then, the MHRA has launched the Innovative Licensing and Access Pathway (ILAP), a new accelerated assessment procedure for marketing authorization applications that enables companies to enter the UK market faster. On January 1, 2024, the MHRA launched an International Recognition Procedure for Great Britain (England, Scotland and Wales) marketing authorization applications whereby the MHRA will, when considering such applications, recognize the approval of medicines by trusted reference regulators in Australia, Canada, Switzerland, Singapore, Japan, United States and EU following its own abbreviated assessment.

Clinical trials regulation and data sharing in the EU

In the EU, a Clinical Trial Application (CTA) must be submitted for each clinical trial to each Member State's national competent authority (NCA) and ethics approval must be sought from an independent Ethics Committee. Once the CTA is approved in accordance with a particular Member State's requirements, the clinical trial may proceed. Under the EU Clinical Trials Regulation 536/2014, which has been in effect since January 31, 2022 replacing the EU Clinical Trials Directive 2001/20/EC, suspected unexpected serious adverse reactions to the drug being trialed occurring during the clinical trial must be reported to the NCA and the Ethics Committee of the Member State where they occurred.

In the EU, Transparency Regulation No 1049/ 2001, EMA Policy 0043, EMA Policy 0070, as well as the Clinical Trials Regulation No 536/2014 set out the obligation for sponsors to make publicly available certain information stemming from clinical studies, whether proactively or in response to third party requests. Interested parties based in the EU may submit a request to the EMA to access information included in the marketing authorization application for authorized medicinal products. Commercially confidential information and protected personal data, however, may not be accessed.

On May 3, 2022, the European Commission published a proposal for a regulation on the European Health Data Space (EHDS), which aims to further enable exchange of electronic health data both for primary use (among national EU healthcare systems for patient care) and secondary use (among private companies and regulators to enable scientific research). Whilst the regulation is currently under discussions among the EU legislators, the text is expected to be finalized by the end of 2023 and for the EHDS to become reality in 2025. This will impose new obligations, but also create opportunities, for entities engaged in health-related research to share and access health data on a scale much larger than what is foreseen under current applicable transparency provisions.

Regulatory framework in the UK following Brexit

The UK officially left the EU on January 31, 2020. A transition period during which EU law remained applicable to the UK began on February 1, 2020 and ended on December 31, 2020. The EU regulatory framework for medicinal products in place before the end of the transition period has been preserved in UK domestic legislation as "retained EU law" but the UK may diverge from EU law in the future should it wish to do so. Pursuant to the Northern Ireland Protocol, the EU pharmaceutical legal framework acquis continues to apply in Northern Ireland and medicines can only be placed in the Northern Ireland market if they comply with EU law. The UK government reached a new agreement with the EU, the "Windsor Framework," which aims to replace the Northern Ireland protocol. According to the Windsor Framework, medicinal products intended for the UK market including Northern Ireland will be authorized by the MHRA and will bear a "UK only" label. This means that medicinal products placed on the market in Northern Ireland will no longer need to be compliant with EU law. These new measures will be implemented beginning January 1, 2025.

Expedited approval pathways

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as Fast Track designation, Breakthrough Therapy designation and Priority Review designation. In addition, Accelerated Approval offers the potential for approval based on a surrogate or intermediate clinical endpoint. In May 2014, the FDA published a final Guidance for Industry titled "Expedited Programs for Serious Conditions Drugs and Biologics," which provides guidance on the FDA programs that are intended to facilitate and expedite development and review of new drug or biological product candidates as well as threshold criteria generally applicable to concluding that a product candidate is a candidate for these expedited development and review programs.

The FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life threatening disease or condition, and nonclinical or clinical data demonstrate the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's review clock for a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

A product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing available therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross disciplinary project lead for the review team; rolling review; and taking other steps to design the clinical trials in an efficient manner.

Accelerated Approval Pathway

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

For the purposes of Accelerated Approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug or biological product, such as an effect on IMM. The FDA has limited experience with Accelerated Approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support Accelerated Approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug or biological product.

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

The Accelerated Approval Pathway is contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a drug or biological product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug or biological product from the market on an expedited basis. In addition, all promotional materials for drugs and biological products approved under accelerated regulations are subject to prior review by the FDA.

The EU and UK operate accelerated evaluation and assessment schemes, which include, at EU level, PRIME (PRIority MEdicines) scheme and, at UK level, the Early Access to Medicines Scheme (EAMS), which may be granted in exceptional cases, often when there is unmet medical need for a life-threatening or serious debilitating condition and existing data show a positive benefit/risk balance that means the medicinal product is of a major public health interest. The CHMP of the EMA or the MHRA (or other national competent authority) will make this determination on a case-by-case basis and subject to meeting eligibility criteria. Accelerated assessment takes place within 150 days. Other regulatory facilitations for these pathways include additional scientific advice at key development milestones and frequent guidance and discussions throughout the approval process. In the UK, the MHRA has launched the Innovative Licensing and Access Pathway (ILAP), a new accelerated assessment procedure for marketing authorization applications that enables companies to enter the UK market faster, available since January 1, 2021. On January 1, 2024, the MHRA launched an International Recognition Procedure for Great Britain (England, Scotland and Wales) marketing authorization applications whereby the MHRA will, when considering such applications, recognize the approval of medicines by trusted reference regulators in Australia, Canada, Switzerland, Singapore, Japan, United States and EU following its own abbreviated assessment.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant Orphan Drug Designation to drugs or biological products intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan Drug Designation must be requested before submitting an NDA. After the FDA grants Orphan Drug Designation, the name of the drug or biological product and its potential orphan-designated 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.

The first NDA or BLA applicant to receive FDA approval for a particular drug or biological product to treat a particular disease with FDA Orphan Drug Designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug or biological product for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biological product for the same disease or condition, or the same drug or biological product for a different disease or condition. Among the other benefits of Orphan Drug Designation are tax credits for certain research and an exemption from the NDA or BLA application user fee.

A designated orphan drug or biological product may not receive orphan drug exclusivity if it is licensed for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be rescinded 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 the EU and UK, under Regulation (EC) 141/2000 and the UK Human Medicines Regulations 2012 SI 2012 No. 1916 (as amended), respectively, medicinal products may be granted an orphan drug designation if they are used to treat or prevent life-threatening or chronically debilitating conditions that affect no more than five in 10,000 people in the EU/UK and for which there is no satisfactory method of diagnosis, prevention or treatment when the application is made, or when the medicinal product is of significant benefit to those affected by the condition. In addition, orphan drug designation can be granted to drugs used to treat or prevent life-threatening or chronically debilitating conditions which, for economic reasons, would be unlikely to be developed without incentives.

The application for orphan designation must be submitted to and approved by the EMA in respect of the EU or to the MHRA for Great Britain before an application is made for marketing authorization for the product. Medicinal products which benefit from orphan status, which they successfully maintain post-grant of the marketing authorization, can benefit from up to ten years of market exclusivity in respect of the approved indication. This prevents regulatory authorities in the EU or Great Britain, as the case may be, from granting marketing authorizations for similar medicinal products for the same therapeutic indication, unless another applicant can show that the similar medicinal product in question is safer, more effective or clinically superior to the orphan-designated product or if the marketing authorization holder consents to the second orphan medicinal product application, or where the marketing authorization holder cannot supply the needs of the market.

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 the maintenance of market exclusivity. Conversely, the 10-year exclusivity period can be further extended by two years, when pediatric studies are conducted in accordance with an agreed pediatric investigation plan (PIP) and in completion of all the legal requirements.

It is noted that the general pharmaceutical legislative framework, as well as the framework applicable to orphan and pediatric medicinal products in the EU, is under review. On April 26, 2023, the European Commission adopted a proposal for a new Regulation set to replace Regulation (EC) No 726/2004 and a new Directive to replace Directive 2001/83 on the Community Code relating to medicinal products for human use. If made into law, this proposal will revise the existing general pharmaceutical legislation and may reduce applicable regulatory exclusivities which will significantly affect all medicinal products that will be authorized after the legislative changes have taken effect.

Post-approval requirements

Drugs and biological products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review, through the applicant's submission of a supplemental application, and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug and biological product manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

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

- Restrictions on the marketing or manufacturing of the product, including total or partial suspension of production, complete withdrawal of the product from the market or product recalls;
- Fines, untitled or warning letters or holds on post-approval clinical trials;
- Refusal of the FDA to approve pending NDAs, BLAs or supplements to approved NDAs or BLAs, or suspension or revocation of product license approvals;

- Product seizure or detention, or refusal to permit the import or export of products; or
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs and biological products may be promoted only for the approved indications and consistently with the provisions of the approved labeling. 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.

In addition, the distribution of prescription drug and biological products is subject to the Prescription Drug Marketing Act (PDMA) which regulates the distribution of drugs, biological products and drug or biological product samples at the federal level, and sets minimum standards for the registration and regulation of drug and biological product distributors by the states. Both the PDMA and state laws limit the distribution of prescription drug and biological product samples and impose requirements to ensure accountability in distribution.

Many jurisdictions, including the EU and the UK, require each marketing authorization holder, national competent authority and the EMA to operate a pharmacovigilance system to ensure that the safety of all medicines is monitored throughout the lifetime of a medicinal product. The overall EU pharmacovigilance system operates through cooperation between the EU Member States, EMA and the European Commission. Applicable obligations extend to all activities consisting of procuring, holding, supplying or exporting medicinal products to the public and may therefore be incumbent upon importers, distributors and other economic operators in the supply chain.

Abbreviated new drug applications for generic drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme allowing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application (ANDA) to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug (RLD).

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form and the strength of the drug. An applicant may submit an ANDA suitability petition to request the FDA's prior permission to submit an abbreviated application for a drug that differs from the RLD in route of administration, dosage form, or strength, or for a drug that has one different active ingredient in a fixed combination drug product (i.e., a drug product with multiple active ingredients). At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists may consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Abridged marketing authorization applications for generic and biosimilar drugs in the EU and the UK

Generic and hybrid medicinal products of reference medicinal products authorized via the centralized procedure have automatic access to the centralized procedure. Generic and hybrid products can refer to the complete dossier (i.e., the quality, preclinical and clinical data) of the reference medicinal product in their marketing authorization application, by demonstration of bioequivalence, usually through the submission of the appropriate bioavailability studies after the period of regulatory data protection (also called "data exclusivity") has expired, namely eight years after the grant of the marketing authorization of the reference medicinal product. Applicants will be able to cross-refer to the dossier of the reference medicinal product, as long as the data protection period has expired. This abridged application procedure avoids the requirement to repeat trials and allows generic applicants a faster entry to the market. If a biosimilar of a reference biological product does not meet the conditions in the definition of generic medicinal products, owing to, in particular, differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference biological medicinal product, the results of appropriate preclinical studies or clinical trials relating to these conditions must be provided. The type and quantity of supplementary data to be provided must comply with the relevant criteria stated in Annex I of Directive 2001/83 as amended and the related detailed guidelines. The results of other tests and trials from the reference medicinal product's dossier do not need to be provided.

505(b)(2) New Drug Applications

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant, and for which the applicant has not obtained a right of reference. If the 505(b)(2) applicant can establish that reliance on the FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional bridging studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new drug candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Hatch-Waxman patent certification and the 30-month stay

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Orange Book.

When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that would be required of an ANDA applicant. Specifically, the applicant must certify that (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a statement certifying that its proposed ANDA label does not contain (or carve out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent, known as a Section VIII statement. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

Exclusivity under the Hatch-Waxman Amendments

In addition, under the Hatch-Waxman Amendments, the FDA may not approve an ANDA or 505(b)(2) NDA referencing a particular drug until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity (NCE). For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA or 505(b)(2) NDA may not be submitted to the FDA until the expiration of five years from the date the NDA is approved, unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) NDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it does, however, block the FDA from approving ANDAs or 505(b)(2) NDAs during the period of exclusivity. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Biosimilars and reference product exclusivity

The Biologics Price Competition and Innovation Act of 2009 (BPCIA) created an abbreviated approval pathway for biological product candidates shown to be highly similar, or "biosimilar," to or interchangeable with an FDA licensed reference biological product. Biosimilarity, which requires that a product is highly similar to the reference product notwithstanding minor differences in clinically inactive components, and that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can generally be shown through analytical studies, animal studies, and a clinical study or studies. 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 in any given patient and, for products that are administered multiple times to an individual, the interchangeable biosimilar and the reference biological product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product. A product shown to be biosimilar or interchangeable with an FDA-approved reference biological product may rely in part on the FDA's previous determination of safety and effectiveness for the reference product for approval, which can potentially reduce the cost and time required to obtain approval to market the product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles and have slowed implementation of the BPCIA by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of reference product exclusivity, another company may obtain FDA licensure and market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, there has been discussion of whether Congress should 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 implementation of the BPCIA is subject to significant uncertainty.

In the EU and the UK, an abridged procedure is available for the regulatory approval of biosimilars, on the basis of comparability studies to the reference biological medicine to substantiate the safety and efficacy profile of the biosimilar product. This comparability with the reference biological medicinal product is only available after the period of regulatory data protection has expired namely eight years after the grant of the marketing authorization of the reference biological medicinal product has expired. Recently, the MHRA and the EMA have stated that comparative data may not be required across all therapeutic indications and may be extrapolated to other indications already approved for the reference medicinal product. The interchangeability of biosimilars remains subject to national determination, on a case-by-case basis; however a recent scientific recommendation by the EMA may lead to a default assumption of interchangeability across all biosimilars in the EU and in the UK.

Pediatric studies and exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA, BLA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug or biological product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), sponsors must also submit pediatric study plans prior to the assessment data.

Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with Orphan Drug Designation.

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

Under the European Pediatric Regulation (Regulation (EC) No 1901/2006), which has also been reflected in and retained by UK law, applicants must submit to the national competent authority or the EMA data from pediatric studies in compliance with an agreed PIP for the validation or acceptance of a marketing authorization application, unless the medicine is exempt because of a deferral or waiver. The conduct of the pediatric studies in accordance with the agreed PIP will result in the grant of a reward (period of protection) which will depend on the type of product (i.e., orphan medicinal product will benefit from an extension of the orphan exclusivity by two years, bringing it to 12 years of marketing exclusivity; or an extension of the supplementary protection certificate by six months).

Patent term extension

After NDA approval, owners of relevant drug or biological product patents may apply for up to a five-year patent extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory process. The allowable patent term extension is typically calculated as one-half the time between the effective date of an IND application and the submission date of a NDA or BLA, plus the time between submission date and the approval date of the NDA or BLA, up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years from the date of product approval. Only one patent applicable to an approved drug or biological product is eligible for extension and only those claims covering the approved drug or biological product, a method for using it or a method for manufacturing it may be extended and the application for the extension must be submitted prior to the expiration of the patent in question. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements.

In the EU and the UK, a patent may be extended by up to a maximum of five years and the protection conferred by the certificate shall extend only to the product covered by the authorization to place the corresponding medicinal product on the market (in the EU and UK) and for any use of the product as a medicinal product that has been authorized before the expiry of the certificate. The aim is to compensate for the erosion of patent term between the filing of a patent and the grant of an MA for a medicinal product incorporating the relevant invention. The term of a supplementary protection certification may be extended by a further six months if the pediatric studies have been conducted in accordance with an agreed PIP within the applicable timeframe.

Foreign regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our drug candidates to the extent we choose to sell any products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing or distribution would apply to any product that is approved outside the United States.

We will also be subject to certain ex-U.S. privacy laws in connection with our clinical trial activities outside the United States such as the EU General Data Protection Regulation (EU GDPR), non-compliance with which could result in administrative fines of up to the greater of €20.0 million or 4% of global annual revenues. The EU GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the EU GDPR.

Reimbursement of medicines in Europe

In the EU, pricing and reimbursement methods can differ in each Member State. Some Member States and the UK may require that health technology assessments (HTA) be completed for the product to be recommended for funding under the NHS. The outcome of HTAs is decided on a national basis and some Member States may decide not to reimburse the use of medicines or may reduce the rate of reimbursement. In December 2021, the EU adopted a new Regulation on Health Technology Assessment which allows Member States to carry out joint clinical assessments and operate joint clinical consultations. It is expected that the new Regulation will come into effect in 2025. In the UK, NICE is the body in England and Wales, which conducts HTAs and issues guidance on whether a product is considered to be "cost-effective" and therefore recommended for use and reimbursement under the national health service. This means that if a positive recommendation has been obtained, then the medicinal product will be widely available to patients in England and Wales. For avoidance of doubt, Scotland and Northern Ireland have their own HTA bodies which will conduct their own assessment.

Other healthcare laws

Although we do not currently have any products on the market, in addition to FDA restrictions on marketing of pharmaceutical and biological products, we are also subject to healthcare statutory and regulatory requirements and enforcement by the U.S. federal and state governments. Even though we are not in a position to make patient referrals and do not bill Medicare, Medicaid or other government or commercial third-party payers, our relationships with healthcare providers, physicians and third-party payors will subject us to healthcare statutory and regulatory requirements and enforcement by federal and state governments. These laws include anti-kickback statutes, false claims statutes and other healthcare laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, in cash or in kind, to induce, or in return for, purchasing, leasing, ordering or arranging for, referring, or recommending the purchase, lease or order of any healthcare item or service that may be reimbursable, in whole or in part, under Medicare, Medicaid, or other federal health care program. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ACA) amended the intent element of the federal Anti-Kickback Statute to clarify that a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to commit a violation. Among others, this statute applies to arrangements between pharmaceutical and biological product manufacturers on the one hand and prescribers, pharmacies, purchasers and formulary managers on the other, including, for example, consulting/speaking arrangements, discount and rebate offers, grants, charitable contributions and patient support offerings. A conviction for violation of the federal Anti-Kickback Statute can result in criminal fines and/or imprisonment and requires mandatory exclusion from participation in federal health care programs. Exclusion from the federal healthcare programs may also be imposed if the government determines that an entity has committed acts that are prohibited by the federal Anti-Kickback Statute. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions under the law, the exceptions and safe harbors are drawn narrowly and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false record or statement material to a false claim. The False Claims Act covers claims made to programs where the federal government reimburses (directly or indirectly) individuals and entities, such as under the Medicare and Medicaid programs, as well as programs where the federal government is a direct purchaser, such as when it purchases off of the Federal Supply Schedule. The law also prohibits avoiding, decreasing or concealing an obligation to pay money to the federal government. The government can bring claims directly or through a civil whistleblower or *qui tam* action, and potential liability includes mandatory treble damages and significant per claim penalties currently set at $13,946 up to $27,894 per false claim or statement for penalties assessed after January 15, 2024. Numerous pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug or biological product prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, the ACA amended the federal Anti-Kickback Statute such that a violation of that statute can serve as a basis for liability under the federal False Claims Act. Most states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply to commercially reimbursed items or services or regardless of whether reimbursement from a federal or state healthcare program is available for the item or service. There is also the Federal Criminal False Claims Act, which is similar to the Federal Civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious or fraudulent claim to the federal government.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits, among other things, the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror or payor knows or should know is likely to influence the beneficiary to order or receive a reimbursable item or service from a particular provider, practitioner or supplier (although pharmaceutical and biological product manufacturers are not considered providers, practitioners or suppliers for purposes of this law), and contracting with an individual or entity that the person knows or should know is excluded from participation in a federal health care program. In addition, federal criminal statutes created by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) prohibit, among other things, 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 money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and their respective implementing regulations, including the Final Omnibus Rule published on January 25, 2013, imposes obligations on certain healthcare providers, health plans and healthcare clearinghouses, known as covered entities, as well as their business associates that perform certain services involving the storage, use or disclosure of individually identifiable health information, including mandatory contractual terms, requirements to facilitate certain patient rights, requirements to safeguard the privacy, security, and transmission of individually identifiable health information, and requirements to provide notice to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information. HITECH increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, 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. On December 10, 2020, the Office of Civil Rights within the Department of Health and Human Services (HHS) issued proposed revisions to the HIPAA Privacy Rule aimed at reducing regulatory burdens that may exist in discouraging coordination of care and patient access to their health information, among other changes. While a final rule has not yet been issued, if adopted, these proposed changes may require us to update our policies and procedures to comply with the new requirements. In addition, many state laws govern the privacy and security of health information and other personal information in certain circumstances (such as the California Consumer Privacy Act of 2018, the Virginia Consumer Data Protection Act, and similar state privacy laws in Colorado, Connecticut and Utah, along with health privacy focused laws such as the Washington My Health My Data Act), and these state laws may differ from each other in significant ways and may not have the same effect. These laws are rapidly evolving and may impose additional regulatory compliance burden and legal risks on our operations.

Further, pursuant to the ACA, the Centers for Medicare & Medicaid Services (CMS) has promulgated regulations to implement what is commonly known as the federal Physician Payment Sunshine Act, which, among other things, requires manufacturers of prescription drugs and biological products, among others, to collect and report information on certain payments or transfers of value they make to U.S.-licensed physicians, teaching hospitals, physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants and certified nurse-midwives, as well as investment interests in the manufacturer held by physicians and their immediate family members. The reports must be submitted on an annual basis, and the reported data is made available in searchable form on a public website. Failure to submit required information may result in civil monetary penalties.

In addition, several states require prescription drug and biological product companies to report certain expenses relating to the marketing and promotion of drug and biological products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. Some states require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging. In addition, states such as California, Connecticut, Nevada and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Certain states and local jurisdictions also require the registration of pharmaceutical sales representatives. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

Efforts to ensure that business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. If a company's operations are found to be in violation of any such requirements, it may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of its operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other federal or state government healthcare programs, including Medicare and Medicaid, integrity oversight and reporting obligations, imprisonment, and reputational harm. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause a company to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

In the EU and the UK companies must comply with national general anti-bribery legislation, including the UK Bribery Act 2010, as well as medicines legislation which prohibits the supply, offer or promise of certain gifts and benefits in connection with the promotion of medicinal products to any person qualified to prescribe, recommend, use, procure or supply them. Companies that breach these laws may incur substantial fines and imprisonment.

In the EU and the UK, payments made to healthcare professionals must be publicly disclosed under applicable transparency provisions and agreements with healthcare professionals must be the subject of prior notification and approval by the healthcare professional's employer. Such requirements are set out in national laws, industry codes or professional codes of conduct, applicable in the EU Member States and in the UK. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

U.S. healthcare reform

In the United States there have been, and continue to be, proposals by the federal government, state governments, regulators and third-party payors to control or manage the costs of health care and, more generally, to reform the U.S. healthcare system. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the ACA was enacted, which was intended to substantially change the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, (i) proscribed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and therapeutic biologics that are inhaled, infused, instilled, implanted or injected, (ii) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, (iii) established annual nondeductible fees and taxes on manufacturers of certain branded prescription drugs and therapeutic biologics, apportioned among these entities according to their market share in certain government healthcare programs, (iv) expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 138% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability, (v) expanded the entities eligible for discounts under the 340B Public Health program, (vi) required annual reporting of certain information regarding drug samples that manufacturers and distributors provide to licensed practitioners, (vii) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research, and (viii) established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Some of these cost-savings pilots and projects, such as the Enhancing Oncology Model, are directed specifically at oncology.

The ACA and certain of its provisions have been subject to judicial challenges as well as legislative and regulatory efforts to repeal or replace them or to alter their interpretation or implementation. For example, the Tax Cuts and Jobs Act (TCJA), among other things, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment, or penalty, imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Additionally, the Further Consolidated Appropriations Act of 2020, signed into law December 20, 2019, fully repealed the ACA's "Cadillac Tax" on certain high-cost employer-sponsored insurance plans (for tax years beginning after December 31, 2019), the annual fee imposed on certain health insurance providers based on market share (for calendar year 2021) and the medical device excise tax on non-exempt medical devices. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states who argued that, without the individual mandate, the entire ACA was unconstitutional. The Supreme Court's dismissal of the lawsuit did not specifically rule on the constitutionality of the ACA.

On March 11, 2021, Congress enacted the American Rescue Plan Act of 2021, which included among its provisions a sunset of the ACA's cap on pharmaceutical manufacturers' rebate liability under the Medicaid Drug Rebate Program. Under the ACA, manufacturers' rebate liability was capped at 100% of the average manufacturer price for a covered outpatient drug. Effective January 1, 2024, manufacturers' MDRP rebate liability is no longer capped, potentially resulting in a manufacturer paying more in MDRP rebates than it receives on the sale of certain covered outpatient drugs. The American Rescue Plan Act also temporarily increased premium tax credit assistance for individuals eligible for subsidies under the ACA for 2021 and 2022 and removed the 400% federal poverty level limit that otherwise applies for purposes of eligibility to receive premium tax credits. Most recently, the Inflation Reduction Act of 2022 extended this increased tax credit assistance and removal of the 400% federal poverty limit through 2025. In the future, there may be additional challenges and/or amendments to the ACA. It remains to be seen precisely what any new legislation will provide, when or if it will be enacted, and what impact it will have on the availability and cost of healthcare items and services, including drug and biological products.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted to reduce healthcare expenditures. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions of Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent statutory amendments, will remain in effect through the first six months of the FY 2032 sequestration order unless additional Congressional action is taken, with the exception of a temporary suspension from May 1, 2020 through July 1, 2022 due to the COVID-19 pandemic. The American Taxpayer Relief Act of 2012 made other changes, including the reduction of Medicare payments to several types of providers and an increase in the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, in August 2022, President Biden signed into law the Inflation Reduction Act of 2022, which implements substantial changes to the Medicare program, including drug pricing reforms and changes to the Medicare Part D benefit design. Among other reforms, the Inflation Reduction Act of 2022 imposes inflation rebates on drug and biological product manufacturers for products reimbursed under Medicare Parts B and D if the prices of those products increase faster than inflation beginning in 2023; implements changes to the Medicare Part D benefit that, beginning in 2025, will cap benefit annual out-of-pocket spending at $2,000, with new discount obligations for pharmaceutical manufacturers; and, beginning in 2026, establishes a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with the CMS. CMS has also taken steps to implement the IRA, including: on June 30, 2023, issuing guidance detailing the requirements and parameters of the first round of price negotiations, to take place during 2023 and 2024, for products subject to the "maximum fair price" provision that would become effective in 2026; on August 29, 2023, releasing the initial list of ten drugs subject to price negotiations; on November 17, 2023, releasing guidance outlining the methodology for identifying certain manufacturers eligible to participate in a phase-in period where discounts on applicable products will be lower than those required by the Medicare Part D Manufacturer Discount Program; and on December 14, 2023, releasing a list of 48 Medicare Part B products that had an adjusted coinsurance rate based on the inflationary rebate provisions of the IRA for the time period of January 1, 2024 to March 31, 2024. If federal spending is further reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the NIH to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve research and development, manufacturing, and marketing activities which may delay our ability to develop, market and sell any products we may develop.

Additionally, the cost of prescription pharmaceuticals and biological products has recently been the subject of considerable discussion in the United States. For example, in response to an Executive Order dated July 9, 2021, on September 9, 2021, the HHS issued a Comprehensive Plan for Addressing High Drug Prices that identified potential legislative policies and administrative tools that Congress and the agency can pursue in order to make drug prices more affordable and equitable, improve and promote competition throughout the prescription drug industry, and foster scientific innovation. In addition, on February 2, 2022, the Biden administration signaled its continued commitment to the Cancer Moonshot initiative, which was initially launched in 2016. In its announcement, the administration noted that its new goals under the initiative include addressing inequities in order to ensure broader access to cutting-edge cancer therapeutics and investing in a robust pipeline for new treatments. In alignment with President Biden's Cancer Moonshot initiative, on June 27, 2023, the Center for Medicare Innovation at CMS announced a new model, the Enhancing Oncology Model, that is designed to make high-quality cancer care more affordable to both patients and Medicare. On September 12, 2022, President Biden issued an Executive Order to promote biotechnology and biomanufacturing innovation. The Order noted several methods through which the Biden administration would support the advancement of biotechnology and biomanufacturing in healthcare, and instructed the HHS to submit, within 180 days of the Order, a report assessing how to use biotechnology and biomanufacturing to achieve medical breakthroughs, reduce the overall burden of disease, and improve health outcomes. Additionally, on October 14, 2022 President Biden issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of the HHS to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. The Executive Order further directed the Secretary of the HHS to submit, within 90 days after the date of the Executive Order, a report regarding any models that may lead to lower cost-sharing for commonly used drugs and support value-based payment that promotes high-quality care. Moreover, there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug and biological product pricing, review the relationship between pricing and manufacturer patient support programs, reduce the cost of prescription drugs and biological products under Medicare and reform government program reimbursement methodologies for drug and biological products. While several proposed reform measures will require Congress to pass legislation to become effective, Congress and the Biden administration have each indicated that it will continue to seek new legislative and/or administrative measures to address prescription drug and biological product costs, as discussed in greater detail in the section titled "Risk Factors."

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, to encourage importation from other countries and bulk purchasing. Most recently, on January 5, 2024, the FDA approved Florida's importation plan to allow pharmacists and wholesalers in the state to import certain medications from Canada. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize any product that is ultimately approved, if approved. In addition, several recently passed state laws require disclosures related to state agencies and/or commercial purchasers with respect to certain price increases that exceed a certain level as identified in the relevant statutes. Some of these laws and regulations contain ambiguous requirements that government officials have not yet clarified. Given the lack of clarity in the laws and their implementation, our future reporting actions could be subject to the penalty provisions of the pertinent federal and state laws and regulations.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug or biological 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 authorization under an FDA expanded access program; however, manufacturers are not obligated to provide investigational new drug or biological products under the current federal right to try law.

Human Capital

As of November 30, 2023, we had 284 full-time or part-time employees, of which approximately 40% have earned an M.D. or a Ph.D. As of November 30, 2023, 249 of our full-time or part-time employees are engaged in research and development. From time to time, we retain independent contractors to support our organization. None of our employees are represented by a labor union or covered by collective bargaining agreements, and we believe our relationship with our employees is good.

We consider the intellectual capital of our employees to be an essential driver of our business. We continually evaluate our business needs and opportunities and strive to balance in-house expertise and capacity with outsourced expertise and capacity. Currently, we outsource substantially all clinical trial work to clinical research organizations and drug substance and finished drug product manufacturing to contract manufacturers.

Competitive pay and benefits

Drug development is a complex endeavor which requires deep expertise and experience across a broad array of disciplines. Biotechnology and pharmaceutical companies both large and small compete for a limited number of qualified applicants to fill specialized positions. We monitor our compensation programs closely and provide what we consider to be a very competitive mix of compensation, insurance and wellness benefits for all our employees, as well as participation in our equity and other enhanced benefit programs. To attract qualified applicants, we offer a total rewards package consisting of a base salary and cash target bonus, a comprehensive benefits package and equity compensation for all full-time and part-time employees. Bonus opportunity and equity compensation increase as a percentage of total compensation based on level of responsibility. Actual bonus payout is based on company and individual performance.

Diversity and inclusion

We are committed to creating and maintaining a workplace free from discrimination or harassment on the basis of color, race, sex, national origin, ethnicity, religion, age, disability, sexual orientation, gender identification or expression or any other status protected by applicable law. Our management team and employees are expected to exhibit and promote honest, ethical and respectful conduct in the workplace. All of our employees must adhere to a code of conduct that sets standards for appropriate behavior and are required to attend biennial training to help prevent, identify, report and stop any type of discrimination and harassment. Recruitment, hiring, development, training, compensation and advancement at our company is based on qualifications, performance, skills and experience without regard to gender, race and ethnicity.

As of November 30, 2023, approximately 52% of our full-time and part-time employees were self-reported as female. Of our vice president-level and above employees, approximately 42% were self-reported as female.

In addition, as of November 30, 2023, approximately 57% of our full-time employees were self-reported as ethnic or racial minorities in the United States, with 42% Asian, 2% Black or African American, 8% Hispanic or Latino and 6% of other minority groups or two or more races. Of our vice president-level and above employees, 25% were self-reported as ethnic or racial minorities in the United States, with 17% Asian and 8% Black or African American.

Employee development and training

We focus on attracting, retaining and cultivating talented individuals. We emphasize employee development and training by providing access to a wide range of online and instructor led development and continual learning programs. Employees are encouraged to attend scientific, clinical and technological meetings and conferences and have access to broad resources they need to be successful.

Board of Directors oversight

Our Board of Directors (Board) recognizes the critical importance of our team and the necessity to ensure a diverse, inclusive, and innovative work environment that is centered around a values-based culture. Our Board meets regularly with management to discuss issues impacting our employees, and to focus on ways to support our workforce. Our focus on culture comes from our Board and flows throughout our company. In evaluating our Chief Executive Officer and management team, significant emphasis is place on their contributions to our overall culture.

Our Board's Compensation Committee is responsible for reviewing with management our human resources activities, which include, among other things, matters relating to employee development, management and engagement, pay equity, and our demographics, diversity and inclusion.

Our Board's Nominating and Corporate Governance Committee is responsible for developing and recommending to the Board any company program relating to corporate responsibility and sustainability, including environmental, social and governance matters.

Corporate Information

We were incorporated under the laws of the State of Delaware in August 2009 under the name Kura Therapeutics, Inc. We subsequently changed our name to Nurix, Inc. in February 2012 and then to Nurix Therapeutics, Inc. in October 2018. Our principal executive offices are located at 1700 Owens Street, Suite 205, San Francisco, California 94158, and our telephone number is (415) 660-5320.

