2023 ANNUAL REPORT

NASDAQ: XLO

x·ilio THERAPEUTICS®

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

FORM 10-K

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

For the fiscal year ended December 31, 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: 001-40925

XILIO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**85-1623397**
(State of Other Jurisdiction of incorporation or Organization)	(I.R.S. Employer Identification No.)
828 Winter Street, Suite 300, Waltham, MA	**02451**
(Address of principal executive offices)	(Zip code)

Registrant's telephone number, including area code: (857) 524-2466

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

Title of Class	*Trading Symbols*	*Name of Exchanges on Which Registered*
Common stock, par value $0.0001 per share	**XLO**	**Nasdaq Global Select Market**

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

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

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

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

Indicate by check mark whether the Registrant has submitted electronically; every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.0405 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 232.405 of this chapter) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

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

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

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

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

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to Section 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 ☒

As of June 30, 2023, the last day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the common stock held by non-affiliates of the registrant was approximately $67.7 million based on the closing price of the registrant's common stock on June 30, 2023.

The number of shares of the registrant's common stock outstanding as of March 28, 2024 was 34,473,486.

Documents Incorporated by Reference

Portions of the registrant's definitive proxy statement for its 2024 Annual Meeting of Stockholders, which the registrant intends to file with the Securities and Exchange Commission pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2023, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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References to Xilio

Unless otherwise stated, all references to "us," "our," "we," "Xilio," "Xilio Therapeutics," "the Company" and similar references in this Annual Report on Form 10-K refer to Xilio Therapeutics, Inc. and its consolidated subsidiaries. Xilio Therapeutics and its associated logos are registered trademarks of Xilio Therapeutics, Inc. Other brands, names and trademarks contained in this Annual Report on Form 10-K are the property of their respective owners.

Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "aim," "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "would," or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our ability to secure sufficient additional capital in the near term or implement other strategies needed to alleviate our current doubt about our ability to continue as a going concern;
- our estimates regarding expenses, future revenue and capital requirements and our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash and cash equivalents;
- the initiation, timing, progress and results of our research and development programs, including preclinical studies and clinical trials;
- the potential advantages and benefits of our current and future product candidates, including our beliefs regarding the potential benefits of our current and future product candidates in combination with other agents;
- our strategic plans to develop and, if approved, subsequently commercialize any product candidates we may develop;
- the timing of and our ability to submit applications for, and obtain and, if approved, maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance of our product candidates, if approved;
- our estimates regarding the addressable patient population and potential market opportunity for our current and future product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;

- our competitive position and expectations regarding developments and projections relating to our current or future competitors and any competing therapies that are or become available;

- developments relating to our competitors and our industry;

- our ability to establish and maintain collaborations and strategic partnerships and realize the expected benefits of such arrangements, including our partnership with Gilead Sciences, Inc., or Gilead, and clinical collaboration with F. Hoffmann-La Roche Ltd;

- our expectations regarding milestones, equity investments and other contingent payments under our partnership with Gilead;

- our estimates regarding anticipated future cost savings associated with our strategic portfolio reprioritization and workforce reduction announced in March 2024;

- our expectations regarding the closing on April 2, 2024 of, and the anticipated use of the proceeds from, the private placement announced on March 28, 2024;

- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; and

- the impact of general economic conditions, including inflation.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly those described in the "Risk Factor Summary" and "Risk Factors" section in Part I, Item 1A of this Annual Report on Form 10-K, that could cause actual results or events to differ materially from the forward-looking statements that we make. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results, performance or achievements may be materially different from what we expect. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

Risk Factor Summary

Our business is subject to numerous risks that, if realized, could materially and adversely affect our business, financial condition, results of operations and future growth prospects. These risks are discussed more fully in Part I, Item 1A. "Risk Factors" in this Annual Report on Form 10-K. These risks include, but are not limited to, the following:

- Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern. If we are unable to raise sufficient additional capital in the near term, we may in the future need to implement additional cost reduction strategies, which could include delaying, limiting, reducing or eliminating both internal and external costs related to our operations and research and development programs.

- If we fail to regain compliance with the continued listing requirements of The Nasdaq Stock Market, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

- Our business is highly dependent on the success of our current product candidates, which are in the early stages of development and will require significant additional preclinical and clinical development before we can seek regulatory approval for and commercially launch a product.

- Our approach to the discovery and development of product candidates based on our technological approaches is unproven, and we do not know whether we will be able to develop any products of commercial value.

- Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

- We may encounter substantial delays in the commencement or completion, or termination or suspension, of our clinical trials, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

- Our product candidates may cause undesirable or unexpectedly severe side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

- Interim top-line and preliminary data from our 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.

- We expect to develop certain of our product candidates in combination with third-party drugs and we will have limited or no control over the safety, supply, regulatory status or regulatory approval of such drugs.

- Manufacturing biologics is complex, and we may experience manufacturing problems that result in delays in our development or commercialization programs.

- We face risk related to our reliance on our current and any future third-party contract development and manufacturing organizations, or CDMOs. For example, the CDMO on which we rely may not continue to meet regulatory requirements, may have limited capacity and may experience interruptions in supply, any of which could adversely affect our development and commercialization plans for our product candidates.

- We expect to rely on third parties to conduct, supervise and monitor IND-enabling studies and clinical trials, and if these third parties perform in an unsatisfactory manner, it may harm our business, reputation and results of operations.

- We have entered into, and may in the future seek to enter into, collaborations, licenses, or similar arrangements with third parties for the research, development and commercialization of certain of our current or future product candidates. If any such arrangements are not successful, we may not be able to capitalize on the market potential of those product candidates.

- Certain of our research and development and manufacturing activities take place in China through a third-party CDMO. A significant disruption in our ability to rely on this CDMO could materially adversely affect our business, financial condition and results of operations.

- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

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

- We rely on in-license agreements for patent rights with respect to our product candidates and may in the future acquire or in-license additional third-party intellectual property rights on which we may similarly rely. We face risks with respect to such reliance, including the risk that we could lose these rights that are important to our business if we fail to comply with our obligations under these licenses or that we may be unable to acquire or in-license third-party intellectual property that may be necessary or important to our business operations.

- Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we will obtain marketing approval to commercialize a product candidate.

- The price of our common stock has been and, in the future, could be subject to volatility related or unrelated to our operations, and purchasers of our common stock could suffer a decline in value.