The mark "Nurix" is our registered trademark in Canada, France, Germany, Italy, Japan, Mexico, Spain, the United Kingdom and the United States. The mark "DELigase" is our registered trademarks in the United States. The Nurix logo is our common law trademark. All other service marks, trademarks and trade names appearing in this Annual Report on Form 10-K are the property of their respective owners. Solely for convenience, the trademarks and trade names referred to in this Annual Report on Form 10-K appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and trade names.

Additional Information

Nurix's Internet website address is http://www.nurixtx.com. On our website, we make available, free of charge, our annual, quarterly and current reports, including amendments to such reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the Securities and Exchange Commission (SEC). The SEC maintains a website at www.sec.gov that contains reports as well as other information regarding us and other companies that file materials with the SEC electronically.

Also available on our website is information relating to corporate governance at Nurix and our Board, including our Corporate Governance Guidelines; our Code of Business Conduct and Ethics (for our directors, officers and employees); and our Board Committee Charters. We will provide any of the foregoing information without charge upon written request to our Corporate Secretary, Nurix Therapeutics, Inc., 1700 Owens Street, Suite 205, San Francisco, California 94158.

We use our Investor Relations website (http://ir.nurixtx.com) as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD promulgated by the SEC. These disclosures are included in the "News" and "Events and Presentations" sections of our website. Accordingly, investors should monitor these portions of our website, in addition to following our press releases, SEC filings and public conference calls and webcasts.

The information contained on our website does not constitute, and shall not be deemed to constitute, a part of this Annual Report on Form 10-K, or any other report we file with, or furnish to, the SEC. Our references to the URLs for websites are intended to be inactive textual references only.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K, including the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the accompanying notes and the information contained in our other public filings before deciding whether to invest in shares of our common stock. We cannot assure you that any of the events described below will not occur. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of or that we deem immaterial may also become important factors that adversely affect our business. If any of the following risks occur, our business, financial condition, results of operations, and future prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline, and you could lose part or all of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.

Our net loss was $143.9 million and $180.4 million for the fiscal years ended November 30, 2023 and 2022, respectively. As of November 30, 2023, we had an accumulated deficit of $545.2 million. To date, we have not generated any revenue from product sales and have financed our operations primarily through our collaborations and sales of our equity interests. We are in the early stages of development of our drug candidates. Our lead drug candidates, NX-5948, NX-2127 and NX-1607, are in the early stages of clinical development. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our operating expenses and capital expenditure requirements will increase substantially if and as we:

- increase enrollment in and further development of our Phase 1 clinical trials of our drug candidates NX-5948, NX-2127 and NX-1607;
- submit investigational new drug applications (INDs) and initiate clinical trials of our other drug candidates;
- enter advanced clinical development and scale up external manufacturing capabilities to supply clinical trials;
- expand the capabilities of our DELigase platform and apply our DELigase platform to advance additional drug candidates into preclinical and clinical development;
- conduct process development for manufacturing of our drug candidates;
- seek marketing approvals for any drug candidates that successfully complete clinical trials;
- prepare for negotiations with the pricing authorities and submission to the health technology appraisal (HTA) bodies;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any drug candidates for which we may obtain marketing approval;
- expand, maintain and protect our intellectual property portfolio;
- hire additional clinical, regulatory, manufacturing, quality assurance and scientific personnel; and
- add operational, financial and management information systems and personnel to support our research, product development and future commercialization efforts and support our operations as a public company.

Our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) or other regulatory authorities to perform trials in addition to those we currently expect, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our planned clinical trials or the development of any of our drug candidates.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even 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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

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

We are in the early stages of clinical development of our drug candidates NX-5948, NX-2127 and NX-1607. We expect that it will be many years, if ever, before we have a drug candidate ready for commercialization. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. To become and remain profitable, we must succeed in developing, obtaining marketing approval for and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our drug candidates, discovering additional drug candidates, establishing and maintaining arrangements with third parties for the manufacture of clinical supplies of our drug candidates, obtaining marketing approval for our drug candidates and manufacturing, marketing, selling and obtaining reimbursement for any products for which we may obtain marketing approval.

If one or more of the drug candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved drug candidate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need substantial additional funding. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we conduct our Phase 1 clinical trials of NX-5948, NX-2127 and NX-1607, grow our pipeline of drug candidates, expand the breadth of our DELigase platform, continue research and development and initiate additional clinical trials of and potentially seek marketing approval for our lead programs and other drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, reimbursement and sales and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our research, product development programs or any future commercialization efforts or grant rights to develop and market drug candidates that we otherwise would prefer to develop and market ourselves.

We had cash, cash equivalents and marketable securities of $295.3 million as of November 30, 2023. We believe that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements through at least the next 12 months. However, our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect, and we may need to seek additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. Our future capital requirements will depend on many factors, including:

- the progress, costs and results of our Phase 1 clinical trials for NX-5948, NX-2127 and NX-1607 and any future clinical development of such drug candidates;
- the scope, progress, costs and results of preclinical and clinical development for our other drug candidates and development programs;
- the number and development requirements of other drug candidates that we pursue;
- the scope of, and costs associated with, future advancements to our DELigase platform;
- the success of our collaborations with Gilead Sciences, Inc. (Gilead), Sanofi S.A. (Sanofi) and Seagen Inc. (now a part of Pfizer Inc. (Pfizer)) and any other collaborations we may establish;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our drug candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our drug candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- our ability to establish additional collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of our drug candidates.

We will need to raise substantial additional capital to complete the development and commercialization of our drug candidates. In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives. Adequate additional funds may not be available to us on acceptable terms, or at all.

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

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. Although we may receive potential future milestone payments under our collaborations with Gilead, Sanofi and Pfizer, we do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of common stock. 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 acquisitions or capital expenditures or declaring dividends.

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

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

We commenced operations in 2009, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential drug candidates, undertaking preclinical studies, establishing arrangements with third parties for the manufacture of initial quantities of our drug candidates and conducting early-stage clinical trials. Our lead drug candidates are in the early stages of clinical development and their risk of failure is high. We have not yet demonstrated our ability to successfully: complete any clinical trials, including large-scale, pivotal clinical trials; obtain marketing approvals; manufacture a commercial-scale product or arrange for a third party to do so on our behalf; or conduct market access, sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as an early-stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

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

Risks Related to the Discovery and Development of Our Drug Candidates

We are early in our development efforts. Our lead drug candidates, NX-5948, NX-2127 and NX-1607, are in the early stages of clinical development. If we are unable to advance our drug candidates through clinical development, develop, obtain regulatory approval for and commercialize our drug candidates or experience significant delays in doing so, our business may be materially harmed.

We are early in our development efforts. Our lead drug candidates, NX-5948, NX-2127 and NX-1607, are in the early stages of clinical development and their risk of failure is high. We have invested substantially all of our efforts and financial resources in building our DELigase platform, in the identification and preclinical development of our current drug candidates and in the preparation for and initiation of Phase 1 clinical trials for our lead drug candidates. Our ability to generate revenue from product sales, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our drug candidates. The success of our drug candidates will depend on several factors, including the following:

- sufficiency of our financial and other resources;
- successful completion of preclinical studies;

- successful submission of INDs or Clinical Trial Applications and initiation of clinical trials;
- successful patient enrollment in, and completion of, clinical trials;
- receipt and related terms of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drug candidates as well as obtaining relevant exclusivity extensions (due to the conduct of pediatric studies);
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our drug candidates;
- achieving desirable therapeutic properties for our drug candidates' intended indications;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- establishing a continued acceptable safety profile of our drug candidates and maintaining such a profile following approval; and
- effectively competing with other therapies.

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

In addition, we filed for and received an Innovation Passport designation for NX-1607 in the United Kingdom (UK) in February 2022. The Innovation Passport is the mandated entry point to the Innovative Licensing and Access Pathway (ILAP) in the UK to facilitate approval of and market access to an innovative medicine. Grant of the Innovation Passport paves the way for enhanced engagement with key stakeholders such as the Medicines and Healthcare products Regulatory Agency (MHRA), health technology agencies in the UK such as the National Institute for Health and Care Excellence (NICE) or the Scottish Medicines Consortium (SMC) and NHS England. However, although the goal of ILAP and the Innovation Passport is to reduce the time to market and enable earlier patient access, they do not accelerate conduct of clinical trials or mean that the regulatory requirements are less stringent, nor do they ensure that any NX-1607 marketing authorization application (MAA) will be approved or that any approval will be granted within any particular timeframe. Despite receiving an Innovation Passport designation, we may decide to delay or forego the commercialization of NX-1607 in the UK or the development may otherwise not proceed.

One of our approaches to the discovery and development of drug candidates based on our targeted protein degradation platform is unproven, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any products.

Treating diseases using targeted protein degradation is a new treatment modality. Our future success depends on the successful development of this novel therapeutic approach. Very few small molecule drug candidates designed to control cellular protein levels, such as our BTK degraders, have been tested in humans, none have been approved in the United States or Europe, and the data underlying the feasibility of developing these therapeutic products is both preliminary and limited. Discovery and development of targeted protein degraders that harness ligases to degrade protein targets have been impeded largely by the complexities and limited understanding of the functions, biochemistry and structural biology of E3 ligases as well as by challenges of engineering compounds that promote protein-protein interactions.

We believe that our targeted protein degrader drug candidates may offer an improved therapeutic approach by removing the disease-causing proteins instead of simply inhibiting their activities. However, the scientific research that forms the basis of our efforts to develop our targeted protein degrader drug candidates is ongoing and the scientific evidence to support the feasibility of developing targeted protein degrader-based therapeutic treatments is both preliminary and limited. Further, certain patients have shown inherent (primary) resistance to approved BTK inhibitors and other patients have developed acquired (secondary) resistance to these inhibitors. Both NX-5948 and NX-2127 degrade BTK with mutations that confer resistance to currently marketed BTK inhibitors, and we believe that preliminary data from our ongoing Phase 1 trials of NX-5948 and NX-2127 may provide evidence of clinical benefit to patients with such resistance mutations. However, any inherent primary or acquired secondary resistance to our BTK degraders in patients would prevent or diminish their clinical benefit.

We are in the early stages of clinical development of NX-5948 and NX-2127 and we currently have limited safety data of NX-5948 and NX-2127 in humans. Although some of our drug candidates have produced observable results in animal studies, these drug candidates may not demonstrate the same chemical and pharmacological properties in humans, and may interact with human biological systems in unforeseen, ineffective or harmful ways. As such, there may be adverse effects from treatment with any of our current or future drug candidates that we cannot predict at this time.

Additionally, the regulatory approval process for novel drug candidates such as ours can be more expensive and take longer than for other, better-known or extensively-studied drug candidates. Although other companies are also developing therapeutics based on targeted protein degradation, no regulatory authority has granted approval for any such therapeutic. As a result of these factors, it is more difficult for us to predict the time and cost of targeted protein degrader drug candidate development, and we cannot predict whether targeted protein degradation will result in the development and marketing approval of any products. Any development problems we experience in the future related to any of our targeted protein degrader research programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Advancing our targeted protein degrader drug candidates creates significant challenges for us, including:

- educating medical personnel regarding the potential efficacy and safety benefits, as well as the challenges, of incorporating our drug candidates, if approved, into treatment regimens; and
- establishing the sales and marketing capabilities to gain market acceptance, if approved.

Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate, or from commercializing any targeted protein degrader drug candidates we may develop on a timely or profitable basis, if at all.

Drug development is a lengthy and expensive process, with an uncertain outcome. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.

Our lead drug candidates are in the early stages of clinical development and their risk of failure is high. We are unable to predict when or if any of our drug candidates will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Before we can commence clinical trials for a drug candidate, we must complete extensive preclinical testing and studies that support our planned INDs in the United States or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or similar regulatory authorities outside the United States will accept our proposed clinical programs or if the outcome of our preclinical testing and studies ultimately will support the further development of our programs.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the outcome. A failure of one or more clinical trials can occur at any stage of testing. Clinical trials may produce negative or inconclusive results, and we or any future collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. We will be required to demonstrate with substantial evidence through adequate and well-controlled clinical trials that our drug candidates are safe and effective for use in treating specific conditions in order to obtain marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that any future larger registration clinical trials will be successful because drug candidates in later-stage clinical trials may fail to demonstrate safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Drug candidates that have shown promising results in preclinical studies and early-stage clinical trials may still suffer significant setbacks in subsequent larger registration clinical trials. Additionally, the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later-stage clinical trials.

We may experience numerous unforeseen events during, or as a result of, clinical trials, that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

- we may experience delays in reaching, or may fail to reach, a consensus with regulators on trial design;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing and delivery of drug candidates to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- we may experience delays in reaching, or may fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- regulators or institutional review boards (IRBs) may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- we may face delays under human tissue act legislation and restrictions across various jurisdictions;
- we may experience difficulty in designing clinical trials and in selecting endpoints for diseases that have not been well-studied and for which the natural history and course of the disease is poorly understood;
- the selection of certain clinical endpoints may require prolonged periods of clinical observation or analysis of the resulting data;
- the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our drug candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials;
- we may have to suspend or terminate clinical trials of our drug candidates for various reasons, including a partial or full clinical hold based on a finding that our drug candidates have undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or IRBs may require that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements;
- clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the cost of clinical trials of our drug candidates may be greater than we anticipate;
- the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate;
- regulators may revise the requirements for approving our drug candidates, or such requirements may not be as we anticipate;
- any future collaborators that conduct clinical trials may face any of the above issues and may also conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us; and
- disruptions caused by macroeconomic, political and market conditions, including supply chain disruptions, may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate safety and efficacy sufficient to obtain marketing approval for our drug candidates.

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

- be delayed in obtaining marketing approval for our drug candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements or changes in the way the product is administered; or
- have the product removed from the market after obtaining marketing approval.

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

Further, cancer therapies sometimes are characterized as first-line, second-line or third-line, and the FDA often approves new therapies initially only for third-line or later use, meaning for use after two or more other treatments have failed. When cancer is detected early enough, first-line therapy, usually chemotherapy, hormone therapy, immunotherapy, radiation therapy, surgery, targeted therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy was ineffective. Our current and planned clinical trials for our drug candidates NX-5948, NX-2127 and NX-1607 are and will be with patients who have received one or more prior treatments. Subsequently, for those drug candidates that prove to be sufficiently beneficial, if any, we may seek approval potentially as a first-line therapy, but any drug candidates we develop, even if approved, may not be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

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

We have recently begun to evaluate our lead drug candidates in human clinical trials, and there have been very few clinical trials to date involving small molecule drug candidates designed to control cellular protein levels through targeted protein degradation. It is impossible to predict when or if any drug candidates we may develop will prove safe in humans. There is a limited safety data set for the effects of NX-5948, NX-2127 and NX-1607 in animals and we only recently have begun to test the safety of our drug candidates in humans. There can be no assurance that our current drug candidates or any future drug candidate will not cause undesirable side effects. Unforeseen side effects from our drug candidates could arise at any time during preclinical or clinical development.

A potential risk in any protein modulation product is that healthy proteins or proteins not targeted for modulation will be modulated or that the modulation of the targeted protein in itself could cause adverse events, undesirable side effects or unexpected characteristics. It is possible that healthy proteins or proteins not targeted for modulation could be modulated by our drug candidates in any of our current or future preclinical studies or clinical trials. There also is the potential risk of delayed adverse events following treatment with our drug candidates.

If any drug candidates we develop are associated with serious adverse events or undesirable side effects, or have characteristics that are unexpected, including in preclinical studies, we may need to abandon their development or limit development to certain uses or subpopulations in which the adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, any of which would have a material adverse effect on our business, financial condition, results of operations and prospects. For example, increased bleeding risk and cardiac arrhythmia such as atrial fibrillation have been reported side effects of approved BTK inhibitors. Furthermore, NX-1607 could activate the immune response to unsafe levels and may have the potential to induce hypercytokinemia, or cytokine storm, which is the overstimulation of immune cells and subsequent overproduction of their activating compounds. Many drug candidates that initially showed promise in early-stage testing for treating cancer or other diseases later have been found to cause side effects that prevented further clinical development of the drug candidates or limited their competitiveness in the market.

The results of preclinical studies and early-stage clinical trials may not be predictive of future results. Initial success in clinical trials may not be indicative of results obtained when these trials are completed or in later-stage trials.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials we commence may not be predictive of the results of the later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. In particular, the small number of patients in our planned early clinical trials may make the results of these trials less predictive of the outcomes of later clinical trials. For example, even if successful, the results of our initial clinical trials for NX-5948, NX-2127 and NX-1607 may not be predictive of the results of further clinical trials of these drug candidates or any of our other drug candidates. Moreover, preclinical and clinical data often are susceptible to varying interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in preclinical studies and clinical trials nonetheless have failed to obtain marketing approval of their products. Our future clinical trials may not ultimately be successful or support further clinical development of any of our drug candidates. There is a high failure rate for drug candidates proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies and clinical trials. Any such setbacks in our clinical development could materially harm our business, results of operations, financial condition and prospects.

Interim top-line and preliminary data from our planned clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publish interim top-line or preliminary data from our planned clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation, business, results of operations, financial condition and prospects.

If we experience delays or difficulties in enrolling patients in clinical trials, our receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, we are currently conducting Phase 1 clinical trials for each of our lead drug candidates: NX-5948, NX-2127 and NX-1607. We cannot predict how difficult it will be to enroll patients for these trials. Therefore, our ability to identify and enroll eligible patients for our NX-5948, NX-2127 and NX-1607 clinical trials may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who otherwise would be eligible for our planned clinical trials instead may enroll in clinical trials of our competitors' drug candidates. Moreover, the size of the relevant patient populations for the diseases that our lead drug candidates target is small, and as more companies begin to focus attention and resources on drug candidates to treat the same indications as our drug candidates, we may experience delays or be unable to successfully recruit and enroll a sufficient number of eligible patients in our clinical trials. Patient enrollment is affected by other factors including:

- the severity of the disease under investigation;
- the size of the patient population and process for identifying patients;
- the availability and efficacy of approved medications for the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the drug candidates under study;
- the efforts to facilitate timely enrollment in clinical trials;
- physicians' attitudes and practices with respect to clinical trial enrollment;
- the burden on patients due to inconvenient procedures;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our current or planned clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our current or planned clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

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

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate.

The manufacture of drugs is complex, and we and our third-party manufacturers are early in our manufacturing efforts.

We have established manufacturing relationships with a limited number of suppliers to manufacture raw materials and the drug substance of any drug candidate for which we are currently pursuing, or may in the future pursue, preclinical or clinical development. Our systems for complying with current good manufacturing practices (cGMPs), manufacturing process development with our third-party manufacturers and scale-up are at an early stage. The actual cost to manufacture and process our drug candidates could be greater than we expect and could materially and adversely affect the commercial viability of our drug candidates. We or any of our third-party manufacturers may encounter difficulties in production, including contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If we or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our current or future drug candidates for clinical trials, our ability to obtain marketing approval or our ability to provide supply of our drug candidates for patients, if approved, could be delayed or stopped. For example, in October 2023, following our communication to the FDA of our intention to transition to an improved manufacturing process for NX-2127, the FDA placed a partial clinical hold on our ongoing Phase 1 clinical trial evaluating NX-2127. Currently-enrolled patients who are deriving clinical benefit may continue to receive treatment in accordance with the ongoing study protocol, but no additional patients may be enrolled until the partial clinical hold is resolved. We remain actively engaged in discussions with FDA as part of our efforts to lift the partial clinical hold. However, there can be no assurance that we can address the issues resulting in the partial clinical hold in a timely manner or at all, and we may incur additional expenses in connection with our efforts to advance our NX-2127 program.

We may not be successful in our efforts to identify or discover additional potential drug candidates.

A key element of our strategy is to apply our DELigase platform to address a broad array of targets and new therapeutic areas. The therapeutic discovery activities we are conducting may not be successful in identifying drug candidates that are useful in treating hematologic cancers, immune-mediated diseases or any other diseases. Our research programs initially may show promise in identifying potential drug candidates, yet fail to yield drug candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential drug candidates;
- potential drug candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval or achieve market acceptance; or
- potential drug candidates may not be effective in treating their targeted diseases.

Research programs to identify new drug candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential drug candidate that ultimately proves to be unsuccessful. If we are unable to identify suitable drug candidates for preclinical and clinical development, we will not be able to obtain revenues from the sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

We may not be successful in our efforts to expand the breadth of our DELigase platform.

A key element of our strategy is to expand the capabilities of our DELigase platform and leverage our platform to discover, develop and potentially commercialize additional drug candidates beyond our current portfolio to target diseases in a wide range of organ systems and tissues and treat various disease states. These enhancements require substantial technical, financial and human resources, and may not result in the discovery or development of additional drug candidates or therapies. We may pursue what we believe is a promising opportunity to leverage our platform only to discover that certain of our risk or resource allocation decisions were incorrect or insufficient, or that individual products or our science in general has technology or biology risks that were previously unknown or underappreciated. Our strategy of pursuing the value of our DELigase platform over a long time horizon and across a broad array of human diseases may not be effective. In the event material decisions in any of these areas turn out to be incorrect or sub-optimal, we may experience a material adverse impact on our business and ability to fund our operations and we may never realize what we believe is the potential of our DELigase platform.

We face substantial competition in an environment of rapid technological change, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. Moreover, the biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face and will continue to face competition from third parties that use protein modulation, antibody therapy, adoptive cell therapy, inhibitory nucleic acid, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. The competition is likely to come from multiple sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research institutions that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are aware of a number of biotechnology companies focused on developing small molecules that degrade target proteins or inhibit E3 ligases, including, but not limited to, Accutar Biotechnology Inc., Arvinas, Inc., BeiGene, Ltd., BioTheryX, Inc., C4 Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics Inc., HotSpot Therapeutics, Inc., Kymera Therapeutics, Inc. and Monte Rosa Therapeutics, all of which currently are in preclinical or clinical development. In addition, certain large pharmaceutical companies have disclosed investments in this field, including AbbVie Inc., Amgen Inc., AstraZeneca plc, Bayer AG, Bristol-Myers Squibb Company, Genentech, Inc., GlaxoSmithKline plc and Novartis International AG. Furthermore, we are aware of multiple other BTK degrader programs in clinical development, including programs from AbbVie Inc., Accutar Biotechnology, Inc., BeiGene, Ltd, Haisco Pharmaceutical Group Co., Ltd. and Ubix Therapeutics, Inc.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Further, mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. All of these competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could prevent us from obtaining the orphan designation in the European Union (EU) and/or in the UK and result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our drug candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

If we do not achieve our projected development goals in the time frames we expect and announce, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings and may be associated with payments from third-party collaborators such as Gilead, Sanofi or Pfizer. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, our revenue may be lower than expected, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

Our estimated market opportunities for our drug candidates are subject to numerous uncertainties and may prove to be inaccurate. If we have overestimated the size of our market opportunities, our future growth may be limited.

Our estimated addressable markets and market opportunities for our drug candidates are based on a variety of inputs, including data published by third parties, our own market insights and internal market intelligence and internally generated data and assumptions. We have not independently verified any third-party information and cannot be assured of its accuracy or completeness. Market opportunity estimates, whether obtained or derived from third-party sources or developed internally, are subject to significant uncertainty and are based on assumptions and estimates that may prove inaccurate. Although we believe our market opportunity estimates are reasonable, such information is inherently imprecise. In addition, our assumptions and estimates of market opportunities are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including but not limited to those described in this Annual Report on Form 10-K. If this third-party or internally generated data prove to be inaccurate or if we make errors in our assumptions based on that data, our actual market may be more limited than we estimate it to be. In addition, these inaccuracies or errors may cause us to misallocate capital and other critical business resources, which could harm our business.

Risks Related to Dependence on Third Parties

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

We have sought third-party collaborators for the research, development and commercialization of some of our targeted protein degrader programs. For example, in June 2019 we entered into a collaboration with Gilead; in December 2019 we entered into a collaboration with Sanofi, which was subsequently expanded and amended in January 2021; and in September 2023 we entered into a collaboration with Seagen Inc. (now a part of Pfizer). Each of the foregoing collaborations requires us to conduct certain research activities. Our likely collaborators for any other collaboration arrangements include large and mid-size pharmaceutical companies, biotechnology companies and universities. These and any future arrangements with third parties limit our control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any drug candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into.

Collaborations involving our research programs or any drug candidates we may develop, including our collaborations with Gilead, Sanofi and Pfizer, pose risks to us, including:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations with us.
- Collaborators may not pursue development and commercialization of any drug candidates we may develop or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition or business combination that diverts resources or creates competing priorities.
- Gilead and Sanofi have broad option rights to select up to five targets each, and Pfizer has option rights to multiple targets, for exclusive targeted protein degrader development, so long as not excluded by us under the terms of each collaboration, and may select targets we are considering but have not taken sufficient action to exclude under each collaboration.
- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing.

- Collaborators could develop independently, or develop with third parties, products that compete directly or indirectly with our products or drug candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products.
- Collaborators may not properly obtain, maintain, enforce or defend our intellectual property or proprietary rights or may use our proprietary information in such a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Gilead, Sanofi and Pfizer have the first right to enforce or defend certain intellectual property rights under the applicable collaboration arrangement with respect to particular licensed programs, and although we may have the right to assume the enforcement and defense of such intellectual property rights if the collaborator does not, our ability to do so may be compromised by their actions.
- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or drug candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control. For example, Sanofi may terminate its agreement with us if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug candidates. For example, each of Gilead, Sanofi and Pfizer can terminate its agreement with us in its entirety or with respect to a specific target for convenience upon written notice or in connection with a material breach of the agreement by us that remains uncured for a specified period of time.
- Collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner, or at all. For instance, if a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

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

We may in the future decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of any drug candidates we may develop. These relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute the ownership interest of our existing stockholders, or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators, and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend upon, among other things, our assessment of the proposed collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of several factors. If we license rights to any drug candidates we or our collaborators may develop, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

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

We plan to continue to selectively pursue collaborations with leading biopharmaceutical and biotechnology companies with development and commercial expertise and capabilities. We face significant competition in attracting appropriate collaborators to advance the development of any drug candidates for which we may seek a collaboration. Whether we reach a definitive agreement for a collaboration will depend upon, among other things, our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of preclinical studies and clinical trials, the likelihood of approval by the FDA or other regulatory authorities, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing products, uncertainty with respect to our ownership of technology (which can exist if there is a challenge to such ownership without regard to the merits of the challenge), the terms of any existing collaboration agreements and industry and market conditions generally. The collaborator also may have the opportunity to collaborate on other drug candidates or technologies for similar indications and will have to evaluate whether such a collaboration could be more attractive than one with us.

Collaborations are complex and time-consuming to negotiate, document and execute. In addition, consolidation among large pharmaceutical companies has reduced the number of potential future collaborators, and we may not be able to locate a suitable collaborator. Any collaboration we enter into may limit our ability to enter into future agreements on particular terms or covering similar target indications with other potential collaborators.

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

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for completing such trials.

We rely on third-party contract research organizations (CROs) to conduct our Phase 1 clinical trial programs for NX-5948, NX-2127 and NX-1607 and we will rely on third-party CROs to conduct any clinical trials for other drug candidates. Agreements with these CROs might terminate for a variety of reasons, including for such CRO's failure to perform. Entry into alternative arrangements, if necessary, could significantly delay our product development activities.

Our reliance on these CROs for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols in the applicable IND. Moreover, the FDA and other foreign regulators such as the EMA and the MHRA require compliance with good clinical practice standards, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected.

If these CROs do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our drug candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our drug candidates.

We rely on third-party contract manufacturing organizations (CMOs) for the manufacture of both drug substance and finished drug product for our drug candidates for preclinical and clinical testing and expect to continue to do so for any future clinical trials and commercialization. This reliance on third parties may increase the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on and expect to continue to rely on third-party contract manufacturing organizations (CMOs) for both drug substance and finished drug product. This reliance on CMOs, particularly where one CMO is the sole source of the drug substance or finished drug product, may increase the risk that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We may be unable to establish agreements with CMOs or to do so on acceptable terms. Even if we are able to establish agreements with CMOs, reliance on them entails additional risks, including:

- reliance on the CMO for regulatory, compliance and quality assurance;
- the possible breach of the manufacturing agreement by the CMO;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the CMO at a time that is costly or inconvenient for us.

We have only limited technology transfer agreements in place with respect to our drug candidates, and these arrangements do not extend to commercial supply. We acquire many key materials on a purchase order basis. As a result, we do not have long-term committed arrangements with respect to our drug candidates and other materials. If we receive marketing approval for any of our drug candidates, we will need to establish an agreement for commercial manufacture with a third party.

The CMOs we retain may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions or other adverse regulatory actions, including untitled or warning letters, clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, failure to approve pending applications, license revocation, seizures or recalls of drug candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

The facilities used by our contract manufacturers to manufacture our drug candidates must be approved by the FDA or the EMA or other national or international regulatory agencies pursuant to inspections that will be conducted after we submit our new drug application (NDA) to the FDA or our MAA to the EMA or other regulatory authority. We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, the EMA or comparable foreign regulatory bodies, they will not be able to secure and/or maintain approval for their manufacturing facilities. In addition, we do not have complete control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, the EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our drug candidates or if such regulatory authority withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our drug candidates, if approved.

Our drug candidates and any products that we may develop may compete with other drug candidates and products for access to suitable manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval or could result in withdrawal of marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current CMOs cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement manufacturer or may not be able to reach agreement with any alternative manufacturer.

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

Some of our suppliers may experience disruption to their respective supply chain due to the effects of macroeconomic conditions, which could delay, prevent or impair our development or commercialization efforts.

We obtain certain chemical or biological intermediates in the synthesis of our drug candidates and natural health products (NHPs) for toxicology testing in countries affected by macroeconomic events and conditions, including inflation, increasing interest rates, uncertainty with respect to the federal budget and debt ceiling and potential government shutdowns related thereto, increasing financial market volatility and uncertainty, the impact of war or military conflict, including regional conflicts around the world, and public health pandemics. If we are unable to obtain these chemical or biological intermediates or NHPs in sufficient quantity and in a timely manner due to disruptions in the global supply chain caused by macroeconomic events and conditions, the development, testing and clinical trials of that drug candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Our CMOs may be unable to successfully scale-up manufacturing of our drug candidates in sufficient quality and quantity, which would delay or prevent us from developing our drug candidates and commercializing approved products, if any.

In order to conduct clinical trials of our drug candidates, we will need to manufacture our drug candidates in large quantities. Quality issues may arise during scale-up activities. Our reliance on a limited number of CMOs, the complexity of drug manufacturing and the difficulty of scaling up a manufacturing process could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our drug candidates, cause us to incur higher costs and prevent us from commercializing our drug candidates successfully. Furthermore, if our CMOs fail to deliver the required commercial quality and quantities of materials on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement CMOs capable of production in a timely manner at a substantially equivalent cost, then testing and clinical trials of that drug candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

Risks Related to the Commercialization of Our Drug Candidates

Even if any of our drug candidates receive marketing approval, a drug candidate may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our drug candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, ibrutinib is a well-established current treatment for chronic lymphocytic leukemia (CLL), and doctors may continue to rely on this and other treatments. If our drug candidates do not achieve an adequate level of acceptance, we may not generate sufficient revenue from product sales and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects, in particular compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of our marketing, sales and distribution support;
- the availability of third-party payor coverage and adequate reimbursement;
- the ability to secure a positive HTA recommendation for the product to be prescribed and reimbursed under the national health system;
- the timing of any marketing approval in relation to other product approvals; and
- any restrictions on the use of our products together with other medications.

If we are unable to establish sales and marketing capabilities, we may not be successful in commercializing our drug candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of biopharmaceutical products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales, marketing and distribution capabilities, either by ourselves or through collaboration or other arrangements with third parties.

We currently expect that we may build our own focused, specialized sales and marketing organization to support the commercialization in the United States of drug candidates for which we receive marketing approval and which can be commercialized with such capabilities. There are risks involved with establishing our own sales and marketing capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a drug candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have incurred these commercialization expenses prematurely or unnecessarily. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, reimbursement, customer service, medical affairs and other support personnel;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales and marketing capabilities or enter into arrangements with third parties to perform these services, our revenue from product sales and our profitability, if any, are likely to be lower than if we ourselves were to market and sell any products that we develop. In addition, we may not be successful in entering into arrangements with third parties to market and sell our drug candidates or may be unable to do so on terms that are acceptable to us. Any of these third parties may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates.

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

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a drug candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Our ability to commercialize any drug candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers, national health technology assessment authorities in Europe and other organizations, and if reimbursement and coverage is available, the level of reimbursement and coverage. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A key focus in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, as well as mandating a system of manufacturer rebates to government payors. Increasingly, government authorities and third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be sufficient to cover our costs. Reimbursement may affect the demand for, or the price of, any drug candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval.

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

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

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

- decreased demand for any drug candidates or products that we may develop;
- termination of clinical trials;
- withdrawal of marketing approval, recall, restriction on the approval or a “black box” warning or contraindication for an approved drug;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- injury to our reputation and significant negative media attention;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our product liability insurance coverage as we initiate our clinical trials, as we expand our clinical trials and if we commence commercialization of our drug candidates. Insurance coverage is increasingly expensive. We may not be able to maintain or increase our insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology, our current drug candidates and any future drug candidates that we may develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize technology and drug candidates similar or identical to ours, and our ability to successfully commercialize our technology and drug candidates may be impaired, and we may not be able to compete effectively in our market.

Our commercial success depends, in large part, on our ability to obtain and maintain patent and other intellectual property and proprietary protection in the United States and other countries with respect to our current drug candidates, future drug candidates that we may develop and proprietary technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and drug candidates. If we are unable to obtain or maintain patent protection with respect to our proprietary drug candidates and technology or do not otherwise adequately protect our intellectual property, competitors and other third parties may be able to use our drug candidates and technologies and erode or negate any competitive advantage that we may have, which could have a material adverse effect on our business. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors and other third parties to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Moreover, the patent applications we own, co-own or license may fail to result in issued patents that cover our current and future drug candidates in the United States or in other foreign countries. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, a patent issues from such applications, and then only to the extent the issued claims cover the technology. If the patent applications we hold with respect to our development programs and drug candidates fail to issue, if their breadth or strength of protection is threatened or if they fail to provide meaningful exclusivity for our current and future drug candidates, it could have a material adverse effect on our ability to commercialize our drug candidates and our business.

To protect our proprietary positions, we file patent applications in the United States and other countries related to our novel technologies and drug candidates that are important to our business. The patent application and prosecution process is expensive, complex and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications in all potential jurisdictions at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments, and it is possible that we may be unable to correct such defects. If any current or future licensors or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised and we might not be able to prevent third parties from making, using and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors and other third parties may independently develop equivalent knowledge, methods and know-how, or design around our claimed subject matter. Any of these outcomes could impair our ability to prevent competition from third parties.

Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our therapeutics 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, clinicians may prescribe these products "off-label." 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. Consequently, the types of claims in issued patents of our patent portfolio may fail to afford strong protection against third-party infringement.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including U.S. Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. In addition, the protections offered by laws of different countries vary and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law and jurisprudence restricts the patentability of methods of treatment of the human body more than U.S. patent law does. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights, whether owned or in-licensed, are highly uncertain.

We may not be aware of all third-party intellectual property rights potentially relating to our current and future drug candidates or their intended uses, and as a result the impact of such third-party intellectual property rights upon the patentability of our own patents and patent applications, as well as the impact of such third-party intellectual property upon our freedom to operate, is highly uncertain. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions typically are not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we or our licensors were the first to make the inventions claimed in our patents or pending patent applications, or that we or our licensors were the first inventors to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications, whether owned or in-licensed, may not result in patents being issued that protect our technology or drug candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. Moreover, we may be subject to third-party challenges in patent offices in the United States and abroad. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. For example, our pending patent applications may be subject to third-party submissions of prior art to the United States Patent and Trademark Office (USPTO) challenging the validity of one or more claims of our owned or licensed pending patent applications, precluding the granting of a patent based on one of our owned or licensed pending patent applications or we may become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or other post-grant proceedings, in the United States or elsewhere, challenging our or our licensors' patent rights or the patent rights of others. An adverse determination in any such challenge could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drug candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights, which could significantly harm our business and results of operations. Such challenges may result in loss of patent rights or exclusivity, or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drug candidates, or limit the duration of the patent protection of our technology and drug candidates. Such proceedings also may result in substantial cost and require significant time from our scientific personnel and management, even if the eventual outcome is favorable to us. In addition, any threat to the breadth or strength of protection provided by our patents and patent applications could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates.

Even if our patent applications issue as patents and are unchallenged, they may not issue in a form that will provide us with any meaningful protection against competing products or processes sufficient to achieve our business objectives, prevent competitors and other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors and other third parties may be able to design around or circumvent our patents, should they issue, by developing similar or alternative technologies or products in a non-infringing manner. Our competitors and other third parties may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. If the patent protection provided by the patents and patent applications we own or license is not sufficiently broad and strong to impede such competition, our ability to successfully commercialize our drug candidates could be negatively affected and companies may be dissuaded from collaborating with us, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes in patent law in the United States and in non-U.S. jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our drug candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity, and therefore is costly, time-consuming and inherently uncertain. Past or future patent reform legislation in the United States and other countries could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents, may diminish the value of our patents or narrow the scope of our patent protection and may affect the scope, strength and enforceability of our patent rights or the nature of proceedings that may be brought by or against us related to our patent rights.

Additionally, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions and actions by the U.S. Congress, the U.S. Supreme Court, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. Any of the foregoing, including any similar adverse changes in the patent laws of other jurisdictions, could also have a material adverse effect on our business, financial condition, results of operations and prospects.

Even if we are able to obtain patent protection for our drug candidates, the life of such protection is limited, and third parties could develop and commercialize products and technologies similar or identical to ours and compete directly against us after the expiration of our patent rights and our ability to successfully commercialize any product or technology would be materially adversely affected.

The life of a patent and the protection it affords is limited. For example, in the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Even if we successfully obtain patent protection for an approved drug candidate, it may face competition from generic or biosimilar medications. Manufacturers of generic or biosimilar drugs may challenge the scope, validity or enforceability of our patents in court or before a patent office, and we may not be successful in enforcing or defending those intellectual property rights and, as a result, may not be able to develop or market the relevant product exclusively, which would materially adversely affect any potential sales of that product.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after such drug candidates are commercialized. As a result, our patents and patent applications may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a U.S. patent may also be shortened if the patent is terminally disclaimed over an earlier-filed patent. A patent term extension ("PTE") based on regulatory delay may be available in the United States. However, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Laws governing extensions analogous to PTEs in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. If we are unable to obtain PTE or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our therapeutic will be shorter and our competitors may obtain approval of competing products following our patent expiration and may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data to launch their product earlier than might otherwise be the case, and our revenue could be reduced, possibly materially. Upon the expiration of patents that may issue from our pending patent applications, we will not be able to assert such patent rights against potential competitors and other third parties, which would materially adversely affect our business, financial condition, results of operations and prospects.

We may need to license intellectual property from third parties, such licenses may not be available or may not be available on commercially reasonable terms and we may not be successful in obtaining or maintaining necessary rights to our drug candidates through acquisitions and in-licenses.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our drug candidates. It may be necessary for us to use the patented or proprietary technology of a third party to commercialize our own technology or drug candidates, in which case we would be required to obtain a license from such third party. Because our development programs may in the future require the use of proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license, or use these third-party proprietary rights. A license to such intellectual property may not be available or may not be available on commercially reasonable terms, which could have a material adverse effect on our business, financial condition, results of operations and prospects. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our drug candidates.

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, also may be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our drug 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. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional drug candidates we may seek to acquire. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or drug candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, and third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on our business.

Our commercial success depends, in part, upon our ability, and the ability of our collaborators to develop, manufacture, market and sell our drug candidates and future drug candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties.

Numerous third-party U.S. and non-U.S. issued patents exist in the area of biotechnology, including in the area of targeted protein degraders and including patents owned or controlled by our competitors. There is considerable and complex intellectual property litigation in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination and *inter partes* review proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates, future drug candidates and technology, including interference, derivation, reexamination or *inter partes* review proceedings before the USPTO. Our competitors or other third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future and claims may also come from competitors or other third parties against whom our own patent portfolio may have no deterrent effect. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. Other parties may allege that our drug candidates or the use of our technologies infringe patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization.

As we continue to develop and, if approved, commercialize our current and future drug candidates, competitors or other third parties may claim that our technology infringes, misappropriates or otherwise violates their intellectual property rights. There are and may in the future be additional U.S. and foreign-issued patents and pending patent applications owned by third parties in the fields in which we are pursuing drug candidates. For example, we are aware of a patent owned by a third party with a claim that covers many potential targeted protein degraders. This patent may be alleged to cover one or more of our targeted protein degrader drug candidates, including our NX-5948 and NX-2127 drug candidates. While we believe that we have valid defenses against any assertion of such patent against us, such defenses may be unsuccessful. If we are unsuccessful and any of our targeted protein degrader drug candidates is found to infringe this patent, we could be required to obtain a license to such patent or forced to permanently cease developing, manufacturing, marketing and commercializing the infringing targeted protein degrader drug candidate. We may not be able to obtain any required license on commercially reasonable terms or at all, and even if we were able to obtain a license, it could be non-exclusive, thereby giving the licensor and other third parties the right to use the same technologies licensed to us, and it could require us to make substantial licensing, royalty and other payments. We also could be forced, including by court order, to permanently cease developing, manufacturing, marketing and commercializing the drug candidate. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willingly infringed any such patent. Even if we were ultimately to prevail, any litigation could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Moreover, as the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. 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 drug candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Patent and other types of the intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found, or believe there is a risk we may be found, by a court of competent jurisdiction to infringe, misappropriate or otherwise violate a third party's intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our products and technology. In addition, we could be found liable for monetary damages, which could be significant, including treble damages and attorneys' fees if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from producing or commercializing our drug candidates or future drug candidates or force us to cease some of our business operations, which could materially harm our business. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure, including due to any additional or separate regulatory approval to which the redesigned products may be subject by regulatory authorities, and any redesigned products may be of inferior quality or performance. If we lose a foreign patent lawsuit alleging our infringement of a competitor's patents, we could be prevented from marketing our therapeutics in one or more foreign countries and/or be required to pay monetary damages for infringement or royalties in order to continue marketing. Claims that we have misappropriated the confidential information, trade secrets or other intellectual property of third parties could have a similar negative impact on our business. Any of these outcomes would have a material adverse effect on our business.

Further, we do not know which processes we will use for commercial manufacture of our future products, or which technologies owned or controlled by third parties may prove important or essential to those processes. Many companies have filed, and continue to file, patent applications related to novel protein modulation therapies that target disease-causing proteins and many companies have filed and continue to file patent applications related to ACT. Some of these patent applications have already been allowed or issued and others may issue in the future. Because this area is competitive and of strong interest to pharmaceutical and biotechnology companies, there likely will be additional patent applications filed and additional patents granted in the future, as well as additional research and development programs expected in the future. If a patent holder believes the manufacture, use, sale, offer for sale or importation of one of our drug candidates or future products infringes its patent, the patent holder may sue us even if we have licensed other patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our licensed patent portfolio may therefore have no deterrent effect.

It is also possible that we have failed to identify all relevant third-party patents or applications. Patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. For example, we may incorrectly determine that our drug candidates are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope.

In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale, importation or use of a current or future drug candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our therapeutics. We do not always conduct independent reviews of pending patent applications of and patents issued to third parties.

Furthermore, because patent applications can take many years to issue, may be confidential for 18 months or more after filing and can be revised before issuance, there may be applications now pending that we are not aware of that may later result in issued patents that may be infringed by the manufacture, use, sale or importation of our drug candidates or future products. Additionally, pending patent applications that have been published can, subject to certain limitations, later be amended in a manner that could cover our technologies, our future products or the manufacture or use of our future products. As such, there may be applications of others now pending or recently revived patents of which we are unaware. These patent applications may later result in issued patents, or the revival of previously abandoned patents, that will prevent, limit or otherwise interfere with our ability to make, use or sell our products.

Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. If we were to challenge the validity of an issued U.S. patent in court, such as an issued U.S. patent of potential relevance to some of our drug candidates or future drug candidates or manufacture or methods of use, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This burden is a high one and in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity or enforceability by invalidating the claims of any such U.S. patent or finding that our drug candidates or technology did not infringe any such claims.

We may choose to challenge the enforceability or validity of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in an ex-parte re-exam, *inter partes* review or post-grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party's patent in patent opposition proceedings in the European Patent Office (EPO) or other foreign patent office. The costs of these opposition proceedings could be substantial and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our drug candidates or proprietary technologies.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may be time-consuming, cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities and ongoing business operations. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our future products or processes. 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. Unlike some of our larger competitors and other third parties, we may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. Uncertainties resulting from the litigation of patent litigation and other proceedings could delay our research and development efforts, adversely affect our ability to raise additional funds and could limit our ability to continue our operations. Any of the foregoing could have a material adverse effect on our business.

We may be subject to claims by third parties asserting that we or our employees, consultants, contractors or advisors have misappropriated, wrongfully used or disclosed alleged trade secrets or other intellectual property, or claiming ownership of what we regard as our own intellectual property.

We may hire and employ individuals who were previously employed at, or may have previously provided or may be currently providing consulting services to, universities as well as other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We have received confidential and proprietary information from collaborators, prospective licensees and other third parties. Although we try to ensure that our employees, consultants and advisors do not improperly use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have inadvertently or otherwise improperly used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's former employer. We also may in the future be subject to claims that we have caused such individual to breach the terms of his or her non-competition or non-solicitation agreement or from former employers or other third parties claiming to have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these claims. We may not be successful in defending these claims, and 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. In addition, we may lose personnel as a result of such claims and any such litigation or the threat thereof may adversely affect our ability to hire employees or contract with independent contractors. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our drug candidates, which would have a material adverse effect on our business, results of operations, financial condition and prospects. Even if we are successful, litigation could result in substantial cost and reputational loss and distract our management and other employees from their regular responsibilities.

In addition, although it is our policy to require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Moreover, even when we obtain agreements assigning intellectual property to us, such assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Furthermore, individuals executing agreements with us may have preexisting or competing obligations to a third party, such as an academic institution, and thus an agreement with us may be ineffective in perfecting ownership of inventions developed by that individual. In addition, we or our licensors may in the future be subject to claims by former employees, consultants or other third parties asserting an ownership right in our owned or licensed patents or patent applications. An adverse determination in any such litigation or proceeding 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 stop others from using or commercializing similar technology and therapeutics, without payment to us, or could limit the duration of the patent protection covering our technology and drug candidates. Such challenges may also result in our inability to develop, manufacture or commercialize our drug candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our owned or licensed patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Competitors or other third parties may infringe our patents, the patents of our licensors or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which, regardless of merit, can be expensive, time-consuming, unpredictable and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke those parties to assert counterclaims against us alleging that we infringe their patents or other intellectual property. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensors is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or 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. Grounds for a validity challenge could include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, non-enablement or failure to claim patent-eligible subject matter. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include reexamination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions. Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our drug candidates or prevent third parties from competing with our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which the patent examiner and we or our licensing partners were unaware during prosecution. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose at least part, and perhaps all, of the patent protection on our drug candidates. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention, or decide that the other party's use of our future patented technology falls under the safe harbor to patent infringement under 35 U.S.C. §271(e)(1). An adverse result in any litigation or proceeding involving our patents or patent applications may put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we successfully assert our patents or other intellectual property rights, a court may not award remedies that sufficiently compensate us for our losses. For example, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. The impact of public announcements of the results of hearings related to such awards on the price of our common stock may be uncertain. If securities analysts or investors perceive such results to be negative, it could have a substantial adverse effect on the price of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Some of our competitors or other third parties may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel for significant periods of time during such litigation could outweigh any benefit we receive as a result of the proceedings. In addition, the uncertainties associated with litigation could compromise our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology or other drug candidates, or enter into development partnerships that would help us bring our drug candidates to market. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be able to pursue or guarantee protection of our intellectual property rights in jurisdictions outside the United States.

Patents are of national or regional effect. Filing, prosecuting and defending patents on drug candidates, research programs and technology in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain technology and drug candidates outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors or other third parties may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our drug candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

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

In Europe, beginning June 1, 2023, European applications and patents may be subject to the jurisdiction of the Unified Patent Court (UPC). Also, European applications will have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the UPC. This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. As a single court system can invalidate a European patent, we, where applicable, may opt out of the UPC, and as such, each European patent would need to be challenged in each individual country.

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

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and/or patent application are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent and/or patent application. The USPTO and patent offices in various foreign countries require compliance with a number of procedural, documentary, fee payment and other similar requirements during the patent application process and throughout the life of a granted patent. 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 a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors or other third parties might be able to enter the market, which could have a material adverse effect on our business and competitive position.

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

We may 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. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our drug candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. 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.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

In addition to seeking patents for some of our technology and drug candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, and confidentiality agreements to maintain our competitive position. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third-party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

Trade secrets can be difficult to protect. We seek to protect our trade secrets, proprietary technology and processes, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems; however, such systems and security measures may be breached, and we may not have adequate remedies for any breach. We cannot guarantee that we have entered into such agreements with each party that may have or had access to our trade secrets or proprietary technology and processes and even in cases we have, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or used in an unauthorized manner by third parties. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. Furthermore, despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is expensive, time-consuming and difficult to prove and the outcome is unpredictable. In addition, some courts inside and outside of the United States may be less willing or unwilling to protect trade secrets. As a result, we could lose our trade secrets and third parties could use our trade secrets to compete with our drug candidates and technology.

Moreover, our competitors or other third parties may independently develop knowledge, methods and know-how equivalent to our trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third parties, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third parties, our competitive position would be harmed.

Intellectual property rights do not necessarily address all potential threats.

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

- others may be able to make products that are similar to any drug candidates we may develop or utilize similar technology but that are not covered by the claims of the patents that we own or license now or in the future, or may develop drug candidates for the diseases our drug candidates seek to treat that do not infringe on our intellectual property rights, but which perform better or are more successful than our drug candidates;
- drug candidates utilizing issued patents and other intellectual property that we hold may prove to be ineffective for their intended treatment or we may not obtain regulatory approval for such drug candidates;
- we, or our current or future license partners or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or license now or in the future;
- we, or our current or future license partners or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending owned patent applications or those that we may own or license in the future will not lead to issued patents;
- we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own will result in issued patents with claims directed to our drug candidates or uses thereof in the United States or in other foreign countries;
- the claims of any current patents or patent issuing based on patent applications that we own may not provide protection against competitors or any competitive advantages or may be challenged by third parties;
- issued patents that we may hold rights to in the future may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing drug candidates;
- we may need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose;
- if we enforce and/or defend our patent rights, a court may not hold that our patents are valid, enforceable and infringed;
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent application covering such intellectual property;
- we may fail to adequately protect and police our trademarks and trade secrets; and
- the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving subject matter that is covered by our patent applications.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Approval and Marketing of Our Drug Candidates

The regulatory approval process of the FDA and other national or European regulators is lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain marketing approval for our drug candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and other national or European regulators is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions. We have not obtained marketing approval for any drug candidate, and it is possible that none of our existing drug candidates, or any drug candidates we may seek to develop in the future, will ever obtain marketing approval.

Our drug candidates could be delayed or fail to receive marketing approval for many reasons, including the following:

- the FDA may disagree with our interpretation of data from preclinical studies or clinical trials;
- the FDA may disagree with the design or implementation of our planned clinical trials;
- data collected from clinical trials of our drug candidates may not be sufficient to support the submission of an NDA to the FDA or other submissions necessary to obtain marketing approval in the United States;
- we may be unable to demonstrate to the satisfaction of the FDA that a drug candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA for approval;
- we may be unable to demonstrate that our drug candidates' clinical and other benefits outweigh their safety risks;
- the FDA may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market any of our drug candidates, which would significantly harm our business, results of operations, financial condition and prospects. The FDA has substantial discretion in the approval process, and in determining when or whether regulatory approval will be obtained for any of our drug candidates. Even if we believe the data collected from clinical trials of our drug candidates are promising, such data may not be sufficient to support approval by the FDA.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our drug candidates for fewer or more limited indications than we request, or they may impose significant limitations in the form of narrow indications, warnings or a risk evaluation and mitigation strategy (REMS). In addition, regulatory authorities may not approve the price we intend to charge for our products, may require precautions or contra-indications with respect to conditions of use, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a drug candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that drug candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our drug candidates.

We have received Fast Track designation for NX-5948 and may seek Fast Track designation for other drug candidates in the future. Fast Track designation may not lead to faster development or regulatory review or approval process, and it does not increase the likelihood that our drug candidates will receive marketing approval.

In January 2024, the FDA granted Fast Track designation for NX-5948 in the United States for the treatment of adult patients with relapsed or refractory CLL or small lymphocytic lymphoma after at least two lines of therapy, including a BTK inhibitory and a B-cell lymphoma 2 inhibitor. As part of our business strategy, we may also seek Fast Track designation for other of our drug candidates. Programs with Fast Track designation may be eligible for more frequent interactions with the FDA, and, if relevant criteria are met, eligibility for Accelerated Approval and Priority Review. Fast Track designation applies to the drug candidate and the specific indication for which it is being studied. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular drug candidate is eligible for this designation, we cannot guarantee that the FDA would decide to grant it. If a drug candidate receives Fast Track designation but does not continue to meet the criteria for Fast Track designation, or if our clinical trials are delayed, suspended or terminated, or put on clinical hold due to unexpected adverse events or issues with clinical supply, we will not receive the benefits associated with the Fast Track program.

Furthermore, Fast Track designation does not change the standards for approval. The receipt of Fast Track designation for a drug candidate may not result in a faster development, regulatory review or approval process compared to drug candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if any drug candidate qualifies for FastTrack designation, the FDA may later decide that the drug candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Fast Track designation alone does not guarantee qualification for FDA Priority Review.

Under FDA policies, a drug candidate is eligible for Priority Review, or review within a six-month time frame from the time a complete NDA is accepted for filing, if the drug candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. The FDA determines whether a drug qualifies for Priority Review after an NDA for such drug is submitted to the FDA. Therefore, until we submit NDAs for our drug candidates, we cannot be assured that they will be granted Priority Review. Even if Priority Review is granted for one of our drug candidates, the FDA does not always meet its six-month goal date for Priority Review, and the review process may be extended if the FDA requests additional information or clarification.

We may submit an NDA for our drug candidates under the Accelerated Approval pathway. If we are unable to obtain approval of our drug candidates through the Accelerated Approval Program in the United States, we may be required to conduct additional nonclinical and clinical studies and trials beyond those that we currently contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approval. Even if we receive approval from the FDA through the Accelerated Approval Program, if our confirmatory postmarketing trial does not verify clinical benefit, or if we do not comply with rigorous postmarketing requirements, the FDA may seek to withdraw the approval.

We may submit an NDA for one or more of our drug candidates seeking approval through the Accelerated Approval Pathway. For any approval to market a drug product, we must provide the FDA and foreign regulatory agencies with clinical data that adequately demonstrate the safety and efficacy of the product for the indication applied for in the NDA or other respective regulatory filings. The Accelerated Approval Program is one of several approaches used by the FDA to make prescription drugs more rapidly available for the treatment of serious or life-threatening diseases. Section 506(c) of the Federal Food, Drug and Cosmetic Act (FDCA) provides that the FDA may grant Accelerated Approval to "a product for a serious or life-threatening condition upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on 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." Approval through the Accelerated Approval Program is subject, however, to the requirement that the applicant conduct additional postmarketing clinical trials to verify and describe the drug's clinical benefit, where there is uncertainty as to the relationship of the surrogate endpoint to the clinical benefit, or of the observed clinical endpoint to ultimate outcome. Typically, clinical benefit is verified when postmarketing clinical trials show that the drug provides a clinically meaningful positive therapeutic effect, that is, an effect on how a patient feels, functions, or survives. The FDA may require that these studies be underway prior to Accelerated Approval pursuant to the Food and Drug Omnibus Reform Act of 2022. If such confirmatory trials fail to confirm the drug's clinical profile or risks and benefits, the FDA may withdraw its approval of the drug.

The FDA has broad discretion with regard to approval through the Accelerated Approval Program, and even if we believe that the Accelerated Approval Program is appropriate for one of our drug candidates, we cannot assure you that the FDA will ultimately agree. The FDA may also change its policies with respect to Accelerated Approval over time. For example, in March 2023, the FDA announced the availability of draft guidance on "Clinical Trial Considerations to Support Accelerated Approval of Oncology Therapeutics," in which the agency outlined, and invited public comment on, its "preferred approach" of randomized controlled trials, including those that provide for longer term follow-up that could fulfill a postmarketing requirement to verify clinical benefit. In that draft guidance, the FDA acknowledged that historically, single-arm trial designs and response endpoints have most commonly been used in oncology but noted that such trials have limitations. Furthermore, even if we do obtain approval through the Accelerated Approval Program, we may not experience a faster development process, review or approval compared to conventional FDA procedures.

Even if the FDA reviews an NDA seeking Accelerated Approval, there can be no assurance that approval will be granted on a timely basis, or at all. The FDA may disagree that the design of, or results from, our studies support Accelerated Approval. Additionally, the FDA could require us to conduct further studies or trials prior to granting approval of any type, including by determining that approval through the Accelerated Approval Program is not appropriate and that our clinical trials may not be used to support approval through the conventional pathway. We might not be able to fulfill the FDA's requirements in a timely manner, which would cause delays, or approval might not be granted because our submission is deemed incomplete by the FDA. There also can be no assurance that after subsequent FDA feedback we will continue to pursue approval through the Accelerated Approval Program. A failure to obtain approval through the Accelerated Approval Program could result in a longer time period to obtain approval of our drug candidates, could increase the cost of their development, could delay our ability to commercialize our products and could significantly harm our financial position and competitive position in the marketplace.

Even if we receive approval for one or more of our drug candidates through the Accelerated Approval Program, we will be subject to rigorous postmarketing requirements, including the completion of one or more confirmatory postmarketing trials as the FDA may require, to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw the approval for multiple reasons, including if we fail to conduct any required confirmatory postmarketing trial with due diligence, our confirmatory postmarketing trial does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false and misleading.

Moreover, Congress is considering potential changes to the Accelerated Approval Program that could impact our ability to obtain Accelerated Approval, or increase the burdens associated with postmarketing requirements in the event we do obtain Accelerated Approval. In particular, the FDA must specify certain conditions for required postapproval studies for products that receive Accelerated Approval, which may include enrollment targets and milestones, including the target date for study completion, by the time the drug is approved. The FDA may also require postapproval studies to be underway at the time of Accelerated Approval or within a specified time period following Accelerated Approval for such drugs, and must explain any instances where it does not require such studies.

Any delay in obtaining, or inability to obtain, approval through the Accelerated Approval Program, or any issues in maintaining approval granted under the Accelerated Approval Program, would delay or prevent commercialization of our products, and would materially adversely affect our business, financial condition, results of operations and prospects.

We, as a company, have limited experience in filing for and obtaining regulatory approval to initiate a clinical trial, and we do not have experience completing any clinical trials, including large-scale, pivotal clinical trials or in manufacturing or in quality assurance in order to market a new drug in the United States or in any other jurisdiction.

As a company, we have limited experience in filing for or obtaining regulatory approval to initiate clinical trials, we do not have experience completing any clinical trials, including large-scale, pivotal clinical trials and we rely on third parties to conduct our clinical trials. We also do not have experience in manufacturing or in quality assurance in order to market a new drug and expect to rely on CROs or other third-party consultants or vendors to assist us in this process. Our inexperience may result in failure to or delays in obtaining the required regulatory approvals to initiate clinical trials, to successfully complete clinical trials and to obtain marketing approval for our drug candidates. If we are unable to obtain regulatory and marketing approval for our drug candidates or experience significant delays in our efforts to do so, our business could be substantially harmed.

Failure to obtain marketing approval in foreign jurisdictions would prevent our drug candidates from being marketed abroad and may limit our ability to generate revenue from product sales.

To market and sell our drug candidates in jurisdictions outside the United States, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approvals from foreign regulatory authorities may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Failure to obtain foreign regulatory approvals on a timely basis or non-compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our drug candidates in certain countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any jurisdiction, which would materially impair our ability to generate revenue.

The UK's exit from the EU continues to create political and economic uncertainty, particularly in the UK and the EU. The UK is now being treated as a "third country" by the EU. Although UK legislation has retained existing EU law, new UK legislation is being drafted and the UK has not retained new EU law, including the Clinical Trials Regulation (EU) No 536/2014. This means that some regulatory activities, such as batch testing and Qualified Person certification, conducted in the UK are no longer recognized in the EU; although the UK accepts the batch testing data carried out in many third countries with recognized equivalent high standards to avoid delays and supply disruption due to re-testing. However, the UK and EU have concluded a Trade and Cooperation Agreement (TCA), which has been approved by the UK Parliament, European Council and European Parliament and has limited the disruption to the supply of medicines, particularly by enabling tariff and quota-free trade between the UK and the EU (provided that the rules of origin requirements are met), and has streamlined some issues, for example by enabling mutual recognition of cGMP inspections and certificates. The regulatory framework for medicines that existed before the end of the transition period has also effectively been preserved in UK domestic legislation as "retained EU law." By retaining a snapshot of EU legislation at its core, the UK has prevented substantial divergence in the regulation of medicines (although divergence has appeared in some areas). However, some changes to the UK legislation have been immediately necessary, including the implementation of the Northern Ireland Protocol (NIP), pursuant to which, the EU pharmaceutical legal framework acquis continues to apply in Northern Ireland (subject to periodic consent of the Northern Ireland Legislative Assembly), and only products compliant with EU law can be placed in the Northern Ireland market—adding an extra layer of regulatory complexity. As a result, companies now need to comply with a separate UK regulatory legal framework in order to commercialize medicinal products in Great Britain (namely, England, Wales and Scotland, as EU law continues to apply in Northern Ireland). The UK government has attempted to renegotiate fundamental aspects of the NIP so this is an unpredictable area for companies in the near future. Failed attempts to renegotiate the NIP have led to media reports of the UK potentially triggering Article 16 of the NIP, a safeguarding measure, that may be engaged unilaterally if the application of the NIP leads to serious economic, societal or environmental difficulties that are liable to persist, or to diversion of trade. The UK government has introduced the Northern Ireland Protocol Bill which, if enacted into law, would enable the government to unilaterally disapply parts of the NIP which may lead to changes to the regulatory environment in Northern Ireland, and may trigger retaliatory measures against the UK by the EU. The UK government reached a new agreement with the EU, the "Windsor Framework," which aims to replace the NIP. According to the Windsor Framework, medicinal products intended for the UK market including Northern Ireland will be authorized by the MHRA and will bear a "UK only" label. This means that medicinal products placed on the market in Northern Ireland will no longer need to be compliant with EU law. These new measures will be implemented beginning January 1, 2025. The TCA allows for future deviation from the current regulatory framework, and it is not known if and/or when any deviations may occur, which may have an impact on development, manufacture, marketing authorization, commercial sales and distribution of pharmaceutical products. It is also important to note that obtaining a marketing authorization is not sufficient to gain effective access to the market in the EU and in the UK; companies still need to agree to a reimbursement price for the products and in some jurisdictions, such as the UK and Germany, a further positive recommendation from health technology on cost-effectiveness is required for the products to be actually prescribed and reimbursed by the respective national health systems (see "—Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any" below). If we fail to comply with the regulatory requirements in international markets and thus do not receive applicable marketing approvals, our target market will be reduced, our ability to realize the full market potential of our drug candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, or at all. Our failure to obtain approval of any of our drug candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that drug candidate and our business prospects could decline.

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

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any collaborators, must therefore comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we, and any collaborators, will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA, EMA, MHRA and other regulatory requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance, as well as the corresponding maintenance of records and documentation and reporting requirements. We, our third-party manufacturers, and any collaborators and their third-party manufacturers could be subject to periodic unannounced inspections by the FDA and other regulatory agencies to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any collaborators, receive marketing approval for one or more of our drug candidates, we, any collaborators, and our respective third-party manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any collaborators, are not able to comply with post-approval regulatory requirements, we, and any collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our business, results of operations, financial condition and prospects.

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

Any drug candidate for which we, or any collaborators, obtain marketing approval, as well as the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA, EMA, the MHRA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians, tracking and tracing, serialization, postmarket adverse event reporting and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement REMS. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our drug candidates receive marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

Clinical trials of our drug candidates must be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a drug candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our drug candidates receives marketing approval and we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;

- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the drug may become less competitive in the marketplace; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

The FDA also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of REMS. The FDA and other agencies, including the U.S. Department of Justice (DOJ), closely regulate and monitor the post-approval marketing and promotion of drugs to ensure they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products only for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws. Other jurisdictions, including European countries, have similar provisions which may lead to investigations and enforcement actions by national authorities.

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- suspension of any ongoing clinical trials;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

Non-compliance with EU and UK requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population (as explained further under "—If any of our drug candidates are not considered to be a new active substance or are deemed to fall within the "global marketing authorization" of an existing medicinal product or if pediatric studies are not adequately completed, this may result in lack of regulatory data protection or failure to obtain an extension to existing regulatory data protection," below), also can result in significant financial penalties, and non-compliance with pediatric requirements may prevent regulatory approvals from being granted. Similarly, failure to comply with the EU and UK's requirements regarding the protection of personal information can lead to significant penalties and sanctions.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers which include requirements relating to quality control and quality assurance, as well as the corresponding maintenance of records and documentation and reporting requirements. We, any contract manufacturers we may engage in the future, our collaborators and their contract manufacturers also will be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, such as the requirement to implement a REMS.

If we decide to seek Orphan Drug Designation or other designations from regulators for any of our current or future drug candidates, we may be unsuccessful or may be unable to maintain the benefits associated with these designations, including the potential for supplemental market exclusivity associated with an Orphan Drug Designation.

We may seek Orphan Drug Designation or other designations from regulators for one or more of our current or future drug candidates. Regulatory authorities in some jurisdictions, including the United States, EU and European Economic Area (EEA), Switzerland and the UK, may designate drugs or biological products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological 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 United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug or biological product. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants Orphan Drug Designation, the identity of the drug or biological product 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 process.

If a product that has Orphan Drug Designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including an NDA or BLA, to market the same drug or biological product for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the biological product was designated. As a result, even if one of our drug candidates receives orphan exclusivity, the FDA can still approve or license other drugs or biological products for use in treating the same indication or disease. Further, the FDA can waive orphan exclusivity if we are unable to manufacture sufficient supply of our product.

In addition, Congress is considering updates to the orphan drug provisions of the FDCA in response to a recent decision by the U.S. Court of Appeals for the Eleventh Circuit. Any changes to the orphan drug provisions could change our opportunities for, or likelihood of success in obtaining, orphan drug exclusivity and would materially adversely affect our business, results of operations, financial condition and prospects.