PART I

Item 1. Business

Overview

We are a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology, or I-O, therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. We are leveraging our proprietary platform to build a pipeline of novel, tumor-activated I-O molecules that are designed to optimize the therapeutic index by localizing anti-tumor activity within the tumor microenvironment, including tumor-activated cytokines and antibodies (including bispecifics) and immune cell engagers (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers). Current I-O therapies have curative potential for patients with cancer; however, their potential is significantly curtailed by systemic toxicity that results from activity of the therapeutic molecule outside the tumor microenvironment. Our molecules are engineered to localize activity within the tumor microenvironment with minimal systemic effects, resulting in the potential to achieve enhanced anti-tumor activity and increasing the population of patients who may be eligible to receive our medicines. Our most advanced tumor-activated, clinical-stage product candidates are XTX101, an Fc-enhanced, anti-CTLA-4 monoclonal antibody, or mAb, XTX301, an interleukin 12, or IL-12, therapy, and XTX202, an interleukin 2, or IL-2, therapy. In 2023, we presented clinical data across these programs showing initial clinical validation for each of these molecules and our tumor-activated approach. In addition to our clinical-stage product candidates, we are continuing to leverage our differentiated research platform and expertise in developing tumor-activated I-O therapies to advance preclinical development for tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers).

XTX101

XTX101 is an investigational tumor-activated, Fc-enhanced, high-affinity binding anti-CTLA-4 mAb designed to block CLTA-4 and deplete regulatory T cells when activated (unmasked) in the tumor microenvironment and improve upon the therapeutic index of existing anti-CTLA-4 therapies. In the third quarter of 2023, we entered into a co-funded clinical trial collaboration with F. Hoffmann-La Roche Ltd., or Roche, to evaluate XTX101 in combination with atezolizumab (Tecentriq®) in a multi-center, open-label Phase 1/2 clinical trial. We are currently evaluating the safety and tolerability of the combination in patients with advanced solid tumors in the Phase 1 dose escalation portion of the clinical trial. We plan to select a recommended Phase 2 dose, or RP2D, for XTX101 in combination with atezolizumab in the second quarter of 2024, and subject to the results of the Phase 1 combination dose escalation portion of the trial, we plan to initiate the Phase 2 portion of the trial for XTX101 in combination with atezolizumab in patients with microsatellite stable colorectal cancer, or MSS CRC, in the third quarter of 2024. In addition, we plan to report initial Phase 2 data for XTX101 in combination with atezolizumab in approximately 20 patients with MSS CRC in the fourth quarter of 2024 and in approximately 20 additional patients (40 patients total) in the first quarter of 2025.

XTX301

XTX301 is an investigational tumor-activated IL-12 designed to potently stimulate anti-tumor immunity and reprogram the tumor microenvironment of poorly immunogenic “cold” tumors towards an inflamed or “hot” state. In March 2024, our wholly-owned subsidiary Xilio Development, Inc., or Xilio Development, entered into an exclusive license agreement with Gilead Sciences, Inc., or Gilead, pursuant to which it granted Gilead an exclusive global license to develop and commercialize XTX301 and specified other molecules directed at IL-12. For more information, please see “—License and Collaboration Agreements—Exclusive License Agreement with Gilead” below.

We are currently evaluating XTX301 in an ongoing Phase 1 first-in-human, multicenter, open-label clinical trial designed to evaluate the safety and tolerability of XTX301 as a monotherapy in patients with advanced solid tumors. In January 2024, we reported preliminary safety data into the third dose level in the Phase 1 dose escalation and anticipate reporting safety, pharmacokinetic, or PK, and pharmacodynamic, or PD, data for XTX301 in the fourth quarter of 2024.

XTX202

XTX202 is an investigational tumor-activated, beta-gamma biased IL-2 designed to potently stimulate CD8+ effector T cells and natural killer, or NK, cells without concomitant stimulation of regulatory T cells, or TREGs, when activated (unmasked) in the tumor microenvironment. In March 2024, we announced updated data from our Phase 2 clinal trial evaluating XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic renal cell carcinoma, or RCC, who have progressed on standard-of-care treatment. Together with previously reported data, we believe these additional data further validate our tumor-activated approach and support the broad potential for XTX202 as a combination therapy. In March 2024, we also announced plans to explore strategic opportunities to continue to develop XTX202 in combination with other agents and, as part of a strategic portfolio reprioritization, plans to discontinue further investment in XTX202 as a monotherapy.

Future Opportunities

In addition to our most advanced product candidates, we believe our proprietary platform technology has the potential to develop additional product candidates using our tumor-activated masking approach, which is designed to achieve tumor-specific molecule activation and derive a clinically meaningful improvement in therapeutic index. We are currently leveraging our differentiated platform technology, and our unique expertise in masking antibodies and cytokines, to develop a new generation of tumor-activated bispecific molecules and immune cell engager molecules. Subject to obtaining sufficient additional capital, we plan to advance XTX501, our tumor-activated PD-1/IL-2 bispecific development candidate, into IND-enabling studies. We also plan to continue to make focused investments in our promising research-stage pipeline for additional tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers). We will continue to evaluate opportunities for better tolerated and more efficacious combination therapies, using product candidates from across our portfolio with other cancer therapies, to increase the potential for curative regimens in oncology.

March 2024 Private Placement

On March 28, 2024, we entered into a securities purchase agreement with certain existing accredited investors, including Bain Capital Life Sciences and Rock Springs Capital, to issue and sell an aggregate of 1,953,125 shares of our common stock at a price of $0.64 per share and prefunded warrants to purchase up to an aggregate of 15,627,441 shares of our common stock at a purchase price of $0.6399 per prefunded warrant share, through a private investment in public equity financing. The prefunded warrants will have an exercise price of $0.0001 per share of common stock, be immediately exercisable and remain exercisable until exercised in full. We anticipate receiving aggregate gross proceeds from the private placement of approximately $11.3 million, before deducting placement agent fees and expenses payable by us. The private placement is expected to close on April 2, 2024, subject to the satisfaction of customary closing conditions. We expect to use the proceeds from the private placement to fund working capital and other general corporate purposes.

Our Approach—Improving the Therapeutic Index of I-O Therapies

Our focus is to improve upon two of the foundational mechanisms of I-O: cytokines and checkpoint inhibitors. Since the 1980s, cytokines have been explored as a cancer therapy due to their ability to carry messages between cells and serve as master regulators of the body's response to inflammation and immune attack. Although cytokines have demonstrated compelling clinical efficacy in certain tumors, including the ability to generate sustained complete responses, or CRs, in a subset of patients, their use has been limited by severe systemic toxicity. Similar to cytokines, checkpoint inhibitors have shown the potential to provide meaningful improvements in survival for patients with cancer, but the utilization of these therapies, beyond those that target the immune proteins PD(L)-1, is also limited largely by toxicity. Finally, immune cell engagers, including T cell engaging bispecific molecules, have demonstrated encouraging clinical activity, but treatment is typically associated with significant toxicities including cytokine-release syndrome and on-target/off-tumor cytotoxicity.