We may seek Orphan Drug Designation for our drug candidates in additional orphan indications in which there is a medically plausible basis for the use of these drug candidates. Even when we obtain Orphan Drug Designation, exclusive marketing rights in the United States may be limited if we seek licensure 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 we, through our manufacturer, are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we may seek Orphan Drug Designation for other drug candidates, we may never receive these designations.

In order to obtain orphan designation in the EEA (the UK has a similar legislation), the product must fulfill certain criteria. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as an orphan medicinal product if it meets the following criteria: (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either the prevalence of such condition must not be more than five in 10,000 persons in the EU when the application is made, or without the benefits derived from orphan status, it must be unlikely that the marketing of the medicine would generate sufficient return in the EU to justify the investment needed for 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.

Products receiving orphan designation in the EU may receive 10 years of orphan market exclusivity (which can be further extended by two years if pediatric studies have been conducted in accordance with an agreed pediatric investigational plan). Applications must first satisfy the orphan designation criteria and apply for orphan designation before making the application for marketing authorization. The applicant must then successfully maintain the orphan designation at the time of the MAA in order to qualify for 10 years of orphan market exclusivity. During this 10-year period, the competent authorities of the EU Member States and European Commission may not accept applications or grant marketing authorization for other similar medicinal products for the same orphan therapeutic indication. The protection afforded by orphan market exclusivity in the EU may, in some circumstances, be circumvented by competitor products which are demonstrated not to be "similar" or which are authorized for different therapeutic indications. There may be a risk that products may be prescribed "off-label" for the orphan therapeutic indication by healthcare professions in some EU Member States.

There are also three exceptions to the orphan market exclusivity principle. Marketing authorization may be granted to a similar medicinal product for the same orphan therapeutic indication if:

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

An orphan product can also obtain an additional two years of orphan market exclusivity in the EU if the MAA contains the results of all pediatric studies conducted in accordance with and agreed pediatric investigation plan. The 10-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.

The UK's regulatory legal framework provides for similar periods of protection (namely regulatory data protection, marketing protection and market exclusivity).

It is important to note that the regulatory protection afforded to medicinal products such as data exclusivity, marketing protection, market exclusivity for orphan indications and pediatric extension are currently under review at the EU level. It is expected that the protection currently afforded in the EU will be reduced in the years to come. On April 26, 2023, the European Commission adopted a proposal for a new Directive and a new Regulation. If enacted into law, this proposal will revise and replace the existing general pharmaceutical legislation and will affect the existing period of regulatory protections afforded to medicinal products.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our drug candidates that receive marketing approval, or such authorities do not grant our drug candidates appropriate periods of data or market exclusivity before approving generic versions of our drug candidates, the sales of our drug candidates could be adversely affected.

Once an NDA is approved, the drug covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations." Manufacturers may seek marketing approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications (ANDAs) in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials demonstrating safety and efficacy. Rather, the applicant generally must show that its drug is pharmaceutically equivalent to the reference listed drug, in that it has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug, and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic drugs may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic drugs are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug is typically lost to the generic drug.

The FDA may not approve an ANDA for a generic drug until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug candidate where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an approved NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug candidate. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drug candidates containing the original active agent for other conditions of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Manufacturers may seek to launch these generic drugs following the expiration of the marketing exclusivity period, even if we still have patent protection for our drug.

Competition that our drug candidates may face from generic versions of our drug candidates could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those drug candidates. Our future revenues, profitability and cash flows could also be materially and adversely affected and our ability to obtain a return on the investments we have made in those drug candidates may be substantially limited if our drug candidates, if and when approved, are not afforded the appropriate periods of non-patent exclusivity.

If any of our drug candidates are not considered to be a new active substance or are deemed to fall within the "global marketing authorization" of an existing medicinal product or if pediatric studies are not adequately completed, this may result in lack of regulatory data protection or failure to obtain an extension to existing regulatory data protection.

Where an applicant for a marketing authorization submits a full dossier containing its own pharmaceutical, preclinical tests and clinical trials data, and where the application does not fall within the "global marketing authorization" of an existing medicinal product, the applicant is entitled to eight years of regulatory data protection upon grant of the marketing authorization (the period starts to run from the first marketing authorization in the EU and EEA). During this period, applicants for approval of generics or biosimilars cannot rely on data contained in the marketing authorization dossier submitted for the already authorized, or reference, medicinal product to support their application. After the expiration of the eight-year period of regulatory data protection, the reference medicinal product benefits from a further two-year period of marketing protection. During these two years of marketing protection, no generic or biosimilar medicinal product that relies upon the reference medicinal product's dossier may be placed on the EU market, but a generic or biosimilar MAA can be submitted to the competent regulatory authorities in the EU Member States during this time. The two-year period of marketing protection can further be extended by one year if, during the first eight years of the grant of the first marketing authorization, 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, even if a compound is considered to be a new active substance and the innovator is able to gain the period of regulatory data protection and marketing protection, provided that no other IP or regulatory exclusivities applied, another unrelated company could also apply for a marketing authorization and market another competing medicinal product for the same therapeutic indication if such company obtained its own marketing authorization based on a separate MAA based on a full self-standing scientific data package supporting the application. The period of regulatory data protection and marketing protection applies in the UK (running from the date of the first authorization in Great Britain).

In the EU, pursuant to Regulation 1901/2006, and in the UK pursuant to the Human Medicines Regulations 2012 (as amended), MAAs must include pediatric data based on pediatric investigation plans agreed with the EMA if the MAA concerns (i) a new active substance, or (ii) a new indication, pharmacological form, or route of administration (where the product is protected by a supplementary protection certificate or a patent qualifying for a supplementary certificate). Applicants may obtain waivers or deferrals to these requirements in certain circumstances (for example a waiver may be obtained if the condition only occurs in adult populations). Where required, pediatric studies must cover all sub-sets of the pediatric population for both existing and new indications, pharmacological forms and route of administrations. Limited further exclusions apply, including in relation to generic or biosimilar applications. Certain rewards may be available for completion of pediatric studies. For example, where MAAs include the results of all studies conducted in compliance with an agreed pediatric investigation plan, the holder of the patent or supplementary protection certificate may be entitled to a six-month extension to the supplementary protection certificate. Additionally, the European Commission's new proposed legislation, if implemented, will also affect the current EU legal framework of pediatric medicines.

Our operations and relationships with actual and potential customers, providers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties including criminal sanctions, civil penalties, exclusions from government programs, contractual damages and reputational harm, and could diminish our future profits and earnings.

Our arrangements with third-party payors, physicians, and other potential customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drug candidates for which we obtain marketing approval.

Applicable U.S. federal and state and non-U.S. healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, a criminal law, which prohibits, among other things, persons and entities from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, in cash or in kind, to induce or reward purchasing, leasing, ordering, or arranging for, referring, or recommending the purchase, lease or order of any good or service for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid. 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. Violations of the federal Anti-Kickback Statute can result in significant civil monetary penalties and criminal fines, as well as imprisonment and exclusion from participation in federal healthcare programs;
- the federal Civil False Claims Act, which may be enforced through civil whistleblower or qui tam actions and imposes significant civil penalties, treble damages and potential exclusion from federal healthcare programs against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or for making a false record or statement material to an obligation to pay the federal government or for knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Further, a violation of the federal Anti-Kickback Statute can serve as a basis for liability under the federal Civil False Claims Act. There is also the federal Criminal False Claims Act, which is similar to the federal Civil False Claims Act and imposes criminal liability on those that make or present a false, fictitious or fraudulent claim to the federal government;
- the federal Civil Monetary Penalties Law, which authorizes the imposition of substantial civil monetary penalties against an entity that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal health care programs to provide items or services reimbursable by a federal health care program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;
- federal criminal statutes created by the Health Insurance Portability and Accountability Act (HIPAA), which impose criminal liability for, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program, including private insurance plans, or, in any matter involving a healthcare benefit program, for knowingly and willfully making materially false, fictitious or fraudulent statements in connection with the delivery of or payment for health care benefits;
- HIPAA, as amended by the Health Information Technology for Economic Clinical Health Act, and its implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Food, Drug, and Cosmetic Act and Public Health Service Act which among other things, strictly regulates drug marketing, prohibits manufacturers from marketing such products for off-label use or misbranding or adulterating their products, and regulates the distribution of samples;
- the federal and state laws that require pharmaceutical manufacturers to report certain calculated product pricing metrics to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of product coverage and reimbursement under federal healthcare programs;
- the federal Physician Payment Sunshine Act, which requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, among others, to annually track and report payments and other transfers of value provided to U.S.-licensed physicians, teaching hospitals, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse-midwives, as well as certain ownership and investment interests held in the manufacturer by physicians and their immediate families;

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to our business practices, including sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers;
- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and relevant compliance guidance promulgated by the federal government;
- state 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;
- state and local laws that prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals; require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging; impose payment caps on certain pharmaceutical products deemed by the state to be "high cost"; and require the registration of pharmaceutical sales representatives; and
- state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of drug candidates from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may also be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause us to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

Providing benefits or advantages to induce or reward improper performance generally to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU and the UK. The provision of benefits or advantages to induce or reward improper performance is governed by the national anti-bribery laws of EU Member States, and in respect of the UK, the UK Bribery Act 2010 (Bribery Act). Infringement of these laws may result in substantial fines and imprisonment. EU Directive 2001/83/EC, which is the EU Directive governing medicinal products for human use, provides that, where medicinal products are being promoted to healthcare professionals, no gifts, pecuniary advantages or benefits in kind may be supplied, offered or promised to such individuals unless they are inexpensive and relevant to the practice of medicine or pharmacy. This provision was transposed into the Human Medicines Regulations 2012 and as such remains applicable in the UK.

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

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our drug candidates. 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. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad.

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any drug candidates for which we obtain marketing approval. The biopharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA-approved product.

Healthcare reform measures that may be adopted in the future may result in reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

To date, there have been several U.S. congressional inquiries and proposed and enacted state and federal legislation and regulations designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient support programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. Most notably, the Inflation Reduction Act (IRA), which was signed into law on August 16, 2022, allows Medicare to: beginning in 2026, establish a "maximum fair price" for a fixed number of pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with the Centers for Medicare and Medicaid Services (CMS); and, beginning in 2023, penalize drug companies that raise prices for products covered under Medicare Parts B and D faster than inflation, among other reforms. CMS has recently taken steps to implement the IRA, including:

- On June 30, 2023, issuing guidance detailing the requirements and parameters of the first round of price negotiations, to take place during 2023 and 2024, for products subject to the "maximum fair price" provision that would become effective in 2026;
- On August 29, 2023, releasing the initial list of 10 drugs subject to price negotiations;
- On November 17, 2023, releasing guidance outlining the methodology for identifying certain manufacturers eligible to participate in a phase-in period where discounts on applicable products will be lower than those required by the Medicare Part D Manufacturer Discount Program; and
- On December 14, 2023, releasing a list of 48 Medicare Part B products that had adjusted coinsurance rates based on the inflationary rebate provisions of the IRA for the time period of January 1, 2024 to March 31, 2024 as well as issuing revised guidance for manufacturers in the Medicare Part B and D drug discount programs.

It is unclear how future regulatory actions to implement the IRA, as well as the outcome of pending litigation against the IRA, may affect our products and future profitability.

On October 14, 2022, President Biden issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of the Department of Health and Human Services (HHS) to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. The Executive Order further directed the Secretary of HHS to submit, within 90 days after the date of the Executive Order, a report regarding any models that may lead to lower cost-sharing for commonly used drugs and support value-based payment that promotes high-quality care. On February 14, 2023, the HHS issued a report in response to the October 14, 2022 Executive Order, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D Sponsors to establish a "high-value drug list" setting the maximum co-payment amount for certain common generic drugs at $2; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements or certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments.

We cannot be sure what impact, if any, the foregoing changes will have on the profitability of any of our drug candidates, if approved for commercial use, in the future.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing. These include legislation and regulations regarding price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, legislative action designed to encourage importation from other countries and bulk purchasing. For example, on January 5, 2024, the FDA approved Florida's importation plan, which allows pharmacists and wholesalers to import certain products from Canada. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. Increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any.

In some countries, particularly the countries of the EU and the UK, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we, or our collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. Furthermore, in some European countries, the authorities conduct an HTA to assess the cost-effectiveness of the product (in the UK that HTA assessment is conducted by the National Institute for Health and Care Excellence), which may significantly impact effective access to the market. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Risks Related to Employees, Managing our Growth and Other Legal Matters

If we fail to attract and retain management and other key personnel, we may be unable to continue to successfully develop our current and any future drug candidates, commercialize our drug candidates or otherwise implement our business plan.

Our ability to compete in the highly competitive biopharmaceuticals industry depends upon our ability to attract and retain highly qualified managerial, scientific, medical, sales and marketing and other personnel. We are highly dependent on our management and scientific personnel, including our President and Chief Executive Officer, Arthur T. Sands, M.D., Ph.D., and Chief Scientific Officer, Gwenn Hansen, Ph.D. The loss of the services of Dr. Sands, Dr. Hansen or other members of our senior leadership team could impede, delay or prevent the successful development of our product pipeline, completion of our current and planned clinical trials, commercialization of our products or in-licensing or acquisition of new assets, and could negatively impact our ability to successfully implement our business plan. If we lose the services of such individuals, we might not be able to find suitable replacements on a timely basis or at all, and our business could be harmed as a result. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees.

We employ all of our executive officers and key personnel on an at-will basis and their employment can be terminated by us or them at any time, for any reason and without notice. In order to retain valuable employees at our company, in addition to salary and cash incentives, we provide stock options and restricted stock units (RSUs) that vest over time. The value to employees of stock options and RSUs that vest over time will be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract offers from other companies.

Moreover, we might not be able to attract or retain qualified management and other key personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area where we are headquartered. We could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. If we are unable to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will harm our ability to implement our business strategy and achieve our business objectives.

In addition, we have scientific and clinical advisors who assist us in formulating our development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

We will need to grow our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As our development and commercialization plans and strategies develop, and as we continue our transition into operating as a public company, we expect to expand our employee base for managerial, operational, financial and other resources. In addition, we have limited experience in product development. We filed our first IND in December 2020 and currently have three drug candidates in ongoing Phase 1 trials. As our drug candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. Our inability to successfully manage our growth and expand our operations could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading laws.

We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include:

- intentional, reckless or negligent conduct or disclosure to us of unauthorized activities that violate the regulations of the FDA or similar foreign regulatory authorities;
- healthcare fraud and abuse in violation of U.S. and foreign laws and regulations;
- violations of U.S. federal securities laws relating to trading in our common stock; and
- failures to report financial information or data accurately.

In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations regulate a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. While we have adopted a code of conduct and implemented other internal controls applicable to all of our employees, 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. Additionally, we are subject to the risk that a person could allege 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 civil, criminal and administrative penalties, damages, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs and diminished profits and future earnings, any of which could adversely affect our ability to operate our business or cause reputational harm.

We depend on our information technology systems, and any failure of these systems, or those of our CROs, third-party vendors, collaborators or other contractors or consultants we may utilize, could harm our business. Security breaches, cyber-attacks, loss of data and other disruptions could compromise sensitive information related to our business or other personal information, prevent us from accessing critical information and expose us to liability, which could adversely affect our business, reputation, results of operations, financial condition and prospects.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems, infrastructure and data to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including but not limited to intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems which are designed to prevent data compromise, and rely on commercially available systems, software, tools and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, resulting in a number of third-party vendors that may or could have access to our confidential information.

Despite the implementation of security measures, our internal information technology systems and infrastructure, and those of our current and any future CROs, collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to breach, breakdown or other damage or interruption from service interruptions, system malfunction, computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet (including harmful attachments to emails, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information), persons inside our organization, or persons with access to systems inside our organization. Any of the foregoing may compromise or lead to data leakage of our system infrastructure, or that of our CROs, third-party vendors and other contractors and consultants.

The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources. In addition, the prevalent use of mobile devices and remote work applications that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property or unauthorized access to personal information. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or those of our third-party vendors, CROs and other contractors and consultants, or inappropriate disclosure of confidential, personal or proprietary information, we could incur liability and reputational damage and the further development and commercialization of our drug candidates could be delayed. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be material, and although we have and continue to invest in and implement security measures designed to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If the information technology systems of our third-party vendors, CROs and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring.

We and our third-party service providers regularly defend against and respond to data security incidents, and we cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems, or those of our third-party vendors, CROs and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations, or financial condition. If such an event were to occur that causes interruptions in our operations, or those of our third-party vendors, CROs and other contractors and consultants, it could result in a material disruption or delay of our product development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or those of our third-party vendors and other contractors and consultants, or security breaches could result in the loss, misappropriation, and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. If any such event, including a computer security breach, results in the unauthorized access, use or release of personal information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state data privacy and security laws (and other similar non-U.S. laws), subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. For example, data breaches frequently result in regulatory actions and commercial and class action litigation based on a variety of laws and legal duties, such as the California Consumer Privacy Act (CCPA), which provides for a private right of action in the event of certain data security breaches. Additionally, the SEC also adopted a new cybersecurity rule requiring companies subject to SEC reporting requirements to formally report material cybersecurity incidents, where failure to report may result in regulatory investigations leading to consent orders that may require additional compliance obligations and/or injunctions, fines and other penalties. Such actions could result in significant legal and financial exposure and reputational damages that could have a material adverse effect on our business, financial condition, results of operations and prospects.

Currently, we carry business interruption coverage and cybersecurity insurance to mitigate certain potential losses, but this insurance is limited in amount and may not be sufficient in type or amount to cover us against claims related to a cybersecurity breach and related business and system disruptions. We cannot be certain that such potential losses will not exceed our policy limits, insurance will continue to be available to us on economically reasonable terms, or at all, or any insurer will not deny coverage as to any future claim. In addition, we may be subject to changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements.

We are or may become subject to a variety of stringent privacy and data security laws, regulations, policies and contractual obligations related to data privacy and security, and changes in such laws, regulations, policies and contractual obligations and our failure, or any failure by our third-party vendors, collaborators, contractors or consultants, to comply with them could harm our business and result in enforcement action by regulators and claims from affected individuals.

We maintain and process, and our third-party vendors, collaborators, contractors and consultants maintain and process on our behalf, a large quantity of proprietary and sensitive information, including confidential business information, personal and patient health information in connection with our preclinical studies and clinical trials and personal information of our employees. We are subject to global privacy and data protection laws and regulations that apply to the collection, transmission, storage and use of personal information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information. Failure by us or our third-party vendors, collaborators, contractors and consultants to comply with any of these laws and regulations could result in enforcement actions by data protection authorities against us, including fines or penalties, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations or prospects.

In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. Each of these laws is subject to varying interpretations and the legislative landscape is constantly evolving. In particular, laws and regulations governing the privacy of health information, such as HIPAA, establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining how protected health information may be used, shared or processed in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. Further, if we fail to comply with applicable privacy laws, we could face civil and criminal penalties, or claims for breach of contract. The HHS has enforcement discretion for HIPAA, and any enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, states have shown an increased interest in protecting the privacy of health data. Washington state passed the My Health My Data Act, which will take effect on March 31, 2024, and is focused on the collection of consumer health data. The My Health My Data Act has a broader scope than HIPAA and includes a private right of action—depending on whether this law applies to us, there may be substantial regulatory action and litigation associated with this act. Following Washington, Nevada enacted Senate Bill 370, which will take effect on March 31, 2024, and is similar to the My Health My Data Act and requires in-scope entities to comply with certain requirements regarding consumer health data. Notably, Senate Bill 370 does not include a private right of action nor does it apply to entities that are subject to HIPAA. Connecticut also amended its comprehensive privacy law in 2023, the Connecticut Data Privacy Act, to impose obligations aimed at "consumer health data." Furthermore, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents pursuant to local state laws. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

Personal data privacy remains an evolving landscape at both the U.S. state and international level, with new regulations coming into effect. For example, the CCPA, which came into effect on January 1, 2020, and was amended and expanded by the California Privacy Rights Act (CPRA) as of January 1, 2023, provides California residents expanded privacy rights, including the right to request correction, access, and deletion of their personal information, the right to opt out of certain personal information sharing, and the right to receive detailed information about how their personal information is processed, including by California residents' employers. Additionally, the CCPA, as amended, requires companies that process personal information of California residents to make disclosures to consumers about their data collection, use and sharing practices, allow consumers to opt out of certain data sharing with third parties, complete certain audits and assessments when processing higher risk data and provide a private right of action for data breaches, as described above. Although the CCPA includes limited exceptions—including exceptions for personal health information collected by covered entities or business associates subject to HIPAA among others, the CCPA may regulate or impact our processing of personal information depending on the context. Failure to comply with the CCPA may result in significant civil penalties, injunctive relief, or statutory or actual damages as determined by the California Privacy Protection Agency, the newly created state agency from the CPRA legislation that is charged with creating new rules and enforcing the CCPA, and the California Attorney General, who also still maintains some CCPA enforcement powers. Notably, following California's lead, several other states enacted privacy laws that took effect in 2023: the Colorado Privacy Act, the Connecticut Personal Data Privacy and Online Monitoring Act, the Utah Consumer Privacy Act, and the Virginia Consumer Data Protection Act. Additional state privacy laws are set to take effect in 2024: the Florida Digital Bill of Rights (July 1, 2024), Montana's Consumer Data Privacy Act (October 1, 2024), Oregon's protections for the personal data of consumer enacted through SB 619 (July 1, 2024), and the Texas Data Privacy and Security Act (July 1, 2024). Compliance with this new privacy legislation adds complexity and may require investment in additional resources for compliance programs, thus potentially result in additional costs and expense of resources to maintain compliance.

In the EU, the EU GDPR governs the collection, use, disclosure, transfer, or other processing of personal data. The UK has implemented the EU GDPR as the UK GDPR which sits alongside the UK Data Protection Act 2018 (the UK GDPR, and together with the EU GDPR, the GDPR). The GDPR imposes compliance obligations on controllers, including (among others) mandating burdensome documentation requirements, granting certain privacy rights to individuals to control how companies collect, use, disclose, retain and otherwise process information about them as well as specific requirements for obtaining valid consent where consent is the legal basis for processing, requirements around accountability and transparency, the obligation to consider data protection when any new products or services are developed, the obligation to appoint data protection officers in certain circumstances, the obligation to notify relevant data supervisory authorities of notifiable personal data breaches without undue delay (and no later than 72 hours) after becoming aware of the personal data breach, and the requirement for more detailed notices for clinical trial subjects and investigators. In addition, the EU GDPR prohibits the international transfer of personal data from clinical trial sites and other third parties (e.g., CROs) located in the EEA to jurisdictions that the European Commission does not recognize as having 'adequate' data protection laws, unless a data transfer mechanism has been put in place or a derogation under the EU GDPR can be relied upon. After years of uncertainty following the July 16, 2020 decision of the Court of Justice of the European Union invalidating the EU-U.S. Privacy Shield Framework for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses (EU SCCs), including a requirement for companies to carry out a transfer privacy impact assessment (TIA), on July 10, 2023, the European Commission adopted its Final Implementing Decision granting the U.S. adequacy (Adequacy Decision) for EU-U.S. transfers of personal data for entities self-certified to the EU-U.S. Data Privacy Framework (DPF). Entities relying on EU SCCs for transfers to the United States are also able to rely on the analysis in the Adequacy Decision as support for their TIA regarding the equivalence of U.S. national security safeguards and redress.

Under the UK GDPR, companies not established in the UK but who process personal data in relation to the offering of goods or services to individuals in the UK, or to the monitoring of their behavior will be subject to the UK GDPR—the requirements of which at this time are largely aligned with those under the EU GDPR. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU Member States to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission reassesses and renews/extends that decision, and remains under review by the European Commission during this period.

The UK GDPR also imposes similar restrictions on transfers of personal data from the UK to jurisdictions that the UK Government does not consider adequate, including the U.S.. The UK's Information Commissioner's Office (ICO) published: (i) its own form of EU SCCs, known as the International Data Transfer Agreement to replace the old Standard Contractual Clauses for transfers to outside the UK; (ii) a "UK addendum" to the new EU SCCs which amends the relevant provisions of such clauses to work in a UK context; and (iii) its own version of the TIA and guidance on international transfers (although entities may choose to adopt either the EU or UK-style TIA). Further, on September 21, 2023, the UK Secretary of State for Science, Innovation and Technology established a UK-U.S. data bridge (i.e., a UK equivalent of the Adequacy Decision) and adopted UK regulations to implement the UK-U.S. data bridge ("UK Adequacy Regulations"). Personal data may now be transferred from the UK under the UK-U.S. data bridge through the UK extension to the DPF to organizations self-certified under the UK extension to the DPF.

As a company, we have invested, and expect to continue to invest, significant time and resources in our GDPR compliance program. This is necessary to ensure we can initiate and maintain GDPR-compliant clinical trials in the EU or UK (as applicable). Any failure or perceived failure by us with respect to GDPR compliance could mean we either cannot initiate additional GDPR-compliant clinical trials in the EU or UK (as applicable) or we may face regulatory investigations, significant fines and penalties, reputational damage or be required to change our business practices, all of which could adversely affect our business, financial condition and results of operations. There is a risk that we could be impacted by a cybersecurity incident that results in loss or unauthorized disclosure of personal data, potentially resulting in us facing harms similar to those described above.

Some countries also are considering or have passed legislation requiring local storage and processing of data, or similar requirements, which could increase the cost and complexity for conducting preclinical testing and clinical trials or delivering our future products, if any. Additionally, other countries (e.g., Australia and Japan) have adopted certain legal requirements for cross-border transfers of personal information. These obligations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other requirements or our practices.

It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices, and our efforts to comply with the evolving data protection rules may be unsuccessful. In addition to the possibility of fines, lawsuits, regulatory investigations, public censure, other claims and penalties, and significant costs for remediation and damage to our reputation, we could be materially and adversely affected if legislation or regulations are expanded to require changes in our data processing practices and policies or if governing jurisdictions interpret or implement their legislation or regulations in ways that negatively impact our business. Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms for ensuring compliance with the new data protection rules. In addition to government regulation, privacy advocates and industry groups have and may in the future propose self-regulatory standards from time to time. These and other industry standards may legally or contractually apply to us, or we may elect to comply with such standards. It is possible that if our practices are not consistent or viewed as not consistent with legal and regulatory requirements, including changes in laws, regulations and standards or new interpretations or applications of existing laws, regulations and standards, we may become subject to audits, inquiries, whistleblower complaints, adverse media coverage, investigations, loss of export privileges, or severe criminal or civil sanctions, all of which may have a material and adverse impact on our business, results of operations, reputation, and financial condition. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our business, financial condition, results of operations or prospects.

Any such liability, litigation, investigations and proceedings may or may not be covered by our liability insurance and may subject us to significant penalties and negative publicity, require us to change our business practices, increase our costs, severely disrupt our business, and may result in significant reputational harm and have a material and adverse impact on our business, financial condition, results of operations or prospects.

U.S. federal income tax reform and changes in other tax laws could adversely affect us.

In December 2017, U.S. federal tax legislation commonly referred to as the TCJA was signed into law, significantly reforming the Internal Revenue Code of 1986, as amended (Code). The TCJA, among other things, changed the U.S. federal tax treatment of research and experimental (R&E) expenses. For tax years beginning on or after January 1, 2022, taxpayers are required to capitalize and amortize, rather than deduct, R&E expenses. R&E expenses are amortizable over five years for research performed in the United States and 15 years for research performed outside the United States. Although there are legislative proposals to repeal or defer the capitalization requirement to later years, there can be no assurance that the provision will be repealed or otherwise modified.

Effective for transactions occurring on or after January 1, 2023, the IRA imposed a new one percent excise tax on certain repurchases of stock by publicly traded U.S. domestic corporations. The excise tax is imposed on the repurchasing corporation itself, not its shareholders from which shares are repurchased. For purposes of calculating the base excise tax, repurchasing corporations are permitted to net the fair market value of certain new stock issuances against the fair market value of stock repurchases during the same taxable year. Certain repurchases are not counted in the base of the excise tax.

In addition, new legislation or regulations that could affect our tax burden could be enacted by any governmental authority. We cannot predict the timing or extent of such tax-related developments that could negatively impact our financial results. We use our best judgment in attempting to quantify and reserve for these tax obligations. However, a challenge by a taxing authority, our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax-related assumptions could have a material adverse effect on our business, results of operations, or financial condition.

Our ability to utilize our net operating loss carryforwards may be subject to limitations.

We have incurred substantial losses during our history, do not expect to become profitable in the near future and may never achieve profitability. As of November 30, 2023, we had federal and state net operating loss (NOL) carryforwards of approximately $269.3 million and $410.9 million, respectively. To the extent we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, subject to the restrictions and exceptions described below. Federal NOLs generated in tax years beginning on or before December 31, 2017, may be carried forward 20 tax years and expire on various dates beginning in 2029. Under current law, NOLs arising in tax years beginning after December 31, 2017, may be carried forward indefinitely, but are limited to no more than 80% of the excess, if any, of current year taxable income (without regard to certain deductions). Our state NOLs can be carried forward 20 years and begin expiring in 2029.

Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period), the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset its post-change income or post-change income tax may be limited. We have identified two ownership changes since our inception that have triggered a limitation on pre-change NOLs under Section 382. A majority of our pre-change NOLs remain available within the carryforward period provided by the Code, subject to availability of taxable income. We may have experienced additional ownership changes that have not yet been identified that could result in the expiration of our NOL and credit carryforwards before utilization and we may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which are outside our control. As a result, if we earn net taxable income, our ability to use our pre-change NOLs and tax credit carryovers to offset U.S. federal taxable income and tax liability may be subject to limitations that potentially could result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Future acquisitions, joint ventures, spin outs or strategic alliances or transactions could disrupt our business and harm our financial condition and results of operations.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot be certain that, following any such acquisition, we will achieve the expected synergies to justify the transaction. The risks we face in connection with acquisitions include:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- coordination of research and development efforts;
- retention of key employees from the acquired company;
- changes in relationships with strategic partners as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into our organization;
- the need to implement or improve controls, procedures and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities and other known liabilities;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Our failure to address these risks or other problems encountered in connection with our past or future acquisitions or strategic alliances could cause us to fail to realize the anticipated benefits of these transactions or cause us to incur unanticipated liabilities and harm the business generally. There also is a risk that future acquisitions will result in our incurring debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or results of operations. Additionally, we may not realize the expected value of out-licensing, joint ventures, spin outs or other strategic transactions.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, or other remedial measures and legal expenses, any of which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the Foreign Corrupt Practices Act (FCPA), the Bribery Act and other anticorruption laws that apply in countries where we do business and may do business in the future. The FCPA, the Bribery Act and other anti-corruption or similar laws generally prohibit us, our officers and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We may in the future operate in jurisdictions that pose a high risk of potential FCPA or Bribery Act violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the FCPA, the Bribery Act or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We also are subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United States, UK and authorities in the EU, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, which we collectively refer to as Trade Control Laws.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the FCPA, the Bribery Act, or other legal requirements including Trade Control Laws. If we are not in compliance with the FCPA, the Bribery Act, and other anti-corruption laws or Trade Control Laws, we may be subject to criminal and civil penalties, legal expenses, and disgorgement and other sanctions and remedial measures, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The Securities and Exchange Commission (SEC) also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Likewise, any investigation of any potential violations of the FCPA, the Bribery Act, other anti-corruption laws or Trade Control Laws by U.S., UK or other authorities also could have an adverse impact on our reputation, our business, results of operations and financial condition.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could significantly harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may produce hazardous waste products. Although we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our 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.

We maintain workers' compensation insurance to cover costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis of 2007-2008 caused extreme volatility and disruptions in the capital and credit markets. Similarly, the volatility associated with the COVID-19 pandemic caused significant instability and disruptions in the capital and credit markets and, more recently, the global economy has been impacted by increasing interest rates and inflation, uncertainty with respect to the federal budget and debt ceiling and potential government shutdowns related thereto, as well as the possibility of a recession or further economic downturn. Moreover, there have been recent concerns with respect to the stability of the global banking system. For example, on March 10, 2023, Silicon Valley Bank (SVB), which was one of our banking partners, was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation (FDIC) as receiver. Similarly, on March 12, 2023, Silvergate Capital Corp. and Signature Bank were each swept into receivership. While we only had a minimal amount of our cash directly at SVB and the FDIC took steps to make depositors of SVB whole such that we regained access to this cash, there is no assurance that similar guarantees will be made in the event of further bank closures and continued instability in the global banking system. Our ongoing cash management strategy is to maintain diversity in our deposit accounts across financial institutions, but deposits in these institutions may exceed the amount of insurance provided on such deposits and there can be no assurance that this strategy will be successful. If other banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, then our ability to access our cash, cash equivalents and marketable securities may be threatened, which could have a material adverse effect on our business and financial condition. Furthermore, the capital and credit markets may be adversely affected by regional conflicts around the world and the possibility of a wider global conflict, global sanctions imposed in response to regional conflicts or an energy crisis. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including weakened demand for our drug candidates and in our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy also could strain our suppliers, possibly resulting in supply disruption. We cannot anticipate all of the ways in which the foregoing, and the current economic climate and financial market conditions generally, could adversely impact our business. Furthermore, our stock price may decline due in part to the volatility of the stock market and any general economic downturn.

Our current operations are in the San Francisco Bay Area, and we or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters as to which our business continuity and disaster recovery plans may not be adequate to protect us.