Our goal is to overcome the limitations of current I-O therapies by developing products with an improved efficacy-to-toxicity ratio, or therapeutic index. The toxicities for cytokines, checkpoint inhibitors and immune cell engagers stem from their activity outside of the tumor microenvironment. Our proprietary platform is designed to overcome these systemic toxicities by creating tumor-activated molecules and unleashing the activity of tumor-activated cytokines and antibodies

(including bispecifics) and immune cell engagers (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers) in the tumor microenvironment. These molecules are intended to be inactive until they reach the tumor microenvironment, where they are activated by the unique conditions of the tumor microenvironment, resulting in localized clinical activity with minimal dose-limiting toxicities. To achieve this tumor selectivity, we apply our platform, which includes engineered features and a proprietary protein masking technology that seeks to minimize interaction with healthy tissue and cells by rendering our molecules inactive until reaching the tumor. Our platform is also designed to enable optimal PK by preventing undesired binding and elimination outside of the tumor microenvironment, resulting in geographically localized pharmacology. The engineered features are designed to ensure that our product candidates are stable molecules with well-understood properties and a reproducible manufacturing approach.

Our Strategy

Our vision is to transform the lives of patients with cancer by harnessing the power of highly potent, tumor-selective I-O therapies that deliver deep and durable clinical responses. By leveraging our proprietary platform for tumor-activated molecules, we aim to discover, develop and, ultimately, commercialize I-O therapies that overcome the known limitations of today's approaches and provide effective, tolerable and durable therapeutic options for patients and their physicians.

In order to achieve these goals, the key elements of our strategy are to:

- **Rapidly advance clinical development for XTX101, our tumor-activated, Fc-enhanced anti-CTLA-4, through our co-funded clinical collaboration with Roche.** In the third quarter of 2023, we entered into a co-funded clinical trial collaboration with Roche to evaluate XTX101 in combination with atezolizumab (Tecentriq®) in a multi-center, open-label Phase 1/2 clinical trial. We are currently evaluating XTX101 in combination with atezolizumab (Tecentriq®) in Phase 1 combination dose escalation. We plan to select a RP2D for XTX101 in combination with atezolizumab in the second quarter of 2024, and subject to the results of the Phase 1 combination dose escalation portion of the trial, we plan to initiate the Phase 2 portion of the trial for XTX101 in combination with atezolizumab in patients with MSS CRC in the third quarter of 2024. In addition, we plan to report initial Phase 2 data for XTX101 in combination with atezolizumab in approximately 20 patients with MSS CRC in the fourth quarter of 2024 and in approximately 20 additional patients (40 patients total) in the first quarter of 2025.

- **Rapidly advance clinical development for XTX301, our tumor-activated IL-12, through our partnership with Gilead.** In March 2024, we entered into an exclusive license agreement with Gilead to develop and commercialize XTX301, as well as other molecules directed at IL-12. We are currently evaluating XTX301 in Phase 1 monotherapy dose escalation, and we anticipate reporting safety, PK and PD data for XTX301 in the fourth quarter of 2024. Under our license agreement with Gilead, we are responsible for conducting clinical development for XTX301 in the ongoing Phase 1 clinical trial through an initial planned Phase 2 dose expansion, and then following the delivery by us of a specified clinical data package for XTX301, Gilead can elect to transition responsibilities for the development and commercialization of XTX301 to Gilead, subject to the terms of the license agreement and payment by Gilead of a transition fee.

- **Explore opportunities for strategic partnerships to evaluate XTX202, our tumor-activated, beta-gamma biased IL-2, in combination with other agents.** In March 2024, we announced additional data from our Phase 2 clinical trial evaluating XTX202 in patients with metastatic RCC or unresectable or metastatic melanoma. Together with previously reported data, we believe these additional data further validate our tumor-activated approach and support the broad potential for XTX202 as a combination therapy. In March 2024, we also announced plans to explore strategic opportunities to continue to develop XTX202 in combination with other agents and, as part of a strategic portfolio reprioritization, plans to discontinue further investment in XTX202 as a monotherapy.

- **Leverage our promising research platform to advance differentiated, tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers).** We believe our proprietary platform technology has the potential to develop additional product candidates using our tumor-activated masking approach. In particular, we are currently leveraging our

differentiated platform technology and our unique expertise in masking antibodies and cytokines to develop a new generation of tumor-activated bispecific molecules and immune cell engager molecules. Subject to obtaining sufficient additional capital, we plan to advance XTX501, our tumor-activated PD-1/IL-2 bispecific development candidate, into IND-enabling studies. We also plan to continue to make focused investments in our promising research-stage pipeline for additional tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers). We will continue to evaluate opportunities for better tolerated and more efficacious combination therapies, using product candidates from across our portfolio with other cancer therapies, to increase the potential for curative regimens in oncology.

- **Leverage the broad applicability of our proprietary platform for tumor-activated I-O molecules through strategic collaborations and partnerships.** We believe the collective components of our proprietary platform technology and the reproducibility it enables in our drug discovery and development efforts present a meaningful opportunity for us to leverage our platform in combination with other agents in oncology. We plan to continue to explore strategic collaborations and partnership that would enable us to access capital, accelerate the development of our current product candidates or additional product candidates or programs, evaluate our current or additional product candidates in combination with other agents, and expand our capabilities, pipeline opportunities and product offerings, particularly where a collaborator may have expertise or capabilities that are synergistic or additive to our own.