Our current operations are located in our facilities in San Francisco, California. Any unplanned event, such as earthquake, flood, fire, explosion, extreme weather condition, medical epidemic, power shortage, telecommunication failure or other natural or man-made accident or incident that results in our being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our drug candidates or interruption of our business operations, and have a material adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Our Common Stock

Our quarterly results of operations may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our results of operations to be subject to quarterly fluctuations. Our net loss and other results of operations will be affected by numerous factors, including:

- variations in the level of expense related to the ongoing development of our drug candidates, DELigase platform, or future development programs;
- results of preclinical studies and clinical trials, or the addition or termination of clinical trials or funding support by us or by existing or future collaborators or licensing partners;
- our execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our drug candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such drug candidates;
- regulatory developments affecting our drug candidates or those of our competitors; and
- changes in general market and economic conditions, including increasing interest rates, inflation, uncertainty with respect to the federal budget and debt ceiling and potential government shutdowns related thereto, instability in the global banking system and the possibility of a recession or further economic downturn.

If our quarterly results of operations fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our results of operations may, in turn, cause the price of our common stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Our stock price may be volatile and you could lose all or part of your investment.

The trading price of our common stock may be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. As a result of this volatility, investors may not be able to sell their common stock at or above the purchase price. The market price for our common stock may be influenced by many factors, including the other risks described in this "Risk Factors" section and the following:

- results of preclinical studies and clinical trials of our drug candidates, or those of our competitors or our existing or future collaborators;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our drug candidates;
- the success of competitive products or technologies;
- introductions and announcements of new products by us, our collaboration partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our drug candidates, clinical trials, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or in those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or drug candidates;
- developments concerning our current or future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the pharmaceutical and biotechnology sectors;

- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our drug candidates and products;
- our ability or inability to raise additional capital and the terms on which any additional capital is raised;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may provide to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- cybersecurity events;
- terrorist acts, acts of war or periods of widespread civil unrest, including the increasingly volatile global economic conditions resulting from regional conflicts around the world;
- effects of public health crises, pandemics and epidemics;
- natural disasters and other calamities; and
- general economic, industry and market conditions, including increasing interest rates, inflation, uncertainty with respect to the federal budget and debt ceiling and potential government shutdowns related thereto, instability in the global banking system and the possibility of a recession or further economic downturn.

In addition, the stock market in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme price and volume fluctuations that often have been unrelated or disproportionate to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

A sale of a substantial number of shares of our common stock may cause the price of our common stock to decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. However, future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options or vesting and settlement of outstanding restricted stock units, or the perception that such sales may occur, could adversely affect the market price of our common stock.

We also expect that significant additional capital may be needed in the future to continue our planned operations. To raise capital, 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. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is and will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not have any control over the analysts or the content and opinions included in their reports. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and clinical trials and results of operations fail to meet the expectations of analysts, our stock price would likely decline. If one or more of such analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause a decline in our stock price or trading volume.

The future sale and issuance of equity or of debt securities that are convertible into equity will dilute our share capital.

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. For example, in March 2021, we sold an additional 5,175,000 shares of our common stock in a follow-on public offering. In addition, we currently have on file with the SEC a shelf registration statement on Form S-3 which allows us to offer and sell up to $450.0 million of our registered common stock, preferred stock, debt securities, warrants, subscriptions rights and or units from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. In August 2021, we entered into an Equity Distribution Agreement with Piper Sandler & Co. (Piper Sandler) pursuant to which, from time to time, we may offer and sell through Piper Sandler up to $150.0 million of the common stock registered under the shelf registration statement pursuant to one or more "at the market" offerings. In June 2022, we issued and sold 2,000,000 shares of common stock under the Equity Distribution Agreement to Piper Sandler for net proceeds of approximately $19.3 million, after deducting offering commissions and expenses paid by us. As of November 30, 2023, we had $130.0 million of common stock remaining available for sale pursuant to the Equity Distribution Agreement. Sales of our common stock under the Equity Distribution Agreement with Piper Sandler could be subject to business, economic or competitive uncertainties and contingencies, many of which may be beyond our control, and which could cause actual results from the sale of our common stock to differ materially from expectations. In addition, in July 2022, we entered into separate Securities Purchase Agreements with certain purchasers to issue and sell pre-funded warrants to purchase an aggregate of 6,814,920 shares of our common stock in registered direct offerings for gross proceeds to us of $95.0 million before deducting offering expenses. Such pre-funded warrants are immediately exercisable, have an exercise price of $0.001 and may be exercised at any time after the date of issuance. To the extent additional capital is raised through the sale and issuance of shares or other securities convertible into shares, the ownership interest of our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or equity securities. No prediction can be made as to the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

We will not receive a significant amount, or potentially any, additional funds upon the exercise of our pre-funded warrants; however, any exercise would increase the number of shares eligible for future resale in the public market and result in substantial dilution to our stockholders.

As of November 30, 2023, we have issued pre-funded warrants to purchase a total of 6,814,920 shares of our common stock, of which 6,097,560 were outstanding as of November 30, 2023. Each pre-funded warrant is exercisable for $0.001 per share of common stock underlying such pre-funded warrant, which may be paid by way of a cashless exercise, meaning that the holder may not pay a cash purchase price upon exercise, but instead would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. Accordingly, we will not receive a significant amount, or potentially any, additional funds upon the exercise of the pre-funded warrants. To the extent such pre-funded warrants are exercised, additional shares of common stock will be issued for nominal or no additional consideration, which will result in substantial dilution to the then existing holders of our common stock and will increase the number of shares eligible for resale in the public market. Sales of substantial numbers of such shares in the public market could adversely affect the market price of the common stock, causing our stock price to decline.

There is no public market for our pre-funded warrants.

There is no public trading market for our pre-funded warrants issued, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Global Market (Nasdaq). Without an active market, the liquidity of the pre-funded warrants will be limited, and the value of the pre-funded warrants may be adversely impacted.

Additionally, each holder of pre-funded warrants will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise. However, any holder may increase or decrease such percentage to any other percentage (not in excess of 19.99%) upon at least 61 days' prior notice from the holder to us.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Our restated certificate of incorporation and our amended and restated bylaws contain provisions that could delay or prevent a change in control of our company. These provisions also could make it difficult for stockholders to elect directors who are not nominated by current members of our board of directors or to take other corporate actions, including effecting changes in our management. These provisions:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only our board of directors to establish the number of directors and fill vacancies on our board;
- provide that directors may be removed only "for cause" and only with the approval of two-thirds of our stockholders;
- require super-majority voting to amend some provisions in our restated certificate of incorporation and amended and restated bylaws, unless such amendments are approved by two-thirds of our board of directors, in which case stockholders can approve by a simple majority;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting; and
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings.

In addition, Section 203 of the Delaware General Corporation Law (DGCL) may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

Our restated certificate of incorporation and our amended and restated bylaws contain exclusive forum provisions for certain claims, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our restated certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our restated certificate of incorporation, or our amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine.

Moreover, Section 22 of the Securities Act of 1933, as amended (the Securities Act) creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder and our amended and restated bylaws provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (a Federal Forum Provision). Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court. Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder and neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder must be brought in federal court. Our stockholders will not be deemed to have waived our compliance with the federal securities laws and the regulations promulgated thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions, including the Federal Forum Provision. These provisions may limit our stockholders' ability to bring a claim in a judicial forum they find favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. Alternatively, if a court were to find the choice of forum provision contained in our restated certificate of incorporation and/or amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

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

As a public company, we incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations which impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Compliance with these rules and regulations may strain our financial and management systems, internal controls, and employees. For example, the Exchange Act requires, among other things, that we file annual, quarterly, and current reports with respect to our business and results of operations and the disclosure requirements under the Exchange Act are subject to change from time to time. For example, in 2023 the SEC adopted rules requiring disclosure of material cybersecurity incidents suffered by public companies, as well as annual disclosure regarding cybersecurity governance and risk management. Complying with these new disclosure obligations once applicable to our company, or any or any additional new disclosure requirements that may apply to us in the future, could cause us to incur substantial costs and could increase negative publicity surrounding any incident that we are required to disclose. Any failure or perceived failure by us to comply with these obligations may also subject us to enforcement action or litigation, any of which could harm our business.

Therefore, as a result of being a public company, our management and other personnel are required to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements also could make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. Moreover, these rules and regulations often are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

If we fail to maintain effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, which could harm our results of operations, investors' views of us and, as a result, the value of our common stock.

Pursuant to the rules and regulations of the SEC, we are required to furnish a report by our management on, among other things, our internal control over financial reporting. To achieve compliance with these rules and regulations, we engage in a process to document and evaluate our internal control over financial reporting, which is both costly and time-consuming. Effective internal control over financial reporting is necessary for us to provide reliable financial reporting and, together with adequate disclosure controls and procedures, are designed to prevent material misstatements due to fraud or error. Any failure to design new or improved internal controls necessary to address risks of material misstatement in our interim or annual financial statements, or difficulties encountered in their implementation or operation, could cause us to fail to meet our reporting obligations. Ineffective internal control over financial reporting could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

The reporting on our assessment of the effectiveness of our internal control over financial reporting needs to include disclosure of any material weaknesses identified in our internal control over financial reporting. Moreover, in the event that we qualify as a large accelerated filer or accelerated filer under SEC rules in future years, our independent registered public accounting firm will be required to audit the effectiveness of our internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act (Section 404(b)). Any mandatory or voluntary compliance with Section 404(b) will result in increased costs, expenses, and management resources. Undetected material weaknesses in our internal control over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation. For example, we previously identified material weaknesses in our internal control over financial reporting for the fiscal year ended November 30, 2021, related to controls over segregation of duties in our journal entry and account reconciliation processes, and certain information technology general controls. The material weaknesses identified did not result in any misstatement of our financial statements and during the year ended November 30, 2022, the material weaknesses was remediated. However, we cannot assure you that the measures we have taken to date, and actions we may take in the future, will prevent or avoid potential future material weaknesses.

We are also required to disclose changes made in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, internal control over financial reporting on a quarterly basis. To comply with the requirements of being a public company, we have undertaken, and may need to further undertake in the future, various actions, such as implementing new internal controls and procedures and hiring additional accounting staff.

Moreover, our current controls and any new controls that we develop may become inadequate because of changes in conditions in our business. Further, material weaknesses in our disclosure controls and procedures and internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective internal control over financial reporting or any difficulties encountered in their implementation or improvement could harm our results of operations or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods, which could cause the price of our common stock to decline. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

We are a "smaller reporting company" and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We became a "smaller reporting company" as of May 31, 2022. We will continue to be a smaller reporting company so long as either (i) the market value of our stock held by non-affiliates is less than $250.0 million as of the prior May 31 or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million as of the prior May 31. As a smaller reporting company, we may take advantage of many of the same exemptions from disclosure requirements as an emerging growth company, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Not applicable.

Item 2. Properties and Facilities

Our principal executive office is located in San Francisco, California, where we lease a total of 77,222 square feet of office and laboratory spaces that we use for our administrative, research and development and other activities. The lease for 19,320 square feet of space expires in June 2024, and the lease for 57,902 square feet of space expires in April 2025. Additionally, we lease a total of 50,094 square feet of office and laboratory space in The Woodlands, Texas that expires in February 2035. We believe that our existing facilities are suitable and adequate for our current requirements and operations.

Item 3. Legal Proceedings

From time to time, we may be involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any legal proceedings that, in the opinion of management, would have a material adverse effect on our business or consolidated financial statements. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity and reputational harm and other factors.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information for Common Stock

Our common stock has been listed on the Nasdaq Global Market under the symbol "NRIX" since July 24, 2020. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of close of business on February 5, 2024, there were 16 holders of record of our common stock. The actual number of stockholders 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 and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, to finance the growth and development of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination regarding the declaration and payment of dividends will fall within the discretion of our Board of Directors, and will depend on various factors, including our operating results, financial condition, and capital requirements, restrictions that may be imposed by applicable law, and other factors deemed relevant by our Board of Directors.

Stock Price Performance Graph

As a "smaller reporting company" as defined by Item 10 of Regulation S-K, we are not required to provide this information.

Use of Proceeds from Registered Securities

None.

Securities Authorized for Issuance under Equity Compensation Plans

Information regarding our equity compensation plans and the securities authorized for issuance thereunder is set forth in Part III, Item 12 of this Annual Report on Form 10-K.

Unregistered Sales of Equity Securities

None.

Purchases of Equity Securities by Issuers and Affiliated Purchasers

None.

Item 6. [Reserved]

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. As discussed in the section titled "Special Note Regarding Forward Looking Statements," the following discussion and analysis contains forward looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward looking statements. Factors that could cause or contribute to these differences include, but are not limited to, those identified below and those discussed in the section titled "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K.

Overview

We are a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative small molecules and antibody therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer, inflammatory conditions and other challenging diseases. Leveraging our extensive expertise in E3 ligases together with our proprietary DNA-encoded libraries, we have built DELigase, an integrated discovery platform to identify and advance novel drug candidates targeting E3 ligases, a broad class of enzymes that can modulate proteins within the cell. Our drug discovery approach is to either harness or inhibit the natural function of E3 ligases within the ubiquitin-proteasome system to selectively decrease or increase cellular protein levels. Our wholly owned, clinical stage pipeline includes targeted protein degraders of Bruton's tyrosine kinase (BTK), a B-cell signaling protein, and inhibitors of Casitas B-lineage lymphoma proto-oncogene B (CBL-B), an E3 ligase that regulates activation of multiple immune cell types including T cells and NK cells. Our partnered drug discovery pipeline consists of multiple programs under collaboration agreements with Gilead Sciences, Inc. (Gilead), Sanofi S.A. (Sanofi) and Seagen Inc. (now a part of Pfizer Inc. (Pfizer)), within which we retain certain options for co-development, co-commercialization and profit sharing in the United States for multiple drug candidates.

Targeted Protein Degradation

Our portfolio of targeted protein degraders of BTK, a B-cell signaling protein, comprises NX-5948, an orally bioavailable BTK degrader for the treatment of relapsed or refractory B-cell malignancies and potentially autoimmune diseases, and NX-2127, an orally bioavailable BTK degrader that also degrades cereblon neosubstrates IKZF1 (Ikaros) and IKZF3 (Aiolos) for the treatment of relapsed or refractory B-cell malignancies.

NX-5948: We are currently treating patients in a Phase 1a/1b dose-escalation and cohort expansion study in patients with relapsed or refractory B-cell malignancies. In January 2024, the U.S. Food and Drug Administration (FDA) granted Fast Track designation for NX-5948 for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two lines of therapy, including a BTK inhibitor (BTKi) and a B-cell lymphoma 2 (BCL2) inhibitor.

NX-2127: We are currently treating patients in a Phase 1a/1b dose-escalation and cohort expansion study of NX-2127 in patients with relapsed or refractory B-cell malignancies. We have initiated Phase 1b expansion cohorts for patients with relapsed CLL, diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL). Enrollment of new patients in this clinical trial is paused pending resolution of a partial clinical hold, which followed our communication to the FDA of our intention to transition to an improved manufacturing process. Patients already enrolled who are receiving clinical benefit may continue treatment.

Targeted Protein Elevation

Our targeted protein elevation program includes NX-1607, an orally bioavailable inhibitor of CBL-B, an E3 ligase that regulates the activation of multiple immune cell types including T cells and NK cells. NX-1607 is targeted for immuno-oncology indications.

We are currently treating patients in a Phase 1a/1b dose-escalation and cohort expansion study of NX-1607 in patients with a range of oncology indications. This study also includes a cohort within the Phase 1a dose escalation study testing NX-1607 in combination with paclitaxel, a taxane chemotherapy commonly used across a range of relapsed and refractory solid tumor indications. NX-1607 was awarded an Innovative Passport from the UK Medicines and Healthcare products Regulatory Agency to accelerate time to market and facilitate patient access to novel drugs to treat serious and life-threatening diseases.

Drug Discovery Pipeline

In addition to our clinical stage drug candidates, we are extending our protein modulation portfolio, both on our own and with partners by developing new targeted protein degraders and ligase inhibitors for a number of targets for which we believe the protein modulation modality can be clinically advantageous over existing therapies. These existing and future programs may have the potential to address diseases with significant unmet need, including cancer, autoimmunity, inflammation, and other challenging diseases.

We have entered into several revenue generating collaborations with large biopharmaceutical companies, including with Gilead, Sanofi and Seagen (now a part of Pfizer), to leverage our DELigase platform for drug discovery. These collaborations allow us to further advance our future pipeline with multiple currently identified targets included in these collaborations. In aggregate, we have received $413.0 million in non-dilutive financing from our collaborators to date, and as of November 30, 2023, we are eligible to receive up to $8.1 billion in potential future fees and milestone payments, as well as royalties on future product sales. We retain certain options for co-development, co-commercialization and profit sharing in the United States for multiple drug candidates, pursuant to these collaborations.

Collaborations and License Agreements

Gilead

In June 2019, we entered into a global strategic collaboration agreement with Gilead (as subsequently amended, the Gilead Agreement) to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with cancer and other challenging diseases using our DELigase platform to identify novel agents that utilize E3 ligases to induce degradation of five specified drug targets. In August 2019 and September 2022, we entered into the First Amendment and the Second Amendment, respectively, to the Gilead Agreement to clarify certain language of the Gilead Agreement. These amendments had no impact on revenue recognition.

Under the Gilead Agreement, Gilead has the option to license drug candidates directed to up to five targets resulting from the collaboration and is responsible for the clinical development and commercialization of drug candidates resulting from the collaboration. We retain the option to co-develop and co-promote, under a profit share structure, up to two drug candidates in the United States, provided that we may only exercise such option once per licensed product and Gilead retains the right to veto our option selection for any one drug candidate of its choice. The collaboration excludes our current internal protein degradation programs for which we retain all rights, and also excludes our future internal programs, provided that we have distinguished future programs as excluded from the scope of the collaboration. In March 2023, Gilead exercised the option, which did not represent a material right at contract inception, since it was not offered for free or at a discount, to exclusively license one target (Gilead License Option Exercise), the first development candidate resulting from the Gilead Agreement. Pursuant to the Gilead Agreement, we received a license option exercise payment of $20.0 million in April 2023 for the Gilead License Option Exercise. The license to the functional intellectual property and all goods and services related to the Gilead License Option Exercise were transferred during the second quarter of fiscal year 2023.

Over time, Gilead may elect to replace the initial drug targets with other drug targets. For drug targets that are subject to the collaboration, we are obligated to use commercially reasonable efforts to undertake a research program in accordance with a research plan agreed to by the parties and established on a target-by-target basis. We have primary responsibility under the Gilead Agreement for performing preclinical research activities (including target validation, drug discovery, identification or synthesis) pursuant to a research plan. Each party will bear its own costs in the conduct of research activities. Gilead will be responsible for any development, commercialization and manufacturing activities, unless we exercise our co-development and co-promotion option. For those programs that we exercise our option to co-develop and co-promote, we and Gilead will split U.S. development costs as well as U.S. profits and losses evenly, and we will be eligible to receive royalties on net ex-U.S. sales and reduced milestone payments.

Upon signing the Gilead Agreement, Gilead paid us an upfront payment of $45.0 million, plus $3.0 million in additional fees. In addition, from the signing of the Gilead Agreement to November 30, 2023, we received payments of $47.0 million for research milestones and additional payments and $20.0 million for a license option exercise payment. As of November 30, 2023, we are eligible to receive up to approximately $2.3 billion in total additional payments based on certain additional fees, payments and the successful completion of certain preclinical, clinical, development and sales milestones. We also are eligible to receive mid-single digit to low tens percentage tiered royalties on annual net sales from any commercial products directed to the optioned collaboration targets, subject to certain reductions and excluding sales in the United States of any products for which we exercise our option to co-develop and co-promote, for which the parties share profits and losses evenly.

Subject to earlier expiration in certain circumstances, the Gilead Agreement expires on a licensed product-by-licensed product and country-by-country basis upon the later of (1) the expiration of the last to expire patent with a valid claim covering the applicable licensed product in the applicable country, (2) the expiration of any regulatory exclusivity for the applicable licensed product in the applicable country or (3) ten years after the first commercial sale of the applicable licensed product in the applicable country covered by the Gilead Agreement, provided that the term for any profit-shared licensed product in the United States will expire upon the expiration or termination of the applicable profit-share term as set forth in an applicable profit-share agreement to be negotiated upon our exercise of our option to co-develop and co-promote such licensed product. If Gilead does not exercise an option to license a drug candidate, then the Gilead Agreement will terminate at the end of the last to expire option period.

We recognized collaboration revenue from the Gilead Agreement of $29.9 million and $23.7 million during the years ended November 30, 2023 and 2022, respectively. As of November 30, 2023 and 2022, there was $10.0 million and $27.4 million, respectively, of deferred revenue related to payments received by us under the Gilead Agreement.

Sanofi

In December 2019, we entered into a strategic collaboration with Genzyme Corporation, a subsidiary of Sanofi, which became effective in January 2020 (as subsequently expanded and amended, the Sanofi Agreement), to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with challenging diseases in multiple therapeutic areas using our DELigase platform to identify small molecules designed to induce degradation of three specified initial drug targets. In January 2021, as part of the existing Sanofi Agreement, Sanofi paid us $22.0 million to exercise its option to expand the number of targets in the Sanofi Agreement from three to a total of five targets.

In January 2021, we entered into the First Amendment to the Sanofi Agreement to modify the research term on all targets. In December 2021, we entered into the Second Amendment to the Sanofi Agreement to extend the substitution deadline on certain targets. In July 2022, we entered into the Third Amendment to the Sanofi Agreement to further extend the substitution deadline on certain targets. The extensions of the substitution deadline had no impact on revenue recognition. Also in July 2022, Sanofi elected to replace certain drug targets, and the substitution extended the research term of those targets by one year to 5.25 years and increased overall forecasted costs, which had an immaterial impact on revenue recognition. In August 2022 and November 2023, we entered into the Fourth Amendment and Fifth Amendment, respectively, to the Sanofi Agreement to modify the research plan for certain targets, which had no impact on revenue recognition.

Under the Sanofi Agreement, Sanofi has exclusive rights and is responsible for the clinical development, commercialization and manufacture of drug candidates resulting from the collaboration while we retain the option to co-develop, co-promote and co-commercialize all drug candidates in the United States directed to up to two targets, one of which must be selected from a list of targets designated at the execution of the Sanofi Agreement or any replacement of such targets, and one of which must be selected from targets identified by Sanofi as part of their January 2021 expansion. Our right to exercise our option to co-develop, co-promote and co-commercialize a given target is dependent on our ability to demonstrate, within a given timeframe, that we have sufficient cash resources and personnel to commercialize the product. The collaboration excludes our current internal protein degradation programs for which we retain all rights, and also excludes our future internal programs, provided that we distinguished future programs as excluded from the scope of the collaboration.

For drug targets that are subject to the collaboration, we have primary responsibility for conducting preclinical research activities (including target validation, drug discovery, identification or synthesis) in accordance with the applicable research plan agreed to by the parties and established on a target-by-target basis. We are obligated to use commercially reasonable efforts to identify relevant target binders and targeted protein degraders in order to identify development candidates. Subject to certain exceptions, each party will bear its own costs in the conduct of such research. Sanofi will be responsible for any development and commercialization activities unless we exercise our co-development and co-promotion option. For those programs that we exercise our option to co-develop, co-promote and co-commercialize, we will be responsible for a portion of the U.S. development costs, and the parties will split U.S. profits and losses evenly, and we will be eligible to receive royalties on ex-U.S. net sales and reduced milestone payments on such optioned products.

Upon signing the Sanofi Agreement, Sanofi paid us an upfront payment of $55.0 million. Subsequently, in January 2021, Sanofi paid us an additional $22.0 million to exercise its option to expand the number of targets beyond the initial targets included in the collaboration. In addition, from the signing of the Sanofi Agreement to November 30, 2023, we received payments of $7.0 million for research milestones. Additionally, we achieved two research milestones in November 2023 and received payments totaling $4.0 million in January 2024 as a result. As of November 30, 2023, we are eligible to receive up to approximately $2.5 billion in total additional payments based on certain additional fees, payments and the successful completion of certain research development, regulatory and sales milestones, as well as mid-single digit to low teen percentage tiered royalties on annual net sales of any commercial products that may result from the collaboration, subject to certain reductions and excluding sales in the United States of any products for which we exercise our option to co-develop and co-promote, for which the parties share profits and losses evenly.

Subject to earlier expiration in certain circumstances, the Sanofi Agreement expires on a licensed product-by-licensed product or profit-shared licensed product-by-profit-shared licensed product basis and country-by-country basis upon on the later of (1) the expiration of the last-to-expire patent with a valid claim covering the applicable licensed product in the applicable country, (2) the expiration of any regulatory exclusivity for the applicable licensed product in the applicable country or (3) ten years after the first commercial sale of the applicable licensed product in the applicable country covered by the Sanofi Agreement.

We recognized collaboration revenue from the Sanofi Agreement of $25.4 million and $15.0 million during the years ended November 30, 2023 and 2022, respectively. As of November 30, 2023 and 2022, there was $24.9 million and $46.2 million, respectively, of deferred revenue related to payments received by us under the Sanofi Agreement.

Pfizer

In September 2023, we entered into a strategic collaboration with Seagen Inc. (now a part of Pfizer Inc.) (the Pfizer Agreement) to develop a suite of targeted protein degraders against multiple targets nominated by Pfizer that are suitable for antibody conjugation. Pfizer will be responsible for conjugating these degraders to antibodies to make Degrader-Antibody Conjugates (DACs), a new class of medicines for use in cancer treatment, and advancing these DAC drug candidates through preclinical and clinical development and commercialization.

Under the Pfizer Agreement, Pfizer has the option to obtain exclusive licenses to develop and commercialize certain degraders, while we retain an option for U.S. profit sharing and co-promotion on two products arising from the collaboration. The collaboration excludes our current internal protein degradation programs for which we retain all rights, and also excludes our future internal programs, provided that we have distinguished future programs as excluded from the scope of the collaboration.

For the targets nominated by Pfizer under the collaboration, we shall use commercially reasonable efforts to identify, synthesize, characterize and deliver targeted protein degraders that selectively bind to and degrade such targets. Development of licensed degraders, with the exception of licensed products for which we exercised our profit-share options, will be at Pfizer's sole cost and expense. For the profit-share products, the parties will share net profits and net losses and global development costs, and we will be eligible to receive royalty and milestone payments on such optioned products.

Under the terms of the Pfizer Agreement, we received an upfront payment of $60.0 million. We are eligible to receive up to approximately $3.4 billion in contingent payments based on specified research, development, regulatory and commercial milestones across multiple programs, and are eligible for mid-single to low double digit percentage tiered royalties on future sales.

Subject to the exceptions described in the Pfizer Agreement, the Pfizer Agreement expires upon the first to occur of (1) the expiration of the last-to-expire option exercise period under the Pfizer Agreement if no such option has been exercised prior to such expiration and (2) the expiration of the last-to-expire royalty term under the Pfizer Agreement.

We recognized collaboration revenue from the Pfizer Agreement of $1.7 million during the year ended November 30, 2023. As of November 30, 2023, there was $58.3 million of deferred revenue related to payments received by us under the Pfizer Agreement.

Financial Overview

Since the commencement of our operations, we have devoted substantially all of our resources to conducting research and development activities, establishing and maintaining our intellectual property portfolio, establishing our corporate infrastructure, raising capital and providing general and administrative support for these operations. We have funded our operations to date primarily from proceeds received under collaboration and license agreements with Celgene Corporation, Gilead, Sanofi and Pfizer and the issuance and sale of common stock, redeemable convertible preferred stock and pre-funded warrants. We do not expect to generate product revenue unless and until we successfully develop and obtain approval for the commercialization of a drug candidate, and we cannot assure you that we will ever generate significant revenue or profits.

Since inception, we have generally incurred significant losses and negative cash flows from operations. During the years ended November 30, 2023 and 2022, we incurred net losses of $143.9 million and $180.4 million, respectively. As of November 30, 2023, we had an accumulated deficit of $545.2 million. These losses have resulted primarily from costs incurred in connection with research and development activities and general and administrative costs associated with our operations.

We do not expect to generate any revenue from commercial product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our drug candidates, which we expect will take a number of years, if ever. We expect our expenses will increase substantially as we advance our drug candidates through preclinical and clinical development; enter advanced clinical development and scale up external manufacturing capabilities to supply clinical trials; apply our DELigase platform to advance additional drug candidates and expand the capabilities of our platform; seek marketing approvals for any drug candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain marketing approval; expand, maintain and protect our intellectual property portfolio; and hire additional clinical, regulatory, manufacturing, quality assurance and scientific personnel. Furthermore, we expect to continue incurring costs associated with operating as a public company, including significant legal, accounting, insurance, investor relations and other administrative and professional services expenses.

Our net losses and cash flows may fluctuate significantly from period to period, depending on, among other things, variations in the level of expense related to the ongoing development of our drug candidates, our DELigase platform or future development programs; the delay, addition or termination of clinical trials; and the execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under such arrangements.

As of November 30, 2023, we had $295.3 million in cash, cash equivalents and marketable securities. We expect that our existing cash, cash equivalents and marketable securities are sufficient to fund our operations for at least the next 12 months. See the section titled "—Liquidity and Capital Resources" for more information. To finance our operations beyond that point, we will need to raise substantial additional capital to complete the development and commercialization of our drug candidates. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

Impact of Current Global Business, Political and Macroeconomic Conditions

Uncertainty in the global business, political and macroeconomic environments present significant risks to our business. We are subject to continuing risks and uncertainties, including increasing financial market volatility and uncertainty, inflation, increasing interest rates, uncertainty with respect to the federal budget and debt ceiling and potential government shutdowns related thereto, instability in the global banking system, cybersecurity events, the impact of war or military conflict, including regional conflicts around the world, and public health pandemics. We are closely monitoring the impact of these factors on all aspects of our business, including the impacts on our clinical trial patients, employees, partner, suppliers, and vendors.

The ultimate extent of the impact of global economic conditions on our business remains highly uncertain and will depend on future developments and factors that continue to evolve. Most of these developments and factors are outside of our control and could exist for an extended period of time. As a result, we are subject to continuing risks and uncertainties and continue to closely monitor the impact of the current conditions on our business. For more information regarding these risks and uncertainties, see the section titled "Risk Factors" in this Annual Report on Form 10-K.

Components of Results of Operations

Collaboration Revenue

We have no products approved for commercial sale and to date have not generated any revenue from the sale of products and do not expect to generate any revenue from the sale of products in the near future.

Our revenue to date has been generated from payments received pursuant to collaboration and license arrangements with strategic partners. Collaboration revenue consists of revenue received from upfront, milestone and contingent payments received from our collaborators. We recognize revenue from upfront payments over the contract term using the cost-based input method. The material right to the two additional targets under the Sanofi Agreement was accounted for using the practical alternative and the expected consideration to be received on the options was included for revenue allocation. We expect to continue recognizing revenue from upfront payments related to our collaboration agreements using the cost-based input method in the foreseeable future.

In addition to receiving upfront payments, we may also be entitled to milestones and other contingent payments upon achieving predefined objectives. If a milestone is considered probable of being reached, and if it is probable that a significant revenue reversal would not occur, the associated milestone amount would also be included in the transaction price.

We expect that any collaboration revenue we generate from our current collaboration and license agreements, and from any future collaboration partners, will fluctuate in the future as a result of the timing and amount of upfront, milestones and other collaboration agreement payments and other factors.

License Revenue

Our license revenue consists of a payment received from the Gilead License Option Exercise that was fully recognized during the second quarter of fiscal year 2023.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the discovery and development of our drug candidates. We expense both internal and external research and development expenses to operations in the periods in which they are incurred. Nonrefundable advance payments for goods or services to be received in future periods for use in research and development activities are deferred and capitalized. The capitalized amounts are then expensed as the related goods are delivered and as services are performed. We track the external research and development costs incurred for each of our drug candidates.

Internal research and development costs include:

- payroll and personnel expenses, including benefits, stock-based compensation and travel expenses, for our research and development functions; and
- depreciation of research and development equipment, allocated overhead and facilities-related expenses.

External research and development expenses consist primarily of costs incurred for the development of our drug candidates and may include:

- fees paid to third parties such as consultants, contractors and contract research organizations to conduct our clinical trials, discovery programs and preclinical studies;
- costs to acquire, develop and manufacture supplies for clinical trials and preclinical studies, including fees paid to third parties such as contract manufacturing organizations; and
- expenses related to laboratory supplies and services.

We expect our research and development expenses to increase substantially for the foreseeable future as we conduct clinical trials for our drug candidates, continue to invest in research and development activities for discovery programs and preclinical studies, pursue regulatory approval of our drug candidates and expand our drug candidate pipeline. The process of conducting the necessary preclinical and clinical research to obtain regulatory approval is costly and time-consuming. To the extent that our drug candidates advance to and continue to advance through clinical trials, our expenses will continue increasing substantially and may become more variable. The actual probability of success for our drug candidates may be affected by a variety of factors, including the safety and efficacy of our drug candidates, investment in our clinical programs, the ability of collaborators to successfully develop our licensed drug candidates, manufacturing capability, competition with other products and commercial viability. As a result of these variables, we are unable to determine when and to what extent we will generate revenue from the commercialization and sale of our drug candidates. We may never succeed in achieving regulatory approval for any of our drug candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of payroll and personnel expenses, including benefits and stock-based compensation, facilities-related expenses and professional fees for legal, consulting and audit and tax services. We expect our general and administrative expenses to increase for the foreseeable future as we continue to improve our infrastructure and operate as a public company. This may include expenses related to compliance with the rules and regulations of the Securities and Exchange Commission and listing standards applicable to companies listed on a national securities exchange, additional insurance, investor relations activities and other administrative and professional services. We also expect our intellectual property expenses to increase as we expand our intellectual property portfolio.