About I-O

The discovery of a role for immunotherapy in the treatment of cancer was made more than 100 years ago, when William Coley treated patients with heat-treated bacterial toxins, resulting in a profound anti-tumor effect in some of those patients. Two of the most important mechanisms within I-O are cytokines and checkpoint inhibitors, with cytokine therapies having been introduced in the 1980s and checkpoint inhibitors in the period after 2011, when the first such product was approved. Both therapeutic approaches are known to provide efficacy in terms of clinical responses and tumor shrinkage. However, toxicities have limited the application of these therapies, resulting in the need to dose-reduce, dose-interrupt or discontinue many patients from treatment. Immune checkpoint inhibitors are associated with immune-related adverse events, or AEs, that may affect any organ system and may be life-threatening or fatal to patients. Cytokines in particular are associated with broad ranging multi-organ toxicities that can be lethal and have limited the development of this class of potential therapies. Anti-PD-1/PD-L1 checkpoint inhibitors have been used broadly because they generally achieve efficacy with minimal systemic toxicity, enabling their administration at their maximally effective doses. Anti-PD-1/PD-L1 treatments have become the most widely utilized immunotherapy agent in oncology, with the U.S. Food and Drug Administration, or FDA, approvals in more than a dozen separate tumor types and $27 billion in worldwide sales in 2020. Our mission is to overcome the limitations of cytokine therapies and checkpoint inhibitors, such as anti-CTLA-4, and make immunotherapies beyond anti-PD-1/PD-L1 treatments more accessible, efficacious and safe for patients with cancer.

The promise and limitations of checkpoint inhibitors

Checkpoint inhibitors have become mainstays in cancer therapy since the FDA approved ipilimumab, an anti-CTLA-4 therapy, in 2011. Similar to cytokines, checkpoint inhibitors have shown the potential to provide meaningful improvements in survival for patients with cancer, but the utilization of these therapies has been limited largely by toxicities. These toxicities, which can be life-threatening or fatal, have resulted in the need to dose-reduce, dose-interrupt or discontinue many patients from treatment. To date, anti-PD-1/PD-L1 checkpoint inhibitors have been used broadly due to their ability to achieve efficacy with minimal systemic toxicity, enabling their administration at their maximally effective doses. In contrast, while the clinical benefit of CTLA-4 blockade to patients with cancer is well-established, the efficacy of current CTLA-4 therapies is impaired by dose-limiting toxicities arising from systemic immune activation. This has reduced the use of anti-CTLA-4 mAbs both as a monotherapy and in combination therapy. We believe XTX101, our tumor-activated, Fc-enhanced high affinity binding anti-CTLA-4, has the potential to overcome these limitations and deliver the full clinical benefit of anti-CTLA-4 mechanisms without the dose-limiting toxicities associated with existing CTLA-4 treatments.

The promise and limitations of cytokines

Cytokines are small signaling proteins that serve as master regulators of the body's response to inflammation and immune attack. There are multiple cytokines, including IL-2, which are approved in a range of oncology and non-oncology indications. Aldesleukin, a high-dose IL-2 therapy, was first approved in 1992 as a monotherapy for patients with melanoma and RCC. Similarly, IL-12 development has been relentlessly pursued due to its unique potential to treat immunologically cold tumors, but currently there are no approved IL-12 therapies. Cytokines such as IL-2 and IL-12 have not achieved therapeutic success in a broad population of patients because their use has been limited by severe toxicity, including fatal outcomes. We believe XTX301, our tumor-activated IL-12 product candidate, has the potential to overcome these limitations and deliver a therapeutic dose with low systemic toxicity and the ability to achieve a broad therapeutic index. We also believe that XTX202, our IL-2 product candidate, has broad potential as a combination therapy based on the safety, PK and PD data reported to date from our Phase 1 and Phase 2 clinical trials.

I-O Combinations

The ability to combine oncology agents has been an important step in developing effective cancer regimens. Combination chemotherapy can be curative in settings where single agents have had limited efficacy and were not considered curative. The substantial dose-limiting toxicities associated with I-O agents has prevented these agents from being combined effectively. The ultimate promise of I-O for patients is dependent upon the ability to develop I-O agents that can be combined at their optimal doses without life-threatening toxicity. The severe toxicity of IL-2 has limited the ability to combine IL-2 with other cancer treatments without compromising the dose administered. Similarly, data from third-party clinical trials has demonstrated that the combination of ipilimumab, an anti-CTLA-4 therapy, with nivolumab, which targets the immune checkpoint protein PD-1, was associated with improved clinical outcomes, but it was limited by significantly higher risk of all-grade and high-grade immune-related AEs such as pruritus, rash, diarrhea, colitis, elevation of the liver enzyme alanine transaminase, known as ALT, hyperthyroidism, hypophysitis and pneumonitis. Importantly, combination therapy generally requires use of low dose ipilimumab at 1 mg/kg rather than the more efficacious dose of 10 mg/kg. Even at the lower dose, ipilimumab combination therapy is poorly tolerated, with AEs causing up to 80% of patients to discontinue treatment, up to 50% of patients requiring emergency room visits and up to 36% of patients requiring hospitalization. The potential of our tumor-activated molecules to minimize the systemic toxicity of I-O could allow us to combine I-O agents to meaningfully improve survival in a broader range of tumor types. We are currently evaluating XTX101, our anti-CTLA-4 product candidate, in combination with atezolizumab, and as discussed above, we plan to explore opportunities to continue to develop XTX202, our IL-2 product candidate, in combination with other agents.

Our Solution: Our Proprietary Platform Enables Tumor-Activated I-O Molecules Designed to Optimize Their Therapeutic Index

I-O therapies have curative potential for patients with cancer. However, this potential has been significantly curtailed to date by dose-limiting toxicities that result from activity of the therapeutic molecule outside the tumor microenvironment. We believe that selectively targeting the activity of I-O agents to the tumor microenvironment can overcome these dose-limiting toxicities and enable maximal therapeutic benefit for patients. Tumor-selective activation could be achieved by harnessing unique characteristics of the tumor microenvironment to activate therapeutic molecules locally that have minimal or non-detectable levels of activity outside of the tumor microenvironment.

Matrix metalloproteases, or MMPs, are enzymes involved in protein degradation that are essential for tumor growth and metastasis because they regulate key processes within the tumor microenvironment, including tumor growth, angiogenesis, invasion and metastasis. MMPs are dysregulated in the tumor microenvironment, resulting in preferential activity of MMPs in the tumor microenvironment by comparison to non-tumor, healthy tissues. As a result, we believe that our platform for tumor-activated molecules, which is designed to harness tumor MMP activity, can design molecules that selectively activate within the tumor microenvironment while maintaining minimal or non-detectable levels of activity outside of the tumor microenvironment.

Our platform enables us to engineer a broad range of immune-modulatory molecules, including tumor-activated cytokines and antibodies (including bispecifics) and immune cell engagers (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers), that contain masking domains designed to minimize their activity outside of

the tumor microenvironment and turn on selectively in the tumor microenvironment where they are preferentially activated by tumor MMPs. Specifically, MMPs enzymatically cleave a protease cleavage site incorporated in a peptide linker that connects the masking protein domain to the active agent. This separates the mask from the active agent, enabling the unmasked agent to promote an anti-tumor response within the tumor microenvironment.

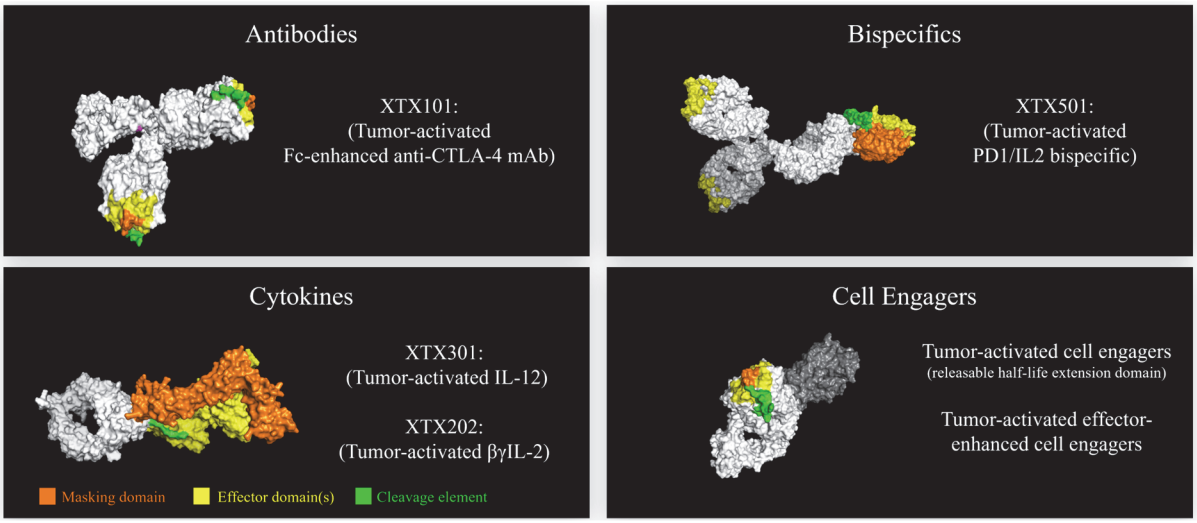
Key features of our tumor-activated molecules exemplify the engineering approach that underpins our platform. Each feature contributes to multiple characteristics of the molecule that are designed to enable tumor selective biological activity and tumor growth inhibition while minimizing toxicity outside of the tumor microenvironment. The general architecture of each of our tumor-activated molecules is:

- a masking domain;
- linker sequences;
- a protease cleavage site;
- a cleavable or retained half-life extension domain for cytokine, immune cell engager and bispecific molecules, as appropriate; and
- the effector domain (i.e., an engineered cytokine, antibody or immune cell engager).

The engineered features are designed to ensure that our product candidates are stable molecules with well-understood properties and a reproducible manufacturing approach. We have applied our masking approach to cytokines and antibodies that regulate immune checkpoints, and with our earlier stage work, we have expanded the application of our platform to tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers).

Our molecules are designed to contain a masking domain that is released by protease cleavage. When the linker sequence, which contains a protease cleavage site, is cleaved by MMPs, the masking domain is released, allowing the unmasked molecule to bind to the target receptor, or in the case of an immune cell engager, bind to the immune cell and tumor antigen to facilitate an immune synapse. Before cleavage by the MMPs in the tumor microenvironment, the engineered molecule is designed to minimize interaction with healthy tissue and cells outside the tumor microenvironment. Specifically, there is no binding to target receptors, and the molecule has a long half-life outside the tumor microenvironment. After cleavage in the tumor microenvironment, the engineered molecule is locally activated and has a relatively short half-life.

Key Features of Xilio's Tumor-Activated Molecules



We believe that the characteristics of our proprietary platform for tumor-activated molecules described above will enable the following key advantages:

- masking that takes advantage of multiple intra-molecular interactions, minimizing the risk of activity outside of the tumor microenvironment and therefore minimizing the risk of toxicity;
- engineering the active molecule such that unmasking in the tumor microenvironment promotes a potent, localized anti-tumor immune response;
- early consideration and incorporation of manufacturing and development aspects into the design of molecules to facilitate production of high-quality drug product for clinical use;
- half-life optimized molecules with prolonged half-life in the inactive (masked) state to support administration to patients on a schedule consistent with other biologics agents; and
- locally activating molecules that have a short half-life in the tumor microenvironment, which minimizes the risk of the activated molecule exhibiting activity outside of the tumor microenvironment and, therefore, further reduces the risk of toxicity.

Our Pipeline

Leveraging our platform technology, we are building a pipeline of tumor-activated I-O molecules to treat cancer, including tumor-activated cytokines and antibodies (including bispecifics) and immune cell engagers (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers). Our goal is to overcome the limitations of current I-O therapies by developing products with an improved therapeutic index. Consistent with this goal, we selected molecules that have prior clinical validation demonstrating therapeutic benefit, but that have been limited by significant toxicities that we believe can be addressed with our approach.

Program	Tumor Types	Mechanism of Action	Stage of Development	Partnerships
XTX101 in combination with atezolizumab [1]	Advanced MSS CRC	anti-CTLA-4 + PD-L1	Phase 1 combination dose escalation ongoing	Co-funded clinical collaboration with Roche
XTX301 [2]	Advanced Solid Tumors	IL-12	Phase 1 monotherapy dose escalation ongoing	Exclusive global license with Gilead
XTX202	Advanced RCC and Melanoma	IL-2βγ	Phase 2 monotherapy enrollment complete [3]	Plan to explore strategic opportunities to develop in combinations [3]
XTX501	Advanced Solid Tumors	PD-1/IL-2 bispecific	Development candidate [4]	
Additional research-stage programs	Undisclosed	Tumor-activated immune cell engagers	Discovery-stage	

1. Evaluating XTX101 in combination with atezolizumab (Tecentriq®) in Phase 1 combination dose escalation trial and planned Phase 2 combination trial in MSS CRC.
2. Evaluating XTX301 in Phase 1 monotherapy dose escalation for the treatment of advanced solid tumors.
3. Plan to discontinue further investment in XTX202 as a monotherapy.
4. Plan to advance in IND-enabling studies, subject to sufficient additional capital.