Interest and Other Income, Net

Interest and other income, net primarily consists of interest earned on our cash, cash equivalents and marketable securities. We expect interest income to vary each reporting period depending on our average bank deposit, money market fund and marketable securities balances during the period and market interest rates.

Critical Accounting Policies and Estimates

Our accounting policies are more fully described in Note 2 of the consolidated financial statements to this Annual Report on Form 10-K. As disclosed in Note 2, the preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions about future events that affect the amounts reported in the financial statements and accompanying notes. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Actual results could differ significantly from those estimates. We believe that the following discussion addresses our most critical accounting policies and estimates, which are those that are most important to the portrayal of our financial condition and results of operations and require management's most difficult, subjective and complex judgments.

Leases

We determine if an arrangement contains a lease and the classification of the lease at inception. An arrangement contains a lease if there is an identified asset and if we control the use of the identified asset throughout the period of use. The evaluation of whether the lease is an operating or a finance lease requires judgments in determining the fair value of the leased asset. Lease right-of-use (ROU) assets and lease liabilities are recognized at the lease commencement date based on the present value of the future minimum lease payments over the lease term at the commencement date. We use our incremental borrowing rate, if an implicit rate is not readily available, and the information available at the date of lease commencement in determining our lease liabilities. Our incremental borrowing rate is based on the rate of interest that we would have to pay to borrow on a collateralized basis over a similar term for an amount equal to the lease payments in a similar economic environment, and the determination of the rate requires us to make certain assumptions and judgements, including on our synthetic credit rating. Leases may include options to extend or early terminate the lease term. If we, using judgement, are reasonably certain that an option will be exercised, then the option will be included in the calculation of the lease term. The determination of the lease liabilities is sensitive to the incremental borrowing rate and the expected lease term. Lease expense for operating leases is recognized on a straight-line basis over the lease term. We do not have any finance leases.

Revenue Recognition

We recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. At contract inception, we assess the goods or services promised within each contract, whether each promised good or service is distinct, and determine those that are performance obligations. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when or as the performance obligation is satisfied.

We enter into collaboration agreements under which we may obtain upfront payments, milestone payments, royalty payments and other fees. Promises under these arrangements may include research licenses, research services, including selection campaign research services for certain replacement targets, the obligation to share information during the research term and the participation of alliance managers and in joint research committees, joint patent committees and joint steering committees. We assess these promises within the context of the agreements to determine the performance obligations.

Exclusive license rights: If a license to our intellectual property is determined to be distinct from the other promises identified in the arrangement, we recognize revenue from nonrefundable, upfront payments allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license and the underlying intellectual property. If the license is the predominant promise, and it is determined that the license represents functional intellectual property, revenue is recognized at the point in time when control of the license is transferred. If it is determined that the license does not represent functional intellectual property, revenue is recognized over time using an appropriate method of measuring progress.

Research and collaboration licenses: Collaboration agreements may include research licenses and research and development services to be performed by us. For research licenses that are bundled with other promises, we utilize 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 proportional performance for purposes of recognizing revenue from non-refundable, upfront payments. We evaluate the measure of proportional performance each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes research, development or regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price. We use the most likely amount method for research, development and regulatory milestone payments. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. If it is probable that a significant revenue reversal would not occur, the associated milestone amount is included in the transaction price.

Customer options: Customer options, such as options granted to allow a licensee to extend a license or research term, to select additional research targets or to choose to research, develop and commercialize licensed compounds, are evaluated at contract inception to determine whether those options provide a material right (i.e., an optional good or service offered for free or at a discount) to the customer. If the customer options represent a material right, the material right is treated as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the standalone selling price. As a practical alternative to estimating the standalone selling price of a material right when the underlying goods or services are both (i) similar to the original goods or services in the contract and (ii) provided in accordance with the terms of the original contract, we allocate the total amount of consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to any material right are recognized as revenue when or as the related future goods or services are transferred or when the option expires.

For performance obligations satisfied over time, we recognize revenue using the cost-based input method and evaluate the measure of proportional performance each reporting period and, if necessary, adjust the measure of performance and related revenue recognition. To measure the proportional performance, we are required to make our best estimates of forecasted expenditures and development timelines, which are subject to uncertainties, including the timing of replacement targets, if any, associated with pharmaceutical product development. Forecasted total expenditures are driven primarily by the number of full-time employees, and the assumptions over the number of full-time employees require significant management judgement. The number of full-time employees may change based on the progress and timing of our product development, and may be influenced by resource allocation decisions on internal programs and overall constraint on resources. The model is highly sensitive to changes in resources assigned over the research term. Forecasted total expenditures also include other direct costs related to product development, including third-party contract costs, and may also require management's estimate of costs and market conditions that may impact costs.

Results of Operations

Comparison of the years ended November 30, 2023 and 2022

Our results of operations for the years ended November 30, 2023 and 2022 are summarized as follows (in thousands):

	Year ended November 30,		
	2023	2022	Change
Revenue:			
Collaboration revenue	$ 56,987	$ 38,627	$ 18,360
License revenue	20,000	—	20,000
Total revenue	76,987	38,627	38,360
Operating expenses:			
Research and development	189,148	184,497	4,651
General and administrative	42,902	37,997	4,905
Total operating expenses	232,050	222,494	9,556
Loss from operations	(155,063)	(183,867)	28,804
Interest and other income, net	11,115	3,507	7,608
Net loss	$ (143,948)	$ (180,360)	$ 36,412

Collaboration Revenue

Our collaboration revenue for the years ended November 30, 2023 and 2022 is summarized as follows (in thousands):

	Year ended November 30,		
	2023	2022	Change
Gilead	$ 29,947	$ 23,674	$ 6,273
Sanofi	25,350	14,953	10,397
Pfizer	1,690	—	1,690
Total collaboration revenue	$ 56,987	$ 38,627	$ 18,360

Our collaboration revenue increased by $18.4 million during the year ended November 30, 2023, compared to the year ended November 30, 2022, primarily due to increased effort resulting in a higher percentage of completion of performance obligations under our collaborations with Gilead and Sanofi in the current period. The increase was also due to higher achievement of research milestones that resulted in higher revenue recognized in each period and impacted the cumulative catch up in revenue for activities satisfied in previous periods. In addition, we recognized revenue of $1.7 million related to activities performed during the fourth fiscal quarter ended November 30, 2023 pursuant to the Pfizer Agreement.

License Revenue

Our license revenue was $20.0 million for the year ended November 30, 2023, and is related to the Gilead License Option Exercise. There was no license revenue for the year ended November 30, 2022.

Research and Development Expenses

Our research and development expenses for the years ended November 30, 2023 and 2022 are summarized as follows (in thousands):

	Year ended November 30,		
	2023	2022	Change
Compensation and related personnel costs	$ 72,876	$ 65,336	$ 7,540
Stock-based compensation	18,709	16,878	1,831
Supplies and contract research	43,943	47,814	(3,871)
Preclinical activities	1,652	5,912	(4,260)
Contract manufacturing	7,770	13,562	(5,792)
Clinical costs	17,500	13,887	3,613
Facility and other costs	26,698	21,108	5,590
Total research and development expenses	$ 189,148	$ 184,497	$ 4,651

Our research and development expense increased by $4.7 million during the year ended November 30, 2023, compared to the year ended November 30, 2022. There was an increase in compensation and related personnel costs and in non-cash stock-based compensation expense that were primarily attributable to higher headcount and the issuance of restricted stock units (RSUs) and incentive stock options. There was also an increase in clinical costs as we continued our clinical trial programs and ongoing patient enrollment and an increase in facility and other costs primarily driven by investments in equipment and expenses related to our leases of office and laboratory space, including the lease in The Woodlands, Texas. There was a decrease in research related costs as we concluded certain studies and sponsored research agreements and a decrease in contract manufacturing as we stabilized the supply needed for our clinical trials.

General and Administrative Expenses

Our general and administrative expenses increased by $4.9 million during the year ended November 30, 2023, compared to the year ended November 30, 2022. There was an increase in non-cash stock-based compensation expense primarily driven by the increased issuance of RSUs and incentive stock options and an increase in professional service costs related to the Pfizer Agreement, offset by a decrease in outside consulting costs.

Interest and Other Income, Net

Our interest and other income, net increased by $7.6 million during the year ended November 30, 2023, compared to the year ended November 30, 2022, primarily attributable to higher interest rates earning higher interest income on our deposits, money market funds and marketable securities.

Liquidity and Capital Resources

Sources of Liquidity

In July 2020, we closed our initial public offering (IPO) and issued 12,550,000 shares of our common stock (including the exercise by the underwriters of their option to purchase an additional 1,550,000 shares of common stock in August 2020) at a price to the public of $19.00 per share for net proceeds of $218.1 million, after deducting underwriting discounts and commissions of $16.7 million and expenses of $3.6 million.

In March 2021, we completed a follow-on offering and issued 5,175,000 shares of our common stock (including the exercise by the underwriters of their option to purchase an additional 675,000 shares of common stock) at a price to the public of $31.00 per share for net proceeds of $150.2 million, after deducting underwriting discounts and commissions of $9.6 million and expenses of $0.6 million.

In August 2021, we entered into an Equity Distribution Agreement with Piper Sandler & Co. (Piper Sandler) pursuant to which, from time to time, we may offer and sell through Piper Sandler up to $150.0 million of the common stock registered under our shelf registration statement on Form S-3 pursuant to one or more "at the market" offerings. We are not required to sell any shares at any time during the term of the Equity Distribution Agreement. We agreed to pay Piper Sandler a commission of 3% of the gross sales price of any shares sold pursuant to the Equity Distribution Agreement. In June 2022, we issued and sold 2,000,000 shares of common stock under the Equity Distribution Agreement at a price of $10.0001 per share of common stock for net proceeds of approximately $19.3 million after deducting offering commissions and expenses paid by us (the June 2022 ATM Offering). As of November 30, 2023, we had $130.0 million of common stock remaining available for sale under the Equity Distribution Agreement.

In July 2022, we entered into separate securities purchase agreements with certain purchasers to issue and sell pre-funded warrants to purchase an aggregate of 6,814,920 shares of our common stock in registered direct offerings (RDOs) at a price of $13.939 per pre-funded warrant. Net proceeds from the RDOs were approximately $94.8 million, after deducting offering expenses of $0.2 million. The pre-funded warrants were immediately exercisable, have an exercise price of $0.001 and may be exercised at any time after the date of issuance. A holder of the pre-funded warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of our common stock outstanding immediately after giving effect to such exercise. A holder of the pre-funded warrants may increase or decrease this percentage not in excess of 19.99% by providing us at least 61 days' prior notice. As of November 30, 2023, a total of 6,097,560 pre-funded warrants remained available for exercise.

Funding Requirements

As of November 30, 2023, our operations have primarily been funded through the net proceeds from equity offerings of $650.5 million and proceeds from collaborations of $409.0 million. We do not have any products approved for sale, and we have not generated any revenue from product sales. As of November 30, 2023, we had $295.3 million in cash, cash equivalents and marketable securities.

We expect that our existing cash, cash equivalents and marketable securities are sufficient to meet our cash requirements and continue operating activities, including the clinical trials of our drug candidates NX-5948, NX-2127 and NX-1607 and the expansion of our intellectual property portfolio and infrastructure, for at least the next 12 months. We will need substantial additional funding to support our continuing operations and pursue our long-term business plan. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing and distribution arrangements. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug candidates and the extent to which we may enter into additional collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated preclinical studies and clinical trials.

In the long term, our ability to support our working capital and capital expenditure requirements will depend on many factors, including the following:

- the progress, costs and results of our ongoing Phase 1 clinical trials for our lead drug candidates NX-5948, NX-2127 and NX-1607, and any future clinical development of such drug candidates;

- the scope, progress, costs and results of preclinical and clinical development for our other drug candidates and development programs;
- the number and development requirements of other drug candidates that we pursue;
- the scope of, and costs associated with, future advancements to our DELigase platform;
- the success of our collaborations with Gilead, Sanofi, Pfizer and any other collaborations we may establish;
- the costs, timing and outcome of regulatory review of our drug candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our drug candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our drug candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- our ability to establish additional collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of our drug candidates.

We considered whether there are conditions or events that raise substantial doubt about our ability to continue as a going concern and evaluated the funds necessary to maintain operations. If we are unable to obtain additional funding, we will be required to implement plans that are within our control, which may include the delay or scaling back of certain research and development programs, to maintain liquidity and operations. Additionally, we may be required to obtain funds through arrangements with others that may require us to relinquish rights to certain of our technologies or products that we would otherwise seek to develop or commercialize ourselves, or cease operations. If we do raise additional capital through public or private equity or convertible debt offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Our contractual obligations mostly consist of our operating lease obligations for our facilities in San Francisco, California and The Woodlands, Texas. Our total operating lease commitments as of November 30, 2023, were approximately $42.4 million, of which $7.6 million is expected to be paid within the next 12 months. In addition, we enter into agreements in the normal course of business with contract research organizations for clinical trials and with vendors for preclinical studies and other services and products for operating purposes, which are generally cancelable upon written notice.

We did not have during the periods presented, and we do not currently have, any commitments or obligations, including contingent obligations, arising from arrangements with unconsolidated entities or persons that have or are reasonably likely to have a material current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, cash requirements or capital resources.

Cash flows

Our cash flows for the years ended November 30, 2023 and 2022 are summarized as follows (in thousands):

	Year ended November 30,	
	2023	2022
Cash used in operating activities	$ (81,365)	$ (159,807)
Cash provided by investing activities	68,301	27,198
Cash provided by financing activities	3,217	117,192
Net decrease in cash, cash equivalents and restricted cash	$ (9,847)	$ (15,417)

Operating activities

Net cash used in operating activities was $81.4 million for the year ended November 30, 2023, and consisted of our net loss of $143.9 million, offset by non-cash adjustments of $42.5 million and a decrease in net assets of $20.1 million. Non-cash adjustments primarily consisted of stock-based compensation expenses of $33.7 million, depreciation and amortization expenses of $7.5 million and amortization of operating lease ROU assets of $6.1 million, offset by net accretion of discount on marketable securities of $5.4 million. The decrease in net assets consisted of an increase in deferred revenue of $19.5 million mainly from the upfront payment received pursuant to the Pfizer Agreement, an increase in accrued expenses and other liabilities of $3.1 million primarily related to the accrual of annual incentive compensation, a decrease in prepaid expenses and other assets of $2.1 million primarily due to the recognition of expenses for prepaid services and an increase in accounts payable of $1.6 million from outstanding payments to vendors, offset by a decrease in operating lease liabilities of $6.3 million due to payments made on operating leases.

Net cash used in operating activities was $159.8 million for the year ended November 30, 2022, and consisted of our net loss of $180.4 million and an increase in net assets of $19.0 million, offset by non-cash adjustments of $39.6 million. The increase in net assets consisted primarily of a decrease in deferred revenue of $26.6 million as we increased effort in our programs and recognized revenue, a decrease in operating lease liabilities of $4.9 million due to payments made on operating leases and an increase in prepaid expenses and other assets of $1.1 million primarily related to increased prepaid clinical and contract manufacturing costs and software license costs, offset by an increase in accrued expenses and other liabilities of $7.5 million primarily related to the accrual of contract research, laboratory supplies and annual incentive compensation and a decrease in accounts receivable of $6.0 million related to payments received under the Gilead Agreement. Non-cash adjustments primarily consisted of stock-based compensation expenses of $28.1 million, amortization of operating lease ROU assets of $5.5 million and depreciation and amortization expenses of $5.3 million.

Investing activities

Net cash provided by investing activities was $68.3 million for the year ended November 30, 2023, and consisted of the maturity of marketable securities of $323.0 million, offset by the purchase of marketable securities of $246.3 million and purchases of property and equipment of $8.4 million.

Net cash provided by investing activities was $27.2 million for the year ended November 30, 2022, and consisted of the maturity of marketable securities of $278.8 million, offset by the purchase of marketable securities of $239.4 million and purchases of property and equipment of $12.2 million.

Financing activities

Net cash provided by financing activities was $3.2 million for the year ended November 30, 2023, and consisted primarily of proceeds from the issuance of common stock under our Employee Stock Purchase Plan.

Net cash provided by financing activities was $117.2 million for the year ended November 30, 2022, and consisted primarily of net proceeds from the issuance of pre-funded warrants in the RDOs of $94.8 million and from the issuance of common stock in the June 2022 ATM Offering of $19.4 million.

Information About Segments

We currently operate in a single business segment. See additional information in our financial statements contained in Part II, Item 8 of this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

As a “smaller reporting company” as defined by Item 10 of Regulation S-K, we are not required to provide this information.

Item 8. Financial Statements and Supplementary Data

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Nurix Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Nurix Therapeutics, Inc. and its subsidiaries (the "Company") as of November 30, 2023 and 2022, and the related consolidated statements of operations, of comprehensive loss, of stockholders' equity and of cash flows for the years then ended, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of November 30, 2023 and 2022, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (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 of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company will need substantial additional funding to support its continuing operations and pursue its long-term business plan. Management's plans in regard to this matter are described in Note 1.

Critical Audit Matters

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

Revenue Recognition - Estimated Costs of Internal Full-Time Employees (FTEs) - Sanofi

As described in Note 3 to the consolidated financial statements, the Company's consolidated revenue was $76.9 million for the year ended November 30, 2023 of which there was revenue of $25.4 million generated from the Company's collaboration agreement with Sanofi. During the contract term, management uses a cost-based input method, which the Company determined most faithfully depicts the transfer of its performance obligation to Sanofi, to recognize revenue based on the actual costs incurred as a percentage of total estimated costs as the Company completes its performance obligation under the contract. Costs consist primarily of internal FTE and third-party contract costs related to the Sanofi agreement. The cumulative effect of revisions to estimated costs to complete the Company's performance obligation is recorded in the period in which changes are identified and amounts can be reasonably estimated. Total estimated costs are primarily driven by the number of estimated FTEs, which requires significant management judgment.

The principal considerations for our determination that performing procedures relating to revenue recognition - estimated costs of internal FTEs is a critical audit matter are (i) the high degree of auditor judgment and subjectivity in performing procedures relating to the estimated costs of internal FTEs due to the significant judgment by management when determining the estimate and (ii) the significant audit effort in evaluating the significant assumption related to the number of estimated FTEs.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others, evaluating and testing management's process for determining the estimated costs of internal FTEs, which included evaluating the reasonableness of the significant assumption related to the number of estimated FTEs, by (i) performing a comparison of management's estimated costs of internal FTEs to the actual internal FTE costs driven by the number of estimated FTEs; (ii) testing the completeness and accuracy of the data used by management in the estimate; (iii) evaluating management's timely identification of changes in estimated costs of internal FTEs driven by the number of estimated FTEs; and (iv) evaluating whether the estimate and assumption were consistent with evidence obtained in other areas of the audit.

/s/ PricewaterhouseCoopers LLP
San Jose, California
February 15, 2024

We have served as the Company's auditor since 2014.

NURIX THERAPEUTICS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	November 30,	
	2023	2022
Assets		
Current assets:		
Cash and cash equivalents	$ 54,627	$ 64,474
Marketable securities, current	233,281	244,667
Prepaid expenses and other current assets	7,595	9,308
Total current assets	295,503	318,449
Marketable securities, non-current	7,421	63,879
Operating lease right-of-use assets	31,142	12,345
Property and equipment, net	16,808	17,163
Restricted cash	901	901
Other assets	3,823	4,022
Total assets	$ 355,598	$ 416,759
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,401	$ 5,064
Accrued expenses and other current liabilities	24,970	22,428
Operating lease liabilities, current	7,489	5,530
Deferred revenue, current	48,098	37,633
Total current liabilities	86,958	70,655
Operating lease liabilities, net of current portion	23,125	6,434
Deferred revenue, net of current portion	45,022	35,974
Total liabilities	155,105	113,063
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Preferred stock, $0.001 par value— 10,000,000 shares authorized as of November 30, 2023 and 2022; no shares issued and outstanding as of November 30, 2023 and 2022	—	—
Common stock, $0.001 par value— 500,000,000 shares authorized as of November 30, 2023 and 2022; 48,718,552 and 47,172,299 shares issued and outstanding as of November 30, 2023 and 2022, respectively	49	47
Additional paid-in capital	746,299	709,220
Accumulated other comprehensive loss	(655)	(4,319)
Accumulated deficit	(545,200)	(401,252)
Total stockholders' equity	200,493	303,696
Total liabilities and stockholders' equity	$ 355,598	$ 416,759

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

NURIX THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)

	Year Ended November 30,	
	2023	2022
Revenue:		
Collaboration revenue	$ 56,987	$ 38,627
License revenue	20,000	—
Total revenue	76,987	38,627
Operating expenses:		
Research and development	189,148	184,497
General and administrative	42,902	37,997
Total operating expenses	232,050	222,494
Loss from operations	(155,063)	(183,867)
Interest and other income, net	11,115	3,507
Net loss	$ (143,948)	$ (180,360)
Net loss per share, basic and diluted	$ (2.65)	$ (3.71)
Weighted-average number of shares outstanding, basic and diluted	54,337,901	48,607,990

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

NURIX THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)

	Year Ended November 30,	
	2023	2022
Net loss	$ (143,948)	$ (180,360)
Other comprehensive loss, net of tax:		
Unrealized gain (loss) on available-for-sale marketable securities	3,664	(3,711)
Total comprehensive loss	$ (140,284)	$ (184,071)

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

NURIX THERAPEUTICS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share amounts)

	Common stock		Additional paid-in capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
	Shares	Amount				
Balance as of November 30, 2021	44,664,371	$ 45	$ 563,757	$ (608)	$ (220,892)	$ 342,302
Issuance of pre-funded warrants, net of issuance costs of $234	—	—	94,759	—	—	94,759
Issuance of common stock in "at the market" financing, net of issuance costs of $672	2,000,000	2	19,326	—	—	19,328
Exercise of stock options	325,596	—	1,078	—	—	1,078
Vesting of restricted stock units	46,028	—	—	—	—	—
Vesting of early exercised stock options	—	—	145	—	—	145
Issuance under employee stock purchase plan	136,304	—	1,955	—	—	1,955
Stock-based compensation	—	—	28,200	—	—	28,200
Unrealized loss on available-for-sale marketable securities	—	—	—	(3,711)	—	(3,711)
Net loss	—	—	—	—	(180,360)	(180,360)
Balance as of November 30, 2022	47,172,299	47	709,220	(4,319)	(401,252)	303,696
Exercise of pre-funded warrants	717,360	2	—	—	—	2
Exercise of stock options	120,826	—	986	—	—	986
Vesting of restricted stock units	441,103	—	—	—	—	—
Vesting of early exercised stock options	—	—	117	—	—	117
Issuance under employee stock purchase plan	266,964	—	2,229	—	—	2,229
Stock-based compensation	—	—	33,747	—	—	33,747
Unrealized gain on available-for-sale marketable securities	—	—	—	3,664	—	3,664
Net loss	—	—	—	—	(143,948)	(143,948)
Balance as of November 30, 2023	48,718,552	$ 49	$ 746,299	$ (655)	$ (545,200)	$ 200,493

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

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

	Year Ended November 30,	
	2023	**2022**
Cash flows from operating activities		
Net loss	$ (143,948)	$ (180,360)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	7,533	5,349
Stock-based compensation	33,673	28,131
Net amortization (accretion) of premium (discount) on marketable securities	(5,421)	426
Loss on disposal of property and equipment	556	9
Amortization of operating lease right-of-use assets	6,121	5,459
Other	—	201
Changes in operating assets and liabilities:		
Accounts receivable	—	6,000
Prepaid expenses and other assets	2,139	(1,094)
Accounts payable	1,614	85
Deferred revenue	19,513	(26,627)
Operating lease liabilities	(6,268)	(4,871)
Accrued expenses and other liabilities	3,123	7,485
Net cash used in operating activities	(81,365)	(159,807)
Cash flows from investing activities		
Purchases of marketable securities	(246,334)	(239,366)
Maturities of marketable securities	323,036	278,808
Purchases of property and equipment	(8,401)	(12,244)
Net cash provided by investing activities	68,301	27,198
Cash flows from financing activities		
Proceeds from issuances of pre-funded warrants, net of issuance costs	—	94,759
Proceeds from issuances of common stock in equity financing, net of issuance costs	—	19,400
Proceeds from exercise of stock options and pre-funded warrants	988	1,078
Proceeds from issuance under employee stock purchase plan	2,229	1,955
Net cash provided by financing activities	3,217	117,192
Net decrease in cash, cash equivalents and restricted cash	(9,847)	(15,417)
Cash, cash equivalents and restricted cash at beginning of period	65,375	80,792
Cash, cash equivalents and restricted cash at end of period	$ 55,528	$ 65,375
Supplemental disclosures of non-cash investing and financing activities:		
Additions to property and equipment included in accounts payable and accrued expenses and other liabilities	$ 632	$ 1,373
Capitalized stock-based compensation related to internal-use software development	$ 74	$ 69
Right-of-use assets recognized in exchange for lease obligations	$ 23,995	$ 5,068
Vesting of early exercised stock options	$ 117	$ 145
Deferred issuance costs recognized related to equity financing	$ —	$ 72

	As of November 30,	
	2023	**2022**
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 54,627	$ 64,474
Restricted cash	901	901
Cash, cash equivalents and restricted cash	$ 55,528	$ 65,375

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

1. Organization

Description of Business

Nurix Therapeutics, Inc. (the Company) was incorporated in the state of Delaware on August 27, 2009, and is headquartered in San Francisco, California. The Company is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative small molecules and antibody therapies based on the modulation of cellular protein levels as a novel treatment approach for cancer, inflammatory conditions and other challenging diseases. Leveraging the Company's expertise in E3 ligases together with its proprietary DNA-encoded libraries, the Company has built DELigase, an integrated discovery platform to identify and advance novel drug candidates targeting E3 ligases, a broad class of enzymes that can modulate proteins within the cell. The Company's drug discovery approach is to either harness or inhibit the natural function of E3 ligases within the ubiquitin-proteasome system to selectively decrease or increase cellular protein levels. The Company's wholly owned, clinical stage pipeline includes targeted protein degraders of Bruton's tyrosine kinase, a B-cell signaling protein, and inhibitors of Casitas B-lineage lymphoma proto-oncogene B, an E3 ligase that regulates activation of multiple immune cell types including T cells and NK cells. The Company's partnered drug discovery pipeline consists of multiple programs under collaboration agreements with Gilead Sciences, Inc. (Gilead), Sanofi S.A. (Sanofi) and Seagen Inc. (now a part of Pfizer Inc. (Pfizer)), within which the Company retains certain options for co-development, co-commercialization and profit sharing in the United States for multiple drug candidates.

Equity Distribution Agreement

In August 2021, the Company filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission, which was amended in February 2023. This shelf registration statement, which includes a base prospectus, allows the Company at any time to offer and sell up to $450.0 million of the Company's registered common stock, preferred stock, debt securities, warrants, subscriptions rights and or units or any combination of securities described in the prospectus in one or more offerings. In addition, in August 2021, the Company entered into an Equity Distribution Agreement with Piper Sandler & Co. (Piper Sandler) pursuant to which, from time to time, the Company may offer and sell through Piper Sandler up to $150.0 million of the common stock registered under the shelf registration statement pursuant to one or more "at the market" offerings.

The Company is not required to sell any shares at any time during the term of the Equity Distribution Agreement. The Company agreed to pay Piper Sandler a commission of 3% of the gross sales price of any shares sold pursuant to the Equity Distribution Agreement. In June 2022, the Company issued and sold 2,000,000 shares of common stock under the Equity Distribution Agreement at a price of $10.0001 per share of common stock for net proceeds of $19.3 million, after deducting offering commissions and expenses paid by the Company. As of November 30, 2023, the Company had $130.0 million of common stock remaining available for sale under the Equity Distribution Agreement.

Registered Direct Offerings

In July 2022, the Company entered into separate securities purchase agreements with certain purchasers to issue and sell pre-funded warrants to purchase an aggregate of 6,814,920 shares of the Company's common stock in registered direct offerings (RDOs) at a price of $13.939 per pre-funded warrant. Net proceeds from the RDOs were $94.8 million, after deducting offering expenses of $0.2 million. Refer to Note 7 for more information regarding the pre-funded warrants issued in the RDOs.

Liquidity and Management Plans

As of November 30, 2023, the Company had cash, cash equivalents and short-term marketable securities of $287.9 million, working capital of $208.5 million and an accumulated deficit of $545.2 million. The Company's operations have historically been financed through the issuance of common stock, redeemable convertible preferred stock and pre-funded warrants and proceeds received under the Company's collaboration and license agreements. Since inception, the Company has generally incurred significant losses and negative net cash flows from operations. The Company does not expect its existing cash, cash equivalents and marketable securities to be sufficient to fund the completion of its clinical trials through commercialization and will need substantial additional funding to support its continuing operations and pursue its long-term business plan. The Company anticipates incurring additional losses until such time, if ever, that it can generate significant sales of its drug candidates currently in development.

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. Management believes that its cash, cash equivalents and short-term marketable securities are sufficient to continue operating activities for at least 12 months following the issuance date of these consolidated financial statements. Future capital requirements will depend on many factors, including the timing and extent of spending on research and development and payments the Company may receive under its collaboration agreements with Sanofi, Gilead and Pfizer or future collaboration agreements, if any. There can be no assurance that, in the event the Company requires additional financing, such financing will be available at terms acceptable to the Company if at all. If additional capital is not available, failure to generate sufficient cash flows from operations, raise additional capital and reduce discretionary spending could have a material adverse effect on the Company's ability to achieve its intended business objectives. Management considered whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern and evaluated the funds necessary to maintain operations. If the Company is unable to obtain additional funding, management will be required to implement plans that are within the Company's control, which may include the delay or scaling back of certain research and development programs, to maintain liquidity and operations. Based on the Company's current forecast of future operating results and management's plans to improve liquidity, the Company has concluded that its cash, cash equivalents and short-term marketable securities are sufficient to continue operating activities for at least 12 months following the issuance date of these consolidated financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The Company's consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) and include the accounts of the Company and its wholly owned subsidiaries, including DeCART Therapeutics Inc., which was legally dissolved in July 2022. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities at the date of the financial statements and reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to the useful lives of long-lived assets, the measurement of stock-based compensation, accruals for research and development activities, income taxes and revenue recognition. The Company also makes certain commencement date estimates for its leases, including the incremental borrowing rate, the expected lease term and the fair value of the leased asset. The Company bases its estimates on historical experience and on other relevant assumptions that are reasonable under the circumstances. Actual results could materially differ from those estimates. Refer to Note 3 for more information regarding the estimates related to revenue recognition.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash, cash equivalents and marketable securities. The Company's marketable securities consist of debt securities issued by highly rated corporate entities, the U.S. federal government or state and local governments. The Company's exposure to any individual corporate entity is limited by policy. Deposits may, at times, exceed federally insured limits. The Company invests its cash equivalents in highly rated money market funds. During the periods presented, the Company has not experienced any losses on its deposits of cash, cash equivalents or marketable securities.

Other Risks and Uncertainties

The Company is subject to a number of risks similar to other clinical stage biopharmaceutical companies, including, but not limited to, changes in any of the following areas that the Company believes could have a material adverse effect on its future financial position or results of operations: risks related to the successful discovery and development of its drug candidates, ability to raise additional capital, development of new technological innovations by its competitors and delay or inability to obtain drug substance and finished drug product from the Company's third-party contract manufacturers necessary for the Company's drug candidates, protection of intellectual property rights, litigation or claims against the Company based on intellectual property rights and regulatory clearance and market acceptance for any of the Company's products candidates for which the Company receives marketing approval.

Moreover, the Company is subject to risks and uncertainties as a result of global business, political and macroeconomic events and conditions, including increasing financial market volatility and uncertainty, inflation, increasing interest rates, uncertainty with respect to the federal budget and debt ceiling and potential government shutdowns related thereto, potential instability in the global banking system, cybersecurity events, the impact of war or military conflict, including regional conflicts around the world, and public health pandemics. The extent to which business, political and macroeconomic factors, including increasing financial market volatility and uncertainty, will impact the Company's business will depend on future developments that are highly uncertain and cannot be predicted at this time.

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. The extent to which the increasing financial market volatility and uncertainty may directly or indirectly impact the Company's financial statements is highly uncertain and subject to change.

The Company relies on single source manufacturers and suppliers for the supply of its drug candidates. Disruption from these manufacturers or suppliers would have a negative impact on the Company's business, financial position and results of operations.

Segments

The Company operates and manages its business as one reportable and operating segment. Operating segments are defined as components of an enterprise where separate financial information is evaluated regularly by the chief operating decision maker (CODM) in deciding how to allocate resources and assess performance. The Company's CODM is the Chief Executive Officer, who reviews consolidated financial information on a company-wide basis for purposes of allocating resources and assessing financial performance.

Cash and Cash Equivalents

The Company considers all highly liquid marketable securities with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents, which consist of money market funds, are stated at fair value.

Restricted Cash

The Company had $0.9 million of restricted cash recorded as a non-current asset as of each of November 30, 2023 and 2022. Restricted cash as of each of November 30, 2023 and 2022 consisted of $0.1 million that serves as collateral for a business credit card account and $0.8 million for letters of credit required under operating leases. These balances are included within the cash, cash equivalents and restricted cash balance in the accompanying consolidated statements of cash flows.

Fair Value of Financial Instruments

The carrying amounts of the Company's financial instruments, including cash equivalents, accounts payable and accrued liabilities included in the Company's consolidated financial statements approximate their fair value due to the nature of the financial instruments. Refer to Note 5 for more information regarding the fair value of the Company's marketable securities.

Marketable Securities

Marketable securities consist of money market funds, U.S. Treasuries, corporate debt securities, U.S. government agency securities, corporate commercial paper and foreign government securities. The Company's marketable securities are classified as available-for-sale and carried at estimated fair values and reported in cash equivalents, short-term marketable securities or long-term marketable securities. Management determines the appropriate classification of the marketable securities at the time they are acquired and evaluates the appropriateness of such classifications at each consolidated balance sheet date. Marketable securities with contractual maturities greater than 12 months are considered long-term marketable securities.

The Company regularly reviews its marketable securities for declines in estimated fair value below amortized cost. The factors considered in determining whether a credit loss exists include the creditworthiness of the security issuers, the number of marketable securities in an unrealized loss position, the severity and duration of the unrealized losses, and whether it is more likely than not that the Company will be required to sell the marketable securities before the recovery of their amortized cost basis. The cost of marketable securities sold is based on the specific identification method. In circumstances when an unrealized loss is determined to be credit-related, or when the Company intends to sell or is more likely than not required to sell a security before it recovers its amortized cost basis, the difference between the fair value and the amortized cost of the security is recognized as interest and other income, net in the consolidated statements of operations, and an allowance for credit loss is recorded on the consolidated balance sheet. In circumstances when the decline in fair value is non-credit related, the difference is reported in accumulated other comprehensive income (loss), net of tax as a separate component of stockholders' equity.

The Company excludes accrued interest from both the fair value and the amortized cost basis of marketable securities for the purposes of identifying and measuring an impairment. The Company writes off accrued interest receivables that have become more than 90 days delinquent by reversing interest income. To date, the Company has not written off any accrued interest receivables associated with its marketable securities.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Major improvements are capitalized, while maintenance and repairs are expensed when incurred. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. The useful life of laboratory equipment, computer equipment, furniture and fixtures and software is generally three years. Tenant improvements are depreciated over the shorter of the lease term or the estimated useful life of the improvements. When assets are retired or disposed of, the cost together with related accumulated depreciation is removed from the Company's accounts and the resulting gain or loss is reflected in the Company's consolidated statements of operations.

Leases

The Company determines if an arrangement contains a lease and the classification of the lease at inception. An arrangement contains a lease if there is an identified asset and if the Company controls the use of the identified asset throughout the period of use.The evaluation of whether the lease is an operating or a finance lease requires judgments in determining the fair value of the leased asset. Lease right-of-use (ROU) assets and lease liabilities are recognized at the lease commencement date based on the present value of the future minimum lease payments over the lease term at the commencement date. ROU assets also include any initial direct costs incurred and any lease payments made on or before the lease commencement date, less any lease incentives received. The Company uses its incremental borrowing rate, if an implicit rate is not readily available, and the information available at the date of lease commencement in determining its lease liabilities. The Company's incremental borrowing rate is based on the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment, and the determination of the rate requires the Company to make certain assumptions and judgements, including on its synthetic credit rating. Leases may include options to extend or early terminate the lease term. If the Company, using judgement, is reasonably certain that an option will be exercised, then the option will be included in the calculation of the lease term. The Company elected to combine lease and non-lease components for all underlying assets groups, and not recognize ROU assets or lease liabilities for short-term leases. A short-term lease is a lease that, at the commencement date, has a lease term of 12 months or less and does not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise. Lease expense for operating leases is recognized on a straight-line basis over the lease term. The Company does not have any finance leases.

Internal-Use Software Development Costs

The Company capitalizes qualifying costs incurred during the application development stage related to software developed for internal-use and amortizes them over the estimated useful life of three years. Amortization of such costs begins when the project is substantially complete and ready for its intended use. Capitalized software development costs are classified as property and equipment, net on the consolidated balance sheet. The Company expenses costs incurred related to the planning and post-implementation phases of development as incurred.

Long-Lived Assets

Long-lived assets, such as property and equipment are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be fully recoverable. If circumstances require a long-lived asset or asset group to be tested for possible impairment, the Company first compares undiscounted cash flows expected to be generated by that asset or asset group to its carrying value. If the carrying value of the long-lived asset or asset group is not recoverable on an undiscounted cash flow basis, an impairment is recognized to the extent that the carrying value exceeds its fair value. Fair value is determined through various valuation techniques including discounted cash flow models, quoted market values and third-party independent appraisals, as considered necessary. There were no such impairment losses during the years ended November 30, 2023 and 2022.

Deferred Offering Costs

The Company capitalizes within other assets certain legal, accounting and other third-party fees that are directly related to the Company's in-process equity financings until such financings are consummated. After consummation of an equity financing, these costs are recorded in stockholder's equity as a reduction of additional paid-in capital generated as a result of the offering. Should a planned equity financing be abandoned, terminated or significantly delayed, the deferred offering costs are immediately written off to operating expenses. As of both November 30, 2023 and 2022, there was $0.5 million of deferred offering costs included in other assets on the consolidated balance sheet.

Revenue Recognition

The Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To recognize revenue from a contract with a customer, the Company performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the Company satisfies a performance obligation.

At contract inception, the Company assesses the goods or services promised within each contract, whether each promised good or service is distinct, and determines those that are performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when or as the performance obligation is satisfied.

The Company enters into collaboration agreements under which it may obtain upfront payments, milestone payments, royalty payments and other fees. Promises under these arrangements may include research licenses, research services, including selection campaign research services for certain replacement targets, the obligation to share information during the research and the participation of alliance managers and in joint research committees, joint patent committees and joint steering committees. The Company assesses these promises within the context of the agreements to determine the performance obligations.

Exclusive license rights: If a license to the Company's intellectual property is determined to be distinct from the other promises identified in the arrangement, the Company recognizes revenue from nonrefundable, upfront payments allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license and the underlying intellectual property. If the license is the predominant promise, and it is determined that the license represents functional intellectual property, revenue is recognized at the point in time when control of the license is transferred. If it is determined that the license does not represent functional intellectual property, revenue is recognized over time using an appropriate method of measuring progress.

Research and collaboration licenses: Collaboration agreements may include research licenses and research and development services to be performed by the Company. For research licenses that are bundled 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 proportional performance for purposes of recognizing revenue from non-refundable, upfront payments. The Company evaluates the measure of proportional performance each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes research, development or regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price. The Company uses the most likely amount method for research, development and regulatory milestone payments. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. If it is probable that a significant revenue reversal would not occur, the associated milestone amount is included in the transaction price.

Sales-based milestones and royalties: For arrangements that include sales-based milestone or royalty payments based on the level of sales, and in which the license is deemed to be the predominant item to which the sales-based milestone or royalties relate to, the Company recognizes revenue in the period in which the sales-based milestone is achieved and in the period in which the sales associated with the royalty occur. To date, the Company has not recognized any sales-based milestone or royalty revenue resulting from its collaboration arrangements.

Customer options: Customer options, such as options granted to allow a licensee to extend a license or research term, to select additional research targets or to choose to research, develop and commercialize licensed compounds are evaluated at contract inception to determine whether those options provide a material right (i.e., an optional good or service offered for free or at a discount) to the customer. If the customer options represent a material right, the material right is treated as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the standalone selling price. As a practical alternative to estimating the standalone selling price of a material right when the underlying goods or services are both (i) similar to the original goods or services in the contract and (ii) provided in accordance with the terms of the original contract, the Company allocates the total amount of consideration expected to be received from the customer to the total goods or services expected to be provided to the customer. Amounts allocated to any material right are recognized as revenue when or as the related future goods or services are transferred or when the option expires.

Deferred revenue, which is a contract liability, represents net amounts received by the Company for which the related revenues have not been recognized because one or more of the revenue recognition criteria have not been met. The current portion of deferred revenue represents the amount to be recognized within one year from the consolidated balance sheet date based on the estimated performance period of the underlying performance obligation. The non-current portion of deferred revenue represents amounts to be recognized after one year through the end of the performance period of the performance obligation.

All revenue was derived from customers located in the United States during the years ended November 30, 2023 and 2022.

Research and Development Expenses

The Company expenses all research and development costs as incurred. Research and development costs include, but are not limited to, payroll and personnel expenses, laboratory supplies, preclinical study costs, clinical trial costs, compound manufacturing costs, consulting costs and allocated overhead, including rent, equipment, depreciation and utilities.

The Company records accrued expenses for estimated costs of research and development activities conducted by third-party service providers, which include preclinical studies and clinical trials and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and includes these costs in accrued expenses and other current liabilities on the consolidated balance sheet.

The Company estimates the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. The Company makes significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, the Company adjusts its accrued estimates. The Company's accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers. The Company records advance payments to service providers as prepaid assets, which are expensed as the contracted services are performed.

Stock-Based Compensation

The Company accounts for stock-based compensation using a fair value-based method, which requires the recognition of compensation expense for costs related to all stock-based payments including stock options, restricted stock units (RSUs) and purchase rights under the Company's 2020 Employee Stock Purchase Plan (ESPP). The Company estimates the fair value of stock options and purchase rights granted under the ESPP on the date of grant using the Black-Scholes option pricing model, which is impacted by the fair value of the Company's common stock, as well as changes in assumptions regarding a number of highly complex and subjective variables. The model requires management to make a number of assumptions including expected volatility, expected term, risk-free interest rate and expected dividend yield. The Company determines the fair value of stock options, RSUs and purchase rights under the ESPP using the market closing price of the Company's common stock on the date of grant.

For stock-based payments with service conditions only, the Company uses the straight-line method to allocate compensation cost to reporting periods over the requisite service period, which is generally the vesting period. Stock-based compensation expense for non-employee stock-based awards is also measured based on the grant date fair value with the estimated fair value expensed over the period for which the non-employee is required to provide service in exchange for the award. For stock-based payments with performance conditions, the Company evaluates the probability of achieving performance conditions at each reporting date. The Company begins to recognize compensation cost using an accelerated attribution method when it is deemed probable that the performance condition will be met. The Company accounts for forfeitures as they occur.

Income taxes

The Company accounts for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Valuation allowances are established when in management's estimate, it is more likely than not, that the deferred tax assets will not be recovered.

Financial statement effects of uncertain tax positions are recognized when it is more likely than not, based on the technical merits of the position, that it will be sustained upon examination. It is the Company's policy to include penalties and interest expense related to income taxes as a component of the provision for income taxes. Non-income-based taxes are expensed as incurred within operating expenses on the Company's consolidated statements of operations.

Comprehensive loss

Comprehensive loss represents the net loss for the period and other comprehensive income (loss). Other comprehensive income (loss) reflects certain gains and losses that are recorded as a component of stockholders' equity (deficit) and are not reflected in the consolidated statements of operations. The Company's other comprehensive income (loss) consists of changes in unrealized gains and losses on available-for-sale marketable securities.

Net loss per share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock (including non-voting common stock and pre-funded warrants) outstanding during the period, without consideration for all other common stock equivalents. Shares of common stock into which the pre-funded warrants may be exercised are considered outstanding for the purposes of computing net loss per share because the shares may be issued for little or no consideration, are fully vested and are exercisable after the original issuance date. Diluted net loss is calculated by dividing the net loss by the weighted-average number of common stock and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share calculation, options to purchase common stock, options early exercised subject to vesting, RSUs and shares expected to be purchased under the ESPP are considered to be potentially dilutive securities. Diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive given the net loss for each period presented.

Recent Accounting Pronouncements Not Yet Adopted

In November 2023, the Financial Accounting Standards Board (FASB) issued Accounting Standard Update (ASU) No. 2023-07, Segment Reporting (Topic 280)—Improvements to Reportable Segment Disclosures (ASU 2023-07), which is intended to improve reportable segment disclosure requirements, primarily through enhanced disclosures about significant segment expenses. ASU 2023-07 should be applied on a retrospective basis. ASU 2023-07 is effective for annual periods beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024. Early adoption is permitted. The Company is in the process of evaluating the impact of this new guidance on its disclosures.

In December 2023, the FASB issued ASU 2023-09—Income Taxes (Topic 740): Improvements to Income Tax Disclosures (ASU 2023-09), which is intended to enhance the transparency and decision usefulness of income tax disclosures, primarily by amending disclosure requirements for the effective tax rate reconciliation and income taxes paid. ASU 2023-09 should be applied on a prospective basis, and retrospective application is permitted. ASU 2023-09 is effective for annual periods beginning after December 15, 2024. Early adoption is permitted. The Company is in the process of evaluating the impact of this new guidance on its disclosures.

3. Collaboration Agreements

Gilead

In June 2019, the Company entered into a global strategic collaboration agreement with Gilead (as subsequently amended, the Gilead Agreement) to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with cancer and other challenging diseases using the Company's DELigase platform to identify novel agents that utilize E3 ligases to induce degradation of five specified drug targets. In August 2019 and September 2022, the Company entered into the First Amendment and the Second Amendment, respectively, to the Gilead Agreement to clarify certain language of the Gilead Agreement. These amendments had no impact on revenue recognition.

Under the Gilead Agreement, Gilead has the option to license drug candidates directed to up to five targets resulting from the collaboration and is responsible for the clinical development and commercialization of drug candidates resulting from the collaboration. The Company retains the option to co-develop and co-promote, under a profit share structure, up to two drug candidates in the United States, provided that the Company may only exercise such option once per licensed product and Gilead retains the right to veto the Company's option selection for any one drug candidate of its choice. The collaboration excludes the Company's current internal protein degradation programs for which the Company retains all rights, and also excludes the Company's future internal programs, provided that the Company has distinguished future programs as excluded from the scope of the collaboration. In March 2023, Gilead exercised the option, which did not represent a material right at contract inception, since it was not offered for free or at a discount, to exclusively license one target (Gilead License Option Exercise), the first development candidate resulting from the Gilead Agreement. Pursuant to the Gilead Agreement, the Company received a license option exercise payment of $20.0 million in April 2023 for the Gilead License Option Exercise. The license to the functional intellectual property and all goods and services related to the Gilead License Option Exercise were transferred during the second quarter of fiscal year 2023.

Over time, Gilead may elect to replace the initial drug targets with other drug targets. For drug targets that are subject to the collaboration, the Company is obligated to use commercially reasonable efforts to undertake a research program in accordance with a research plan agreed to by the parties and established on a target-by-target basis. The Company has primary responsibility under the Gilead Agreement for performing preclinical research activities (including target validation, drug discovery, identification or synthesis) pursuant to a research plan. Each party will bear its own costs in the conduct of research activities. Gilead will be responsible for any development, commercialization and manufacturing activities, unless the Company exercises its co-development and co-promotion option. For those programs that the Company exercises its option to co-develop and co-promote, the Company and Gilead will split U.S. development costs as well as U.S. profits and losses evenly, and the Company will be eligible to receive royalties on net ex-U.S. sales and reduced milestone payments.

Upon signing the Gilead Agreement, Gilead paid the Company an upfront payment of $45.0 million plus $3.0 million in additional fees. In addition, from the signing of the Gilead Agreement to November 30, 2023, the Company has received payments of $47.0 million for research milestones and additional payments and $20.0 million for a license option exercise payment. As of November 30, 2023, the Company is eligible to receive up to approximately $2.3 billion in total additional payments based on certain additional fees, payments and the successful completion of certain preclinical, clinical, development and sales milestones. The Company also is eligible to receive mid-single digit to low tens percentage tiered royalties on annual net sales from any commercial products directed to the optioned collaboration targets, subject to certain reductions and excluding sales in the United States of any products for which the Company exercises its option to co-develop and co-promote, for which the parties share profits and losses evenly.

Subject to earlier expiration in certain circumstances, the Gilead Agreement expires on a licensed product-by-licensed product and country-by-country basis upon the later of (1) the expiration of the last to expire patent with a valid claim covering the applicable licensed product in the applicable country, (2) the expiration of any regulatory exclusivity for the applicable licensed product in the applicable country or (3) ten years after the first commercial sale of the applicable licensed product in the applicable country covered by the Gilead Agreement, provided that the term for any profit-shared licensed product in the United States will expire upon the expiration or termination of the applicable profit-share term as set forth in an applicable profit-share agreement to be negotiated upon the Company's exercise of its option to co-develop and co-promote such licensed product. If Gilead does not exercise an option to license a drug candidate, then the Gilead Agreement will terminate at the end of the last to expire option period.

The Company identified the following promises in the Gilead Agreement: (1) the research licenses, (2) the research services, including selection campaign research services for certain replacement targets, (3) the obligation to share information during the research term and (4) the participation in the joint research committee and joint steering committee. The Company determined that the research licenses, the obligation to share information and the participation in joint committees are not capable of being distinct from the research services due to the specialized nature of the research services to be provided by the Company, and, accordingly, the promises identified were combined as one single performance obligation. The Company also concluded that, at the inception of the Gilead Agreement, Gilead's options to obtain an exclusive development, manufacturing and commercialization license for each collaboration target, to extend the five-year research term and to perform selection campaign research services for certain replacement targets do not represent material rights and are not considered performance obligations because they do not contain a significant and incremental discount. The Company concluded that Gilead's target reservation right is not a performance obligation as it does not require any specific action from the Company and it is rather an exclusivity right and an attribute of other performance obligations in the Gilead Agreement, such as the research licenses.

In order to determine the transaction price, the Company evaluated all the payments to be received during the duration of the contract. Certain milestone payments and additional fees were considered variable consideration, which were not included in the transaction price based on the most likely amount method as of November 30, 2023. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that the transaction price at the inception of the Gilead Agreement consisted of the upfront payment of $45.0 million and $3.0 million in additional fees. Upon the achievement of research milestones and additional fees related to target reservations, $47.0 million in variable consideration was added to the transaction price, and a cumulative effect was recorded as revenue in the period the transaction price increased. The transaction price is recognized as collaboration revenue using the cost-based input method over the estimated research term of five years. The contract term was determined to be the five-year initial research term which represents the estimated timing of completion of the identified deliverables. Additionally, the Company considered the impact of Gilead terminating the Gilead Agreement prior to the completion of the research services during the initial five-year research term and determined that there were significant economic costs to Gilead for doing so, and as such, did not adjust the contract term.

Using the cost-based input method, which the Company determined most faithfully depicts the transfer of its performance obligation to Gilead, the Company recognizes revenue based on actual costs incurred as a percentage of total estimated costs as the Company completes its performance obligation under the contract. Costs consist primarily of internal full-time employee (FTE) and third-party contract costs related to the Gilead Agreement. The cumulative effect of revisions to estimated costs to complete the Company's performance obligation is recorded in the period in which changes are identified and amounts can be reasonably estimated. Total estimated costs are primarily driven by the number of estimated FTEs, which requires significant management judgment.

For the year ended November 30, 2023, the Company recognized collaboration revenue related to the Gilead Agreement of $29.9 million, of which $20.3 million was included in deferred revenue as of November 30, 2022, and $7.9 million was related to performance obligations satisfied in previous periods. For the year ended November 30, 2022, the Company recognized collaboration revenue related to the Gilead Agreement of $23.7 million, of which $18.4 million was included in deferred revenue as of November 30, 2021, and $4.0 million was related to performance obligations satisfied in previous periods. As of November 30, 2023, deferred revenue related to the Gilead Agreement was $10.0 million, all of which was current. As of November 30, 2022, deferred revenue related to the Gilead Agreement was $27.4 million, of which $18.2 million was current.

Sanofi

In December 2019, the Company entered into a strategic collaboration with Genzyme Corporation, a subsidiary of Sanofi, which became effective in January 2020 (as subsequently expanded and amended, the Sanofi Agreement), to discover, develop and commercialize a pipeline of targeted protein degradation drugs for patients with challenging diseases in multiple therapeutic areas using the Company's DELigase platform to identify small molecules designed to induce degradation of three specified initial drug targets. In January 2021, as part of the existing Sanofi Agreement, Sanofi paid the Company $22.0 million to exercise its option to expand the number of targets in the Sanofi Agreement from three to a total of five targets.

In January 2021, the Company entered into the First Amendment to the Sanofi Agreement to modify the research term on all targets (the First Sanofi Amendment). In December 2021, the Company entered into the Second Amendment to the Sanofi Agreement to extend the substitution deadline on certain targets. In July 2022, the Company entered into the Third Amendment to the Sanofi Agreement to further extend the substitution deadline on certain targets. The extensions of the substitution deadline had no impact on revenue recognition. Also in July 2022, Sanofi elected to replace certain drug targets, and the substitution extended the research term of those targets by one year to 5.25 years and increased overall forecasted costs, which had an immaterial impact on revenue recognition. In August 2022 and November 2023, the Company entered into the Fourth Amendment and Fifth Amendment, respectively, to the Sanofi Agreement to modify the research plan for certain targets, which had no impact on revenue recognition.

Under the Sanofi Agreement, Sanofi has exclusive rights and is responsible for the clinical development, commercialization and manufacture of drug candidates resulting from the collaboration while the Company retains the option to co-develop, co-promote and co-commercialize all drug candidates in the United States directed to up to two targets, one of which must be selected from a list of targets designated at the execution of the Sanofi Agreement or any replacement of such targets, and one of which must be selected from targets identified by Sanofi as part of their January 2021 expansion. The Company's right to exercise its option to co-develop, co-promote and co-commercialize a given target is dependent on its ability to demonstrate, within a given timeframe, that it has sufficient cash resources and personnel to commercialize the product. The collaboration excludes the Company's current internal protein degradation programs for which it retains all rights, and also excludes future internal programs, provided that the Company distinguished future programs as excluded from the scope of the collaboration.

For drug targets that are subject to the collaboration, the Company has primary responsibility for conducting preclinical research activities (including target validation, drug discovery, identification or synthesis) in accordance with the applicable research plan agreed to by the parties and established on a target-by-target basis. The Company is obligated to use commercially reasonable efforts to identify relevant target binders and targeted protein degraders in order to identify development candidates. Subject to certain exceptions, each party will bear its own costs in the conduct of such research. Sanofi will be responsible for any development and commercialization activities unless the Company exercises its co-development and co-promotion option. For those programs that the Company exercises its option to co-develop, co-promote and co-commercialize, the Company will be responsible for a portion of the U.S. development costs, and the parties will split U.S. profits and losses evenly and the Company will be eligible to receive royalties on ex-U.S. net sales and reduced milestone payments on such optioned products.

Upon signing the Sanofi Agreement, Sanofi paid the Company an upfront payment of $55.0 million. Subsequently, in January 2021, Sanofi paid the Company an additional $22.0 million to exercise its option to expand the number of targets beyond the initial targets included in the collaboration. In addition, from the signing of the Sanofi Agreement to November 30, 2023, the Company has received payments of $7.0 million for research milestones. Additionally, the Company achieved two research milestones in November 2023 and received payments totaling $4.0 million in January 2024 as a result. As of November 30, 2023, the Company is eligible to receive up to approximately $2.5 billion in total additional payments based on certain additional fees, payments and the successful completion of certain research development, regulatory and sales milestones, as well as mid-single digit to low teen percentage tiered royalties on annual net sales of any commercial products that may result from the collaboration, subject to certain reductions and excluding sales in the United States of any products for which the Company exercises its option to co-develop and co-promote, for which the parties share profits and losses evenly.

Subject to earlier expiration in certain circumstances, the Sanofi Agreement expires on a licensed product-by-licensed product or profit-shared licensed product-by-profit-shared licensed product basis and country-by-country basis upon on the later of (1) the expiration of the last-to-expire patent with a valid claim covering the applicable licensed product in the applicable country, (2) the expiration of any regulatory exclusivity for the applicable licensed product in the applicable country or (3) ten years after the first commercial sale of the applicable licensed product in the applicable country covered by the Sanofi Agreement.

The Company identified the following promises in the Sanofi Agreement: (1) the research licenses, (2) the research services, (3) the obligation to share information during the research term and (4) the participation of alliance managers in the joint research committee and joint patent committee. The Company determined that the research licenses, the obligation to share information and the participation in the joint committees are not capable of being distinct from the research services due to the specialized nature of the research services to be provided by the Company, and, accordingly, the promises identified were combined as one single performance obligation. The Company also determined that Sanofi's exclusive right to add up to two additional targets constitutes a material right as it represents a significant and incremental discount that Sanofi would not have received without entering into the Sanofi Agreement. The option to extend the license term does not represent a material right because it does not contain a significant and incremental discount.

In order to determine the transaction price, the Company evaluated all the payments to be received during the duration of the contract. Certain milestone payments and additional fees were considered variable consideration, which were not included in the transaction price based on the most likely amount method as of November 30, 2023. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. At the inception of the Sanofi Agreement, the Company determined that the transaction price consisted of the upfront payment of $55.0 million for three initial drug targets and $22.0 million for two additional targets. Subsequently, upon the achievement of research milestones, $11.0 million in variable consideration was added to the transaction price, which includes $4.0 million added during the three months ended November 30, 2023, and a cumulative effect was recorded as revenue in the period the transaction price increased. Revenue is recognized using the cost-based input method over the research term of 4.25 years, the revised research period that was agreed to in January 2021 in the First Sanofi Amendment, for certain targets, and 5.25 years, the revised research period due to the target substitutions in July 2022, for certain other targets.

Using the cost-based input method, which the Company determined most faithfully depicts the transfer of its performance obligation to Sanofi, the Company recognizes revenue based on actual costs incurred as a percentage of total estimated costs as the Company completes its performance obligation under the contract. Costs consist primarily of internal FTE and third-party contract costs related to the Sanofi Agreement. The cumulative effect of revisions to estimated costs to complete the Company's performance obligation is recorded in the period in which changes are identified and amounts can be reasonably estimated. Total estimated costs are primarily driven by the number of estimated FTEs, which requires significant management judgment.

For the year ended November 30, 2023, the Company recognized collaboration revenue related to the Sanofi Agreement of $25.4 million, of which $21.0 million was included in deferred revenue as of November 30, 2022, and $2.6 million was related to performance obligations satisfied in previous periods. For the year ended November 30, 2022, the Company recognized collaboration revenue related to the Sanofi Agreement of $15.0 million, of which $14.0 million was included in deferred revenue as of November 30, 2021, and $0.6 million was related to performance obligations satisfied in previous periods. As of November 30, 2023, deferred revenue related to the Sanofi Agreement was $24.9 million, of which $20.3 million was current and includes $4.0 million in contract assets representing the unbilled amount related to the research milestones recognized in November 2023. As of November 30, 2022, deferred revenue related to the Sanofi Agreement was $46.2 million, of which $19.4 million was current and includes $1.0 million in contract assets representing the unbilled amount related to the research milestone recognized in November 2022.

Pfizer

In September 2023, the Company entered into a strategic collaboration with Seagen Inc. (now a part of Pfizer Inc.) (the Pfizer Agreement) to develop a suite of targeted protein degraders against multiple targets nominated by Pfizer that are suitable for antibody conjugation. Pfizer will be responsible for conjugating these degraders to antibodies to make Degrader-Antibody Conjugates (DACs), a new class of medicines for use in cancer treatment, and advancing these DAC drug candidates through preclinical and clinical development and commercialization.

Under the Pfizer Agreement, Pfizer has the option to obtain exclusive licenses to develop and commercialize certain degraders, while the Company retains an option for U.S. profit sharing and co-promotion on two products arising from the collaboration. The collaboration excludes the Company's current internal protein degradation programs for which the Company retains all rights, and also excludes the Company's future internal programs, provided that the Company has distinguished future programs as excluded from the scope of the collaboration.

For the targets nominated by Pfizer under the collaboration, the Company shall use commercially reasonable efforts to identify, synthesize, characterize and deliver targeted protein degraders that selectively bind to and degrade such targets. Development of licensed degraders, with the exception of licensed products for which the Company exercises its profit-share options, will be at Pfizer's sole cost and expense. For the profit-share products, the parties will share net profits and net losses and global development costs, and the Company will be eligible to receive royalty and milestone payments on such optioned products.

Under the terms of the Pfizer Agreement, the Company received an upfront payment of $60.0 million. The Company is eligible to receive up to approximately $3.4 billion in contingent payments based on specified research, development, regulatory and commercial milestones across multiple programs, and is eligible for mid-single to low double digit percentage tiered royalties on future sales.

Subject to the exceptions described in the Pfizer Agreement, the Pfizer Agreement expires upon the first to occur of (1) the expiration of the last-to-expire option exercise period under the Pfizer Agreement if no such option has been exercised prior to such expiration and (2) the expiration of the last-to-expire royalty term under the Pfizer Agreement.

The Company identified the following promises in the Pfizer Agreement: (1) the research licenses, (2) the research services, (3) the participation of a gatekeeper and an alliance managers and the participation in various joint committees, and (4) the obligation to share information during the research term. The Company determined that the research licenses, the participation in the joint committees and the obligation to share information are not capable of being distinct from the research services, and, accordingly, the identified promises were combined as one single performance obligation. The Company also determined that, at the inception of the Pfizer Agreement, Pfizer's options to obtain an exclusive development, manufacturing and commercialization license for each collaboration target and to extend the four-year research term do not represent material rights and are not considered performance obligations because they do not contain a significant and incremental discount. Additionally, Pfizer's target reservation right is not a performance obligation as it is an exclusivity right and an attribute of other performance obligations in the Pfizer Agreement, such as the research licenses, and does not require any specific actions from the Company.

In order to determine the transaction price, the Company evaluated all the payments to be received during the duration of the contract. Milestone payments and additional fees were considered variable consideration, which were not included in the transaction price based on the most likely amount method as of November 30, 2023. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that the transaction price at the inception of the Pfizer Agreement consisted of the upfront payment of $60.0 million. The Company has not yet achieved any research milestones and no variable consideration has been added to the transaction price. The transaction price is recognized as collaboration revenue using the cost-based input method over the estimated research term of four years, which represents the estimated period to complete the identified deliverables. Additionally, the Company considered the impact of Pfizer terminating the Pfizer Agreement prior to the completion of the research services during the initial four-year research term and determined that there were significant economic costs to Pfizer for doing so, and as such, did not adjust the contract term.

Using the cost-based input method, which the Company determined most faithfully depicts the transfer of its performance obligation to Pfizer, the Company recognizes revenue based on actual costs incurred as a percentage of total estimated costs as the Company completes its performance obligation under the contract. Costs consist primarily of internal FTE and third-party contract costs related to the Pfizer Agreement. The cumulative effect of revisions to estimated costs to complete the Company's performance obligation is recorded in the period in which changes are identified and amounts can be reasonably estimated. Total estimated costs are primarily driven by the number of estimated FTEs, which requires significant management judgment.

For the year ended November 30, 2023, the Company recognized collaboration revenue related to the Pfizer Agreement of $1.7 million. As of November 30, 2023, deferred revenue related to the Pfizer Agreement was $58.3 million, of which $17.9 million was current.

4. Consolidated Balance Sheet Components

Property and Equipment, Net

Property and equipment, net, consisted of the following (in thousands):

	November 30,	
	2023	2022
Laboratory equipment	$ 32,239	$ 26,385
Leasehold improvements	3,238	3,825
Computer equipment	938	786
Furniture and fixtures	652	452
Software	5,403	4,688
Software in progress	587	697
Total property and equipment, gross	43,057	36,833
Less: Accumulated depreciation and amortization	(26,249)	(19,670)
Total property and equipment, net	$ 16,808	$ 17,163

For the years ended November 30, 2023 and 2022, depreciation and amortization expense was $7.5 million and $5.3 million, respectively, which includes amortization expense related to capitalized software of $1.4 million and $1.2 million, respectively. All long-lived assets are maintained in the United States.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	November 30,	
	2023	2022
Accrued compensation	$ 15,303	$ 13,164
Accrued contract research and lab supplies	7,131	6,426
Accrued professional services	1,755	1,250
Accrued taxes	30	85
Other	751	1,503
Total accrued expenses and other current liabilities	$ 24,970	$ 22,428

5. Fair Value Measurements

In accordance with the authoritative guidance on fair value measurements and disclosures under U.S. GAAP, the Company discloses and recognizes the fair value of its assets and liabilities using a hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to valuations based upon unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements) and the lowest priority to valuations based upon unobservable inputs that are significant to the valuation (Level 3 measurements). The guidance establishes three levels of the fair value hierarchy as follows:

Level 1—Inputs that reflect unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date;

Level 2—Inputs other than quoted prices included within Level 1 that are observable for the asset or liability either directly or indirectly, including inputs in markets that are not considered to be active; and

Level 3—Inputs that are unobservable.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and considers factors specific to the asset or liability.