XTX101, Our Clinical-Stage, Tumor-Activated, Fc-Enhanced, High Affinity Binding Anti-CTLA-4 Product Candidate

XTX101 is an investigational tumor-activated, Fc-enhanced, high-affinity binding anti-CTLA-4 mAb designed to block CLTA-4 and deplete TREGs when activated (unmasked) in the tumor microenvironment and improve upon the therapeutic index of existing anti-CTLA-4 therapies. In the third quarter of 2023, we entered into a co-funded clinical trial collaboration with Roche to evaluate XTX101 in combination with atezolizumab (Tecentriq®) in a multi-center, open-

label Phase 1/2 clinical trial. We are currently evaluating the safety and tolerability of the combination in patients with advanced solid tumors in the Phase 1 dose escalation portion of the clinical trial. Subject to the results of Phase 1 combination dose escalation, we plan to evaluate the safety and efficacy of the combination in the Phase 2 portion of the clinical trial in patients with microsatellite stable colorectal cancer.

Background on CTLA-4

CTLA-4 is an immune checkpoint protein that is well-established as playing a central role in the development of tumors. The scientific insight that led to the early development of CTLA-4 therapeutics is attributable to investigators recognizing CTLA-4 as a protein on T cells that acts as a brake on T cell activation. By removing this brake, T cells were freed to attack cancer. This work led to the development and FDA approval of ipilimumab, a CTLA-4 mAb, for the treatment of unresectable or metastatic melanoma at a dose of 3 mg/kg in 2011 and in additional indications in subsequent years.

While anti-CTLA-4 therapies such as ipilimumab have demonstrated meaningful efficacy across a range of tumor types, autoimmune toxicities have significantly limited their use to date. Clinical trials have shown that 20% of ipilimumab-treated melanoma patients survive at least three years, and a subset survive for 10 years or longer. Ipilimumab remains one of the most impactful drugs for these patients; however, the number of patients who benefit from treatment with ipilimumab remains limited due to its toxicity. Investigation of dose-response in two third-party clinical trials of melanoma patients showed that higher doses of ipilimumab are likely to increase the proportion of patients who benefit; however, the increased dose also resulted in an unacceptable toxicity profile for most patients. In a Phase 2 trial of ipilimumab conducted by Bristol-Myers Squibb Company, a dose range of 0.3 mg/kg to 10 mg/kg was tested and efficacy was measured both by response rate and by clinical outcome. Both the response rate and median overall survival, or mOS, were higher at 10 mg/kg than at 3 mg/kg, with the 0.3 mg/kg dose determined as being ineffective. The rate of severe AEs was 25% at the 10 mg/kg dose, 7% at the 3 mg/kg dose and 0% at the ineffective dose of 0.3 mg/kg. Similarly, as shown in the table below, in a Phase 3 trial conducted by Bristol-Myers Squibb Company, mOS was higher at the 10 mg/kg dose but resulted in unacceptable toxicity for most patients. Therefore, we believe that achieving a three-fold increase in therapeutic index would be transformational.

High-Dose Ipilimumab Improved Survival but Resulted in Unacceptable Toxicity

Dose (mg/kg)	mOS (mo)	Adverse Events: Gr 3/4 irAEs / disconts. (%)
3	**11.5**	**14 / 19**
10	**15.7**	**30 / 31**

Ipilimumab has shown preliminary evidence of promising anti-tumor activity in a range of tumor types outside of its currently approved indications, but successful additional approvals have been limited due to its toxicity. For example, ipilimumab has been observed to be more active when combined with the anti-PD-1/PD-L1 antibody nivolumab. However, the combination of ipilimumab and nivolumab has been shown to cause a greatly increased rate of immune-related toxicity when compared to treatment with either ipilimumab or nivolumab as a monotherapy. Clinical results from patients who express high-affinity FcγR polymorphisms have shown improved responses to ipilimumab, but efforts to improve the potency of the antibody have been limited by perceived toxicity risk. There remains a critical need to develop safe and effective forms of anti-CTLA-4 mAbs that can achieve efficacious doses within the tumor microenvironment.

Our Solution: XTX101, a Tumor-Activated, Fc-Enhanced Anti-CTLA-4

XTX101 is a clinical-stage, tumor-activated, Fc-enhanced anti-CTLA-4 mAb that is designed to improve upon the therapeutic index of existing anti-CTLA-4 therapies by overcoming potency and tolerability limitations. Our goal is to demonstrate an improved safety profile enabling higher anti-CTLA-4 exposure in the tumor that will result in increased efficacy. In preclinical studies, we observed the following tolerability and activity profile of XTX101:

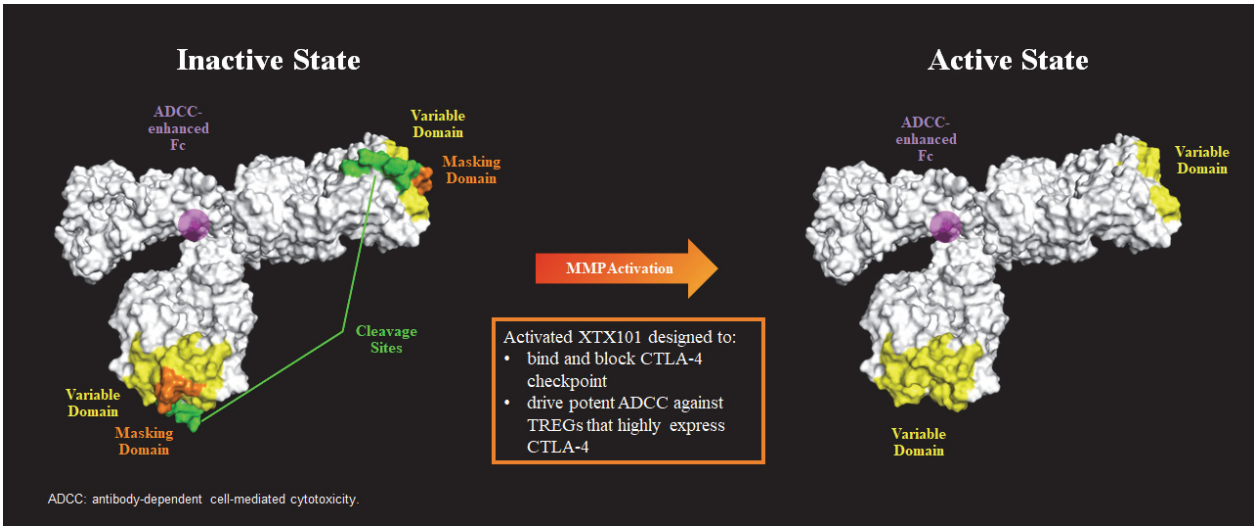
- improved *in vivo* potency and the intra-tumoral PD effects of XTX101 are consistent with the improved potency being a result of the higher affinity binding to the target CTLA-4 and enhanced IgG1-Fc effector function, which

further improves checkpoint inhibition and enhances antibody-dependent cellular cytotoxicity to deplete immune-suppressive TREGs in the tumor microenvironment;

- reduced peripheral immune activity due to masking of the CDR sequences; and
- activation by protease-dependent release of the masks, which acts selectively in the tumor microenvironment and minimizes toxicity associated with systemic immune activation.

XTX101 is designed to enhance the desirable features of an anti-CTLA-4 antibody while mitigating the known limitations of anti-CTLA-4 antibodies due to toxicity. We expect this combination of features to result in an increased therapeutic index.

Tumor-Activated Design Components of XTX101



Preliminary Phase 1 Monotherapy Data Presented in May 2023

In May 2023, we announced initial Phase 1 monotherapy dose escalation data for XTX101. As of a data cutoff date of May 2, 2023, 25 patients had been treated with XTX101, including dose levels ranging from 7 mg to 180 mg administered once every three weeks, or Q3W, and one dose level at 150 mg administered once every six weeks, or Q6W. Of these patients, 20 patients were dosed in monotherapy dose-escalation and five patients were dosed in monotherapy dose-expansion.

Patients had a wide range of advanced and treatment-refractory solid tumors, including colorectal cancer, or CRC, non-small cell lung cancer, or NSCLC, and pancreatic cancer. In addition, 76% of patients had been previously treated with at least three prior lines of anti-cancer therapy, and 44% had been previously treated with at least one I-O agent. As of the data cutoff date, three patients were continuing on treatment with XTX101, and 22 patients had discontinued treatment with XTX101.

Preliminary Safety Data

A recommended Phase 2 dose, or RP2D, and schedule of 150 mg Q6W was determined based on the favorable preliminary safety, PK and PD data for XTX101. At the RP2D, no dose-limiting toxicities were observed, and there was no reported evidence of immune-related endocrine or skin AEs that are commonly associated with systemically active anti-CTLA-4 agents. In addition, evidence of effective masking of XTX101 was demonstrated by low levels of unmasked drug detected in peripheral circulation, and XTX101 achieved target PK exposure at the RP2D, reaching the targeted area under the curve, or AUC, and peak concentration, or C_{max}.

As of the data cutoff date of May 2, 2023:

- Across all dosing levels and dosing intervals, no Grade 4 or Grade 5 treatment-related AEs were reported by investigators.

- Among seven patients who received XTX101 administered at the RP2D of 150 mg on a Q6W dosing schedule, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were diarrhea (14%), fatigue (14%) and decreased appetite (14%). In these patients, no treatment-related colitis or infusion related reaction of any grade was observed. Investigators reported only one Grade 3 treatment-related AE of diarrhea, which occurred after two doses and resolved after five days without steroid use. This patient tolerated two additional doses of XTX101 after dose reduction to 75 mg Q6W without any symptom recurrence. At the RP2D of 150 mg Q6W, this was the only patient with a dose reduction due to an AE, and no patients discontinued treatment due to a treatment-related AE.

- Among 18 patients who received XTX101 administered on a Q3W dosing schedule, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were diarrhea (28%), colitis (28%), infusion related reaction (28%), nausea (17%), vomiting (17%) and abdominal pain (11%). Of these, investigators reported the following Grade 3 treatment-related AEs: diarrhea (6%), colitis (22%) and infusion related reaction (17%). Infusion related reactions were associated with antidrug antibodies. Across all dose levels administered Q3W, two patients had dose reductions due to AEs, and four patients discontinued treatment due to an infusion related reaction.

Preliminary Anti-Tumor Activity Data

A partial response, or PR, was observed at nine weeks in one patient with advanced PD-L1 negative NSCLC with hepatic metastases treated with XTX101 at the 150 mg Q6W dose level and confirmed after the data cutoff date at week 27. The only treatment-related AE reported for this patient was Grade 1 fatigue. In addition, PD markers for anti-CTLA-4 reported for this patient showed minimal immune activation in peripheral circulation, demonstrating evidence of tumor-selective activation of XTX101.

Updated Phase 1 Monotherapy Data Presented at the European Society for Medical Oncology (ESMO) Immuno-Oncology Congress in December 2023

In December 2023, we reported updated Phase 1 monotherapy data for XTX101 at the ESMO Immuno-Oncology Congress. As of a data cutoff date of November 13, 2023, 36 patients with advanced solid tumors had been administered XTX101 monotherapy, including 18 patients at the RP2D and schedule of 150 mg Q6W.

Patients treated at the RP2D of 150 mg Q6W were heavily pre-treated, with 83% of patients receiving three or more lines of anti-cancer therapy and 56% previously treated with an immunotherapy.

Preliminary Safety Data

At the RP2D of 150 mg Q6W, 18 patients (including nine patients previously reported) were evaluable for safety as of the data cutoff date of November 13, 2023:

- Safety data were consistent with previously reported results. XTX101 monotherapy was generally well-tolerated with treatment-related AEs primarily Grade 1 or 2, and no patients discontinued treatment due to a treatment-related AE. In addition, as previously reported, only one patient had a dose reduction due to an AE.

- The most common treatment-related AE of any grade (≥10% incidence) reported by investigators was fatigue (11%).

- As previously reported, investigators reported only two Grade 3 treatment-related AEs: Grade 3 treatment-related AE of diarrhea, which occurred after two doses and resolved after five days without steroid use, and one Grade 3 treatment-related AE of dermatitis.

In addition, no Grade 4 or 5 treatment-related AEs were reported by investigators across all dosing levels and dosing intervals.

Preliminary Anti-Tumor Activity Data

At the RP2D of 150 mg Q6W, 12 patients were evaluable for anti-tumor activity as of the data cutoff date:

- As previously reported, a confirmed PR was observed in a patient with Stage 4 PD-L1 negative NSCLC, including complete resolution of liver metastases. The confirmed PR continued through 36 weeks of treatment with XTX101, with the patient discontinuing treatment after week 36 due to an unrelated AE.

- Additional data reported demonstrated a disease control rate, or DCR, of 33% in late-line and I-O refractory patients administered XTX101 monotherapy at the RP2D of 150 mg Q6W, consisting of the confirmed PR in the NSCLC patient and stable disease in three patients (triple-negative breast cancer, melanoma and MSS CRC (n=1 each)).