The following tables present the Company's investments, which consist of cash equivalents and available-for-sale marketable securities, that are measured at fair value on a recurring basis as of November 30, 2023 and 2022 (in thousands):

November 30, 2023	Level	Amortized cost	Unrealized gain	Unrealized loss	Estimated fair value
Money market funds	Level 1	$ 44,187	$ —	$ —	$ 44,187
U.S. treasury securities	Level 1	160,991	61	(29)	161,023
Corporate debt securities	Level 2	3,487	—	(56)	3,431
U.S. government agency securities	Level 2	69,389	5	(567)	68,827
Long-term marketable securities:					
U.S. government agency securities	Level 2	7,490	—	(69)	7,421
Total		$ 285,544	$ 66	$ (721)	$ 284,889
Included in cash and cash equivalents		$ 44,187	$ —	$ —	$ 44,187
Included in marketable securities, current		$ 233,867	$ 66	$ (652)	$ 233,281
Included in marketable securities, non-current		$ 7,490	$ —	$ (69)	$ 7,421

November 30, 2022	Level	Amortized cost	Unrealized gain	Unrealized loss	Estimated fair value
Money market funds	Level 1	$ 59,452	$ —	$ —	$ 59,452
U.S. treasury securities	Level 1	75,322	—	(1,120)	74,202
Corporate debt securities	Level 2	81,026	—	(1,279)	79,747
U.S. government agency securities	Level 2	8,998	—	(135)	8,863
Corporate commercial paper	Level 2	74,896	—	—	74,896
Foreign government securities	Level 2	7,051	—	(92)	6,959
Long-term marketable securities:					
U.S. treasury securities	Level 1	5,779	—	(98)	5,681
Corporate debt securities	Level 2	3,492	—	(217)	3,275
U.S. government agency securities	Level 2	56,301	1	(1,379)	54,923
Total		$ 372,317	$ 1	$ (4,320)	$ 367,998
Included in cash and cash equivalents		$ 59,452	$ —	$ —	$ 59,452
Included in marketable securities, current		$ 247,293	$ —	$ (2,626)	$ 244,667
Included in marketable securities, non-current		$ 65,572	$ 1	$ (1,694)	$ 63,879

The following table summarizes the available-for-sale marketable securities in an unrealized loss position for which an allowance for credit losses has not been recorded as of November 30, 2023 and 2022, aggregated by investment category and length of time in a continuous unrealized loss position (in thousands):

	Less than 12 months		Greater than 12 months		Total	
November 30, 2023	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss
U.S. treasury securities	$ 46,694	$ (4)	$ 5,936	$ (25)	$ 52,630	$ (29)
Corporate debt securities	—	—	3,431	(56)	3,431	(56)
U.S. government agency securities	23,599	(108)	48,805	(528)	72,404	(636)
Total	$ 70,293	$ (112)	$ 58,172	$ (609)	$ 128,465	$ (721)

	Less than 12 months		Greater than 12 months		Total	
November 30, 2022	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss	Fair Value	Gross Unrealized Loss
U.S. treasury securities	$ 40,747	$ (377)	$ 39,136	$ (841)	$ 79,883	$ (1,218)
Corporate debt securities	14,257	(152)	68,765	(1,344)	83,022	(1,496)
U.S. government agency securities	45,395	(663)	15,391	(851)	60,786	(1,514)
Foreign government securities	—	—	6,959	(92)	6,959	(92)
Total	$ 100,399	$ (1,192)	$ 130,251	$ (3,128)	$ 230,650	$ (4,320)

The accrued interest receivable related to the Company's marketable securities was $0.8 million and $1.1 million as of November 30, 2023 and 2022, respectively, and was included in prepaid expenses and other current assets on the consolidated balance sheet. Long-term marketable securities held by the Company generally mature within two years from the balance sheet date.

The Company classifies its money market funds and U.S. treasury securities, which are valued based on quoted market prices in active markets with no valuation adjustment, as Level 1 assets within the fair value hierarchy.

The Company classifies its marketable securities in corporate debt securities, U.S. government agency securities, corporate commercial paper and foreign government securities as Level 2 assets within the fair value hierarchy. The fair values of these marketable securities are estimated by taking into consideration valuations obtained from third-party pricing services. The pricing services utilize industry standard valuation models, including both income- and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities, prepayment/default projections based on historical data and other observable inputs. There were no transfers of financial instruments between valuation levels during the years ended November 30, 2023 and 2022.

As of November 30, 2023 and 2022, the unrealized losses for available-for-sale marketable securities were non-credit related, and the Company does not intend to sell the securities that were in an unrealized loss position, nor will it be required to sell those securities before recovery of their amortized cost basis, which may be maturity. As of November 30, 2023 and 2022, no allowance for credit losses for the Company's marketable securities was recorded. During the years ended November 30, 2023 and 2022, the Company did not recognize any impairment losses related to marketable securities.

6. Commitments and Contingencies

Legal Proceedings

From time to time, the Company may be involved in legal proceedings in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will be made and that such expenditures can be reasonably estimated. Significant judgment is required to determine both probability and the estimated amount. Legal fees and other costs associated with such actions are expensed as incurred. As of November 30, 2023, the Company was not a party to any material legal proceedings.

Indemnifications

In the ordinary course of business, the Company often includes standard indemnification provisions in its arrangements with its partners, suppliers and vendors, among others. Pursuant to these provisions, the Company may be obligated to indemnify such parties for losses or claims suffered or incurred in connection with its service, breach of representations or covenants, intellectual property infringement or other claims made against such parties. These provisions may limit the time within which an indemnification claim can be made. It is not possible to determine the maximum potential amount under these indemnification obligations due to the limited history of prior indemnification claims and the unique facts and circumstances involved in each particular agreement. The Company has not incurred any material costs as a result of such indemnifications and has not accrued any liabilities related to such obligations in these consolidated financial statements as management believes such liability is immaterial.

In addition, the Company has entered into indemnification agreements with directors and certain officers and employees that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers or employees. No demands have been made upon the Company to provide indemnification under such agreements, and thus, there are no claims that the Company is aware of that could have a material effect on the Company's consolidated financial statements. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is not specified in the agreements. However, the Company currently has directors' and officers' insurance that reduces its exposure and may enable the Company to recover a portion of any future amounts paid.

Operating Leases

The Company leases office and laboratory facilities totaling approximately 57,902 square feet within the same building in San Francisco, California under several lease agreements. The terms of these lease agreements expire in April 2025. The Company has an option to renew these leases for an additional two years, and the renewal term has not been included in the lease term used to calculate the right-of-use asset and lease liability as it is not reasonably certain that the Company will exercise the option.

In July 2021, the Company entered into a lease agreement for the lease of approximately 19,320 square feet of office space in a different building in San Francisco, California. The lease commenced in December 2021 and will expire in June 2024, unless terminated earlier.

In March 2022, the Company entered into a lease agreement for the lease of approximately 46,434 square feet of office space in The Woodlands, Texas. In August 2023, the lease agreement was amended to increase the square footage of the leased premise to 50,094 square feet. The amendment had no impact on the accounting for the lease. The Company has an option to renew for two additional terms of five years each, and the renewal terms have not been included in the lease term used to calculate the right-of-use asset and lease liability as it is not reasonably certain that the Company will exercise the option. The lease commenced in September 2023 when the underlying assets became available for use and will expire in March 2035.

The Company is required to pay base rent plus its proportionate share of operating expenses, as defined in the applicable lease agreement on all of its leases. Variable lease payments related to operating expenses including utilities, maintenance costs and real estate taxes were $6.2 million and $4.4 million for the years ended November 30, 2023 and 2022, respectively. Additionally, for the year ended November 30, 2022, certain leased premises were subject to additional variable lease payments related to landlord-owned improvements which were not estimable at lease inception. The right-of-use asset recognized in exchange for lease obligations for these additional variable lease payments was $1.2 million for the year ended November 30, 2022.

Operating lease expenses, excluding variable lease payments, were $6.8 million and $5.9 million for the years ended November 30, 2023 and 2022, respectively. Short-term lease expense was not material for the periods presented. As of November 30, 2023, the weighted average remaining lease term was 9.1 years and the weighted average discount rate was 6.45%.

Other information related to leases were as follows (in thousands):

	Year Ended November 30,	
	2023	2022
Cash paid for amounts included in the measurement of lease liabilities:		
Cash flows from operating leases	$ 6,973	$ 6,578

The undiscounted future non-cancellable lease payments under the Company's lease agreements as of November 30, 2023 were as follows (in thousands):

Year ending November 30,	Operating Leases
2024	$ 7,646
2025	4,574
2026	2,913
2027	2,993
2028	3,076
2029 to 2035	21,244
Total undiscounted lease payments	42,446
Less: imputed interest	(11,832)
Total operating lease liabilities	$ 30,614
Operating lease liabilities, current	$ 7,489
Operating lease liabilities, net of current portion	23,125
Total operating lease liabilities	$ 30,614

7. Common Stock

The Company's Restated Certificate of Incorporation authorizes the Company to issue up to 500,000,000 shares of common stock, $0.001 par value per share, as of November 30, 2023 and 2022. Holders of common stock are entitled to dividends when and if declared by the Company's board of directors, subject to the prior rights of the holders of shares of preferred stock. The holder of each share of common stock is entitled to one vote. As of November 30, 2023, no dividends have been declared.

In July 2022, the Company issued pre-funded warrants to purchase an aggregate of 6,814,920 shares of the Company's common stock in RDOs at a price of $13.939 per pre-funded warrant. The pre-funded warrants were immediately exercisable, have an exercise price of $0.001 and may be exercised at any time after the date of issuance. A holder of pre-funded warrants may not exercise the warrant if the holder, together with its affiliates, would beneficially own more than 9.99% of the number of shares of the Company's common stock outstanding immediately after giving effect to such exercise. A holder of the pre-funded warrants may increase or decrease this percentage not in excess of 19.99% by providing at least 61 days' prior notice to the Company. As of November 30, 2023, there were pre-funded warrants to purchase an aggregate of 6,097,560 shares of the Company's common stock that remained available for exercise.

The pre-funded warrants were classified as a component of permanent equity in the Company's consolidated balance sheet as they are freestanding financial instruments that are immediately exercisable, do not embody an obligation for the Company to repurchase its own shares and permit the holders to receive a fixed number of shares of common stock upon exercise. All of the shares underlying the pre-funded warrants have been included in the weighted-average number of shares of common stock used to calculate net loss per share attributable to common stockholders because the shares may be issued for little or no consideration, are fully vested and are exercisable after the original issuance date of the pre-funded warrants.

Common stock reserved for future issuance, on an as-if converted basis, as of November 30, 2023 and 2022, consists of the following:

	November 30,	
	2023	2022
Options to purchase common stock issued and outstanding	8,340,968	8,256,957
Shares available for future equity grants	1,614,035	834,291
Shares available for issuance under employee stock purchase plan	1,530,281	1,325,523
Restricted stock units issued and outstanding	1,246,031	784,824
Pre-funded warrants issued and outstanding	6,097,560	6,814,920
Total common stock reserved for future issuance	18,828,875	18,016,515

8. Stock-Based Compensation

Equity Incentive Plans

The Company's 2020 Equity Incentive Plan (the 2020 Plan) serves as the successor to the Company's 2012 Equity Incentive Plan (together with the 2020 Plan, the Stock Plans) and provides for the granting of stock options, stock appreciation rights, restricted stock awards, RSUs, performance awards and stock bonus awards to employees, directors, consultants, independent contractors and advisors of the Company.

Under the Stock Plans, the Company generally grants stock-based awards with service-based vesting conditions only. Options granted typically vest under various different vesting terms over a four-year period and expire ten years from the date of grant. In the case of an incentive stock option granted to an employee who at the time of grant owns stock representing more than 10% of the total combined voting power of all classes of stock, the exercise price shall be no less than 110% of the fair value per share on the date of grant, and the award shall expire five years from the date of grant. In the case of all other stock options, the per share exercise price shall be no less than 100% of the fair value per share on the date of grant. RSUs issued typically vest under various different vesting terms over a two- to four-year period.

Following the effectiveness of the 2020 Plan on July 22, 2020, the Company ceased making grants under the 2012 Plan. However, the 2012 Plan continues to govern the terms and conditions of the outstanding awards granted under it. Shares of common stock subject to awards granted under the 2012 Plan that cease to be subject to such awards by forfeiture or otherwise will be available for issuance under the 2020 Plan.

As of November 30, 2023, there were 1,614,035 shares of common stock reserved for future issuance pursuant to the 2020 Plan.

Stock options

Option activity under the Stock Plans is set forth below:

	Number of options outstanding	Weighted-average exercise price	Weighted-average contractual life (in years)	Aggregate intrinsic value[1] (in thousands)
Balances as of November 30, 2022	8,256,957	$ 19.47	8.44	$ 13,210
Options granted	1,991,212	10.29		
Options exercised	(120,826)	8.16		
Options forfeited	(1,786,375)	20.74		
Balances as of November 30, 2023	8,340,968	$ 17.17	7.77	$ 3,295
Options vested and expected to vest as of November 30, 2023[2]	8,345,877	$ 17.16	7.77	$ 3,295
Options exercisable as of November 30, 2023	4,750,849	$ 17.25	7.12	$ 3,295

(1) The aggregate intrinsic values were calculated as the pre-tax difference between the exercise price of stock options and the quoted market price of the Company's common stock on November 30, 2023 for all in-the-money stock options. The total intrinsic value of stock options exercised during the years ended November 30, 2023 and 2022 was $0.2 million and $4.5 million, respectively.

(2) As of November 30, 2023, a total of 4,909 shares of common stock were early exercised and subject to repurchase by the Company at the lower of (i) the fair value of such shares on the date of repurchase, or (ii) the original exercise price of such shares. The corresponding exercise value was immaterial and recorded as a stock-based compensation liability.

The fair value of options granted during the years ended November 30, 2023 and 2022 was estimated using the Black-Scholes option pricing model on the grant date using the following assumptions:

	November 30,	
	2023	2022
Expected term (years)	5.50 - 6.06	5.50 - 6.07
Expected volatility	74% - 92%	70% - 74%
Risk-free interest rate	3.27% - 4.59%	1.31% - 4.22%
Dividend yield	0%	0%

The expected term represents the weighted-average period the stock-based payments are expected to remain outstanding. The expected term assumption for stock options was determined using the simplified method for "plain-vanilla" options. The expected stock price volatility assumption was determined by examining the historical volatilities for industry peers, as the Company does not have sufficient trading history for its common stock. The risk-free rate assumption is based on the U.S. Treasury instruments. The expected dividend assumption is based on the Company's history and expectation of dividend payouts. The expected dividend yield is 0% as the Company has not paid and does not anticipate paying dividends on its common stock.

During the years ended November 30, 2023 and 2022, the weighted-average grant date fair value of options granted was $7.22 and $11.80 per share, respectively.

Restricted stock units

RSU activity under the Stock Plans is set forth below:

	Number of RSUs	Weighted-average grant date fair value
Balances as of November 30, 2022	784,824	$ 18.97
RSUs granted	1,109,427	10.53
RSUs vested	(441,103)	17.99
RSUs forfeited	(207,117)	14.30
Balances as of November 30, 2023	1,246,031	$ 12.58

During the years ended November 30, 2023 and 2022, the weighted-average grant date fair value of RSUs granted was $10.53 and $19.11 per share, respectively, and the total fair value of RSUs vested was $7.9 million and $0.9 million, respectively.

Employee Stock Purchase Plan

Under the Company's ESPP, eligible employees are entitled to purchase shares of common stock at a discount with accumulated payroll deductions. The purchase price for shares of common stock purchased under the ESPP will be 85% of the lesser of the fair market value of the Company's common stock on (i) the first trading day of the applicable offering period or (ii) the last trading day of each purchase period in the applicable offering period.

During the year ended November 30, 2023, the Company issued 266,964 shares pursuant to the ESPP at a weighted-average price of $8.35 per share. As of November 30, 2023, there were 1,530,281 shares of common stock reserved for issuance pursuant to the ESPP.

The fair value of ESPP granted during the years ended November 30, 2023 and 2022 was estimated using the Black-Scholes option pricing model on the grant date using the following assumptions:

	November 30,	
	2023	2022
Expected term (years)	0.5	0.5
Expected volatility	67%	70% - 101%
Risk-free interest rate	4.98% - 5.54%	0.67% - 3.12%
Dividend yield	0%	0%

Stock-Based Compensation

Stock-based compensation expense related to the Stock Plans and the ESPP that is included in the Company's consolidated statements of operations is as follows (in thousands):

	Year Ended November 30,	
	2023	2022
Research and development	$ 18,707	$ 16,808
General and administrative	14,966	11,323
Total stock-based compensation	$ 33,673	$ 28,131

During the years ended November 30, 2023 and 2022, capitalized stock-based compensation related to internal-use software development was $74,000 and $69,000, respectively. As of November 30, 2023, the total compensation cost related to stock-based awards not yet recognized was $53.1 million, which is expected to be amortized on a straight-line basis over the weighted-average remaining vesting period of approximately 2.09 years.

9. Defined Contribution Plan

The Company sponsors a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code of 1986, as amended (the 401(k) Plan), which provides for the Company to make discretionary matching or discretionary annual contributions to the 401(k) Plan, for its employees. Substantially all of the Company's employees are eligible to participate in the 401(k) Plan. Employees may contribute a percentage of their annual compensation to the plan, subject to statutory limitations. The Company has made contributions to the 401(k) Plan and recorded contribution expense of $1.0 million and $0.9 million during the years ended November 30, 2023 and 2022, respectively.

10. Income Taxes

For the years ended November 30, 2023 and 2022, the Company did not record any current income tax benefit or provision. The Company has generated net operating losses (NOLs) since inception and has established a valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

Loss before provision for income taxes includes the following component (in thousands):

	November 30,	
	2023	2022
Domestic	$ (143,948)	$ (180,360)
	$ (143,948)	$ (180,360)

The effective tax rate differs from the federal statutory rate as follows:

	November 30,	
	2023	2022
Federal statutory income tax rate	21.0 %	21.0 %
State income tax rate	14.1	5.9
Research and development tax credits	4.8	3.5
Stock-based compensation	(4.2)	(2.0)
Change in valuation allowance	(35.6)	(28.4)
Other	(0.1)	—
Total	— %	— %

Deferred Tax Assets and Liabilities

Deferred income taxes reflect the net tax effects of loss and credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the deferred tax assets for federal and state income taxes are as follows (in thousands):

	Year ended November 30,	
	2023	2022
Deferred tax assets:		
Net operating loss carryforwards	$ 92,131	$ 83,775
Research and development tax credits	37,052	27,096
Deferred revenue	11,143	19,950
Stock-based compensation	5,472	3,846
Accrued expenses and other liabilities	3,723	3,797
Operating lease liabilities	8,789	3,199
Capitalized research and experimental expenses	44,348	—
Gross deferred tax assets	202,658	141,663
Valuation allowance	(193,717)	(138,362)
Total deferred tax assets	8,941	3,301
Deferred tax liabilities:		
Operating lease right-of-use assets	(8,941)	(3,301)
Total deferred tax liabilities	(8,941)	(3,301)
Net deferred tax assets	$ —	$ —

Realization of the deferred tax assets is dependent upon future taxable income, the amount, if any, and timing of which are uncertain. The Company has established a valuation allowance to offset deferred tax assets as of November 30, 2023 and 2022 due to the uncertainty of realizing future tax benefits from its NOL carryforwards and other deferred tax assets. The valuation allowance increased by $55.4 million to $193.7 million during the year ended November 30, 2023, primarily related to an increase on the deferred tax asset for research and development (R&D) credits, NOL carryforwards and Section 174 research and development capitalization. The valuation allowance increased by $54.8 million to $138.4 million during the year ended November 30, 2022, primarily related to an increase on the deferred tax asset for R&D credits and NOL carryforwards.

As of November 30, 2023, the Company had NOL carryforwards available to reduce future taxable income, if any, for federal and state income tax purposes of $269.3 million and $410.9 million, respectively. All outstanding federal NOL carryforwards were generated for tax years beginning after December 31, 2017, and carry forward indefinitely. State NOL carryforwards begin expiring in 2029. As of November 30, 2023, the Company had federal and state research credit carryforwards of $32.3 million and $20.2 million, respectively. If not utilized, the federal credit carryforwards will begin expiring in 2032 and the state credits carry forward indefinitely.

Section 382 of the Internal Revenue Code of 1986, as amended (IRC) places a limitation on the utilization of NOL and tax credit carryforwards in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50 percentage points. The Company has identified two ownership changes that have triggered a limitation on pre-change NOLs under Section 382. A majority of the Company's pre-change NOLs remain available within the carryforward period provided by the IRC, subject to availability of taxable income. As a result of the ownership changes, the Company has determined that approximately $0.4 million of NOLs will expire unutilized, and as such, these NOLs are not reflected in the Company's deferred tax asset balance.

Unrecognized Tax Benefits

The Company has recorded a liability related to uncertain tax positions in the financial statements. The Company has unrecognized tax benefits of $15.5 million as of November 30, 2023, all of which are offset by a full valuation allowance. There are no tax benefits included in the balance of unrecognized tax benefits that, if recognized, would affect the effective tax rate. There are no interest and penalties accrued as of November 30, 2023.

A reconciliation of the beginning and ending amounts of unrecognized income tax benefits during the years ended November 30, 2023 and 2022 is as follows (in thousands):

	Years ended November 30,	
	2023	2022
Balance at beginning of period	$ 10,261	$ 6,331
Additions based on tax positions related to current period	5,247	3,930
Balance at end of period	$ 15,508	$ 10,261

The Company files income tax returns in the United States and in various states. In January 2019, the California Franchise Tax Board (FTB) initiated an examination of the Company's California tax return for tax years ending in 2015, 2016, 2017 and 2018. During the year ended November 30, 2021, the FTB issued proposed audit assessments related to revenue sourcing and R&D credits. The Company did not agree with the FTB's assessments and challenged the assessments. Pursuant to a measurement analysis, the Company has not recorded an unrecognized tax benefit related to the FTB's sourcing position. The Company maintains an unrecognized tax benefit related to its California R&D credits for all years. All of the Company's tax years will remain open for examination by the federal and state authorities for three and four years, respectively, from the date of the utilization of any NOLs.

In August 2022, the U.S. Inflation Reduction Act (the Act) was enacted into law. The Act includes various tax provisions, including an excise tax on stock repurchases, expanded tax credits for clean energy incentives and a corporate alternative minimum tax that generally applies to U.S. corporations with adjusted financial statement income in excess of $1.0 billion. The Company does not expect the Act to have a material impact on its financial statements.

In December 2017, the Tax Cuts and Jobs Act (TCJA) was signed into law, significantly reforming the IRC. The TCJA contains a provision impacting Section 174 of the IRC whereby for tax years beginning on or after January 1, 2022, taxpayers are required to capitalize and amortize, rather than deduct, research and experimental (R&E) expenses. The R&E expenses under Section 174 must be amortized over five years for research performed in the United States and 15 years for research performed outside the United States. This rule became effective for the Company during the year ended November 30, 2023. For the year ended November 30, 2023, the Company recorded a deferred tax asset of $44.3 million pursuant to the provisions of Section 174 of the IRC.

11. Net Loss Per Share

The following table sets forth the computation of the Company's basic and diluted net loss per share attributable to common stockholders, which excludes shares which are legally outstanding but subject to repurchase by the Company (in thousands, except share and per share data):

	Year Ended November 30,	
	2023	2022
Numerator:		
Net loss	$ (143,948)	$ (180,360)
Denominator:		
Weighted-average number of shares outstanding, basic and diluted [1]	54,337,901	48,607,990
Net loss per share, basic and diluted	$ (2.65)	$ (3.71)

[1] The shares underlying the pre-funded warrants to purchase shares of the Company's common stock have been included in the calculation of the weighted-average number of shares outstanding, basic and diluted, for the years ended November 30, 2023 and 2022.

The following potentially dilutive securities were excluded from the computation of the diluted net loss per share of common stock for the periods presented because their effect would have been anti-dilutive:

	Years ended November 30,	
	2023	2022
Options to purchase common stock issued and outstanding	8,340,968	8,256,957
Options early exercised subject to vesting	4,909	22,246
Restricted stock units issued and outstanding	1,246,031	784,824
Shares expected to be purchased under employee stock purchase plan	203,314	123,194
Total	9,795,222	9,187,221

12. Related Party Transactions

The Company's Chief Financial Officer is a trustee for the multiple employer welfare association that facilitates the acquisition and administration of the Company's healthcare plans. Expenses related to the healthcare plan premiums were $4.4 million and $4.0 million for the years ended November 30, 2023 and 2022, respectively. As of November 30, 2023 and 2022, the amount recorded in accounts payable and accrued expenses and other current liabilities in connection with this healthcare plan provider was not material.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our President and Chief Executive Officer (CEO) and our Chief Financial Officer (CFO), our principal executive officer and principal accounting and financial officer, respectively, have evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act) as of November 30, 2023.

Disclosure controls and procedures are controls and other procedures that are designed to ensure that information required to be disclosed in our reports filed or submitted under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include controls and procedures designed to ensure that information required to be disclosed in our reports filed under the Exchange Act is accumulated and communicated to management, including our CEO and our CFO, to allow timely decisions regarding required disclosure. Based on their evaluation, the CEO and CFO have concluded that our disclosure controls and procedures were effective as of November 30, 2023.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design safeguards into the process to reduce, though not eliminate, this risk.

Under the supervision and with the participation of our management, including our CEO and CFO, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of November 30, 2023 based on the framework in "Internal Control — Integrated Framework" (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of November 30, 2023.

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. For as long as we remain a "smaller reporting company" as defined by Rule 12b-2 of the Exchange Act and report less than $100 million of annual revenues in our most recent fiscal year, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our internal control over financial reporting.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended November 30, 2023, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspection

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item will be set forth in our definitive proxy statement for our 2024 Annual Meeting of Stockholders (Proxy Statement) to be filed with the Securities and Exchange Commission (SEC) within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference.

We have adopted a code of business conduct and ethics that applies to all employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The code of business conduct and ethics is available on our website at www.nurixtx.com. Amendments to, and waivers from, the code of business conduct and ethics that apply to any director, executive officer or persons performing similar functions will be disclosed at the website address provided above and, to the extent required by applicable regulations, on a Current Report on Form 8-K filed with the SEC.

Item 11. Executive Compensation

The information required by this item will be set forth in the Proxy Statement to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, 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 will be set forth in the Proxy Statement to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference.

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

The information required by this item will be set forth in the Proxy Statement to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item will be set forth in the Proxy Statement to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements

The financial statements filed as part of this Annual Report on Form 10-K are listed in the "Index to Financial Statements" under Part II, Item 8 of this Annual Report on Form 10-K.

(2) Financial Statement Schedules

Financial statement schedules have been omitted in this Annual Report on Form 10-K because they are not applicable, not required under the instructions, or the information requested is set forth in the financial statements or related notes thereto.

(3) Exhibits

The following is a list of exhibits filed with this Annual Report on Form 10-K incorporated herein by reference (numbered in accordance with Item 601 of Regulation S-K):

EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference				Filed or Furnished Herewith
		Form	File No.	Exhibit	Filing Date	
3.1	Restated Certificate of Incorporation	10-Q	001-39398	3.1	October 14, 2020	
3.2	Amended and Restated Bylaws	8-K	001-39398	3.1	December 16, 2022	
4.1	Form of Common Stock Certificate	S-1	333-239651	4.1	July 2, 2020	
4.2	Amended and Restated Investor Rights Agreement, dated March 9, 2020, by and among the Registrant and certain of its stockholders	S-1	333-239651	4.2	July 2, 2020	
4.3	Description of Registrant's Securities	10-K	001-39398	4.3	February 9, 2023	
4.4	Form of Pre-funded Warrant	8-K	001-39398	4.1	July 8, 2022	
10.1	Form of Indemnity Agreement	S-1	333-239651	10.1	July 2, 2020	
10.2*	2012 Equity Incentive Plan, as amended, and forms of award agreements	S-1	333-239651	10.2	July 2, 2020	
10.3*	2020 Equity Incentive Plan and forms of award agreements	S-1/A	333-239651	10.3	July 20, 2020	
10.4*	2020 Employee Stock Purchase Plan and forms of award agreements	S-1/A	333-239651	10.4	July 20, 2020	
10.5*	Employment Agreement, dated July 15, 2020, by and between the Registrant and Arthur T. Sands	S-1/A	333-239651	10.5	July 20, 2020	
10.6*	Letter Agreement, dated June 15, 2020, by and between the Registrant and Arthur T. Sands	S-1	333-239651	10.11	July 2, 2020	
10.7*	Employment Agreement, dated July 15, 2020, by and between the Registrant and Gwenn Hansen	S-1/A	333-239651	10.7	July 20, 2020	
10.8*	Employment Agreement, dated July 15, 2020, by and between the Registrant and Christine Ring	10-K	001-39398	10.7	February 16, 2021	
10.9*	Employment Agreement, dated July 15, 2020, by and between the Registrant and Hans van Houte	10-K	001-39398	10.9	January 28, 2022	
10.10*	Executive Severance and Change in Control Plan, as amended and restated on January 19, 2022, and form of Participation Agreement thereunder	10-K	001-39398	10.11	January 28, 2022	
10.11	Lease Agreement, dated as of March 24, 2014, between ARE-San Francisco No. 26, LLC and the Registrant	S-1	333-239651	10.8	July 2, 2020	
10.12	Lease Agreement, dated as of June 21, 2021, between ARE-San Francisco No. 19 LLC and the Registrant	10-Q	001-39398	10.2	October 14, 2021	

10.13	First Amendment to Lease Agreement, dated June 28, 2023, by and between ARE-San Francisco No. 19 Owner, LLC and the Registrant	10-Q	001-39398	10.1	October 12, 2023	
10.14	Lease Agreement, dated as of March 1, 2022, between 8800 Technology Forest Pl, LLC and the Registrant	10-Q	001-39398	10.1	April 8, 2022	
10.15	First Amendment to Lease Agreement, dated August 25, 2023, by and between 8800 Technology Forest PL, LLC and the Registrant	10-Q	001-39398	10.2	October 12, 2023	
10.16†‡	Collaboration, Option and License Agreement, dated June 10, 2019, by and between the Registrant and Gilead Sciences, Inc., as amended	S-1	333-239651	10.9	July 2, 2020	
10.17	First Amendment to Collaboration, Option and License Agreement, dated August 13, 2019, by and between the Registrant and Gilead Sciences, Inc.	10-Q	001-39398	10.2	October 6, 2022	
10.18‡	Second Amendment to Collaboration, Option and License Agreement, dated September 9, 2022, by and between the Registrant and Gilead Sciences, Inc.	10-Q	001-39398	10.3	October 6, 2022	
10.19†‡	Collaboration and License Agreement, dated December 19, 2019, by and between the Registrant and Genzyme Corporation	S-1	333-239651	10.10	July 2, 2020	
10.20†	First Amendment to Collaboration and License Agreement, dated January 6, 2021, by and between the Registrant and Genzyme Corporation	10-K	001-39398	10.11	February 16, 2021	
10.21†	Second Amendment to Collaboration and License Agreement, dated December 16, 2021, by and between the Registrant and Genzyme Corporation	10-Q	001-39398	10.4	October 6, 2022	
10.22†	Third Amendment to Collaboration and License Agreement, dated July 7, 2022, by and between the Registrant and Genzyme Corporation	10-Q	001-39398	10.5	October 6, 2022	
10.23†‡	Fourth Amendment to Collaboration and License Agreement, dated August 11, 2022, by and between the Registrant and Genzyme Corporation	10-Q	001-39398	10.6	October 6, 2022	
10.24†‡	Fifth Amendment to Collaboration and License Agreement, dated November 3, 2023, by and between the Registrant and Genzyme Corporation					X
10.25†‡	Collaboration and License Agreement, dated September 6, 2023, by and between the Registrant and Seagen Inc.					X

10.26	Equity Distribution Agreement, dated August 4, 2021, by and between the Registrant and Piper Sandler & Co.	S-3	333-258448	1.2	August 4, 2021	
21.1	Subsidiaries of the Registrant	10-K	001-39398	21.1	January 28, 2022	
23.1	Consent of Independent Registered Public Accounting Firm					X
24.1	Power of Attorney (reference is made to the signature page hereto)					X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Principal Financial and Accounting Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1§	Certification of Principal Executive Officer and Principal Financial and Accounting Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
97.1	Compensation Recovery Policy					X
101.INS	Inline XBRL Instance Document - the Instance Document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	Cover Page Interactive Data File (formatted as Inline XBRL and included in Exhibit 101)					X

* *Indicates a management or compensatory plan or arrangement in which directors or executive officers are eligible to participate.*

† *Registrant has omitted portions of the exhibit as permitted under Item 601(b)(10) of Regulation S-K.*

‡ *Registrant has omitted certain schedules pursuant to Item 601(a)(5) of Regulation S-K.*

§ *The certifications furnished in Exhibits 32.1 hereto are deemed to accompany this Annual Report on Form 10-K and are not deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act of the Exchange Act.*

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

NURIX THERAPEUTICS, INC.

Date: February 15, 2024

By: /s/ ARTHUR T. SANDS

Arthur T. Sands, M.D., Ph.D.
President, Chief Executive Officer and Director

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Arthur T. Sands and Hans van Houte, and each of them, as his or her true and lawful attorneys-in-fact, proxies, and agents, each with full power of substitution, for him or her in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, proxies, and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully for all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, proxies, and agents, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ ARTHUR T. SANDS **Arthur T. Sands, M.D., Ph.D.**	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 15, 2024
/s/ HANS VAN HOUTE **Hans van Houte**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	February 15, 2024
/s/ DAVID L. LACEY **David L. Lacey, M.D.**	Chairman and Director	February 15, 2024
/s/ JULIA P. GREGORY **Julia P. Gregory**	Director	February 15, 2024
/s/ LORI A. KUNKEL **Lori A. Kunkel, M.D.**	Director	February 15, 2024
/s/ JUDITH A. REINSDORF **Judith A. Reinsdorf, J.D.**	Director	February 15, 2024
/s/ EDWARD C. SALTZMAN **Edward C. Saltzman**	Director	February 15, 2024
/s/ PAUL M. SILVA **Paul M. Silva**	Director	February 15, 2024