Preliminary Pharmacokinetic Data

As previously reported, consistent with the tumor-selective design for XTX101, preliminary pharmacokinetic analyses demonstrated 96% activation of XTX101 in a melanoma tumor and 73% activation in a metastatic liver lesion in a CRC patient, compared to minimal peripheral activation of XTX101 of 13% in both patients.

Cytokine Programs

The major focus in our cytokine programs is the development of tumor-activated cytokines with exemplary clinical activity and tolerability. These cytokine programs include our clinical-stage, tumor-activated product candidates, XTX301 (IL-12) and XTX202 (IL-2), as well as discovery-stage programs for oncology.

XTX301, Our Clinical-Stage, Tumor-Activated IL-12 Product Candidate

XTX301 is an investigational tumor-activated IL-12 designed to potently stimulate anti-tumor immunity and reprogram the tumor microenvironment of poorly immunogenic "cold" tumors towards an inflamed or "hot" state. In March 2024, our wholly-owned subsidiary Xilio Development entered into an exclusive license agreement with Gilead pursuant to which it granted Gilead an exclusive global license to develop and commercialize XTX301 and specified other molecules directed at IL-12. For more information, please see "—License and Collaboration Agreements—Exclusive License Agreement with Gilead" below.

We are currently evaluating XTX301 in an ongoing Phase 1 first-in-human, multicenter, open-label clinical trial designed to evaluate the safety and tolerability of XTX301 as a monotherapy in patients with advanced solid tumors. In January 2024, we reported preliminary safety data into the third dose level in the Phase 1 dose escalation and anticipate reporting safety, PK and PD data for XTX301 in the fourth quarter of 2024.

Background on IL-12

IL-12 is a potent, pro-inflammatory cytokine produced by antigen-presenting cells such as dendritic cells, macrophages and B cells. IL-12 has two subunits, p35 and p40, that together form a heterodimer protein. IL-12 is a key cytokine in the body's response to pathogen infection, sending a signal to T cells, among others. IL-12 interacts with diverse immune cells, including CD4+ T cells, CD8+ effector T cells, NK cells, monocytes and macrophages. IL-12's broad range of pro-inflammatory functions suggests that it could potentially be highly potent in controlling anti-cancer immunity. IL-12 has been shown in preclinical studies to induce robust anti-tumor effects against many types of malignancies and it has been tested against multiple human cancers in clinical trials. Recombinant human IL-12 has been evaluated in clinical trials, and anti-tumor efficacy was observed in a small number of patients across a range of tumor types.

Unfortunately, systemic IL-12 therapy has historically caused severe AEs in patients with cancer. Life-threatening liver damage, called hepatotoxicity, was identified during the early development of previous IL-12 therapies, which severely limited the dose of IL-12 that could be administered, and further trials to evaluate efficacy were therefore conducted at sub-optimal doses due to the toxicity. In an early Phase 2 trial of recombinant human IL-12, the MTD of 0.5 μg/kg (administered in days 1-5 in a 21-day dosing cycle) caused severe side effects in 70% of patients, or 12 of 17 patients, of whom two died from gastrointestinal bleeding and multi-organ failure, respectively. The severe toxicities indicated that recombinant human IL-12 could not be used systemically due to rapid increases in the cytokines IFN-γ, TNF-α and IL-6 that caused a cytokine storm syndrome characterized by systemic inflammation, multi-organ dysfunction and immune cytopenias. Efforts to overcome these systemic liabilities include alternate drug delivery approaches such as intra-tumoral administration of IL-12 encoding DNA vaccines or administration of oncolytic viruses expressing IL-12. Despite activity in individual lesions, cancer is a systemic disease that cannot be cured with local therapy once it has reached an advanced stage. Therefore, to unleash the potential for IL-12 in the majority of patients with advanced or metastatic cancer, an IL-12 that can be administered systemically but act locally at the tumor site is needed.

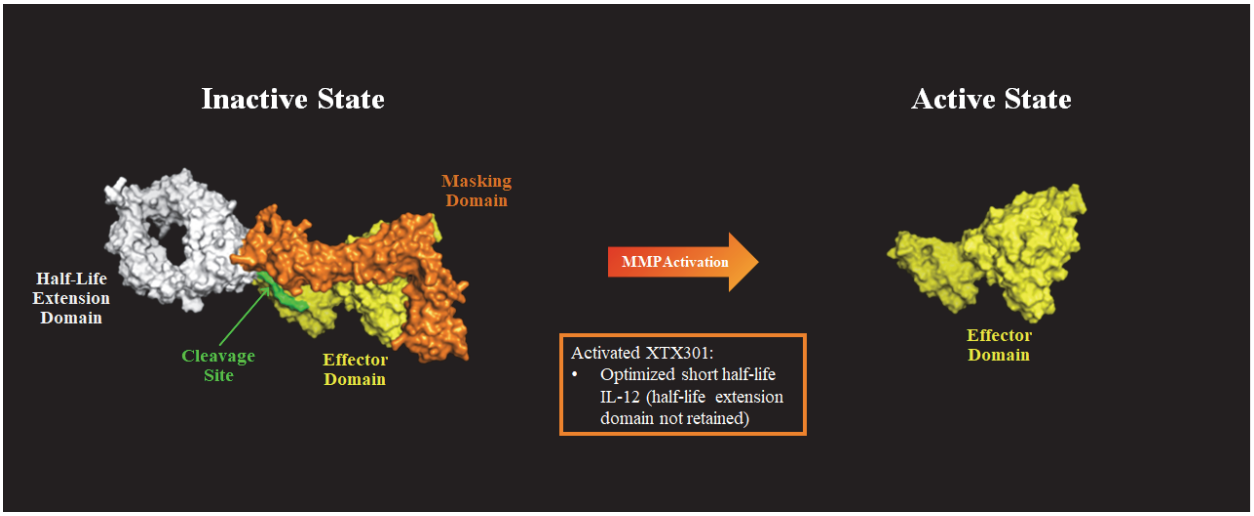
The failure of systemic IL-12 to induce meaningful anti-tumor efficacy is generally attributed to tolerability, which limits the dose and, as a result, the ability to reach therapeutic concentrations within the tumor microenvironment. Therefore, maximizing the amount of IL-12 that reaches the tumor, while minimizing exposure of non-tumor tissue, may be critical for a safe and effective anti-tumor response. Tumor-selective activation is therefore a desirable therapeutic profile.

Our Solution: XTX301, a Tumor-Activated IL-12

Our goal for our IL-12 program is to create a tumor-activated, extended half-life IL-12 therapeutic with minimal peripheral effects. We are using our platform technology and proprietary approach to achieve systemic delivery of tumor-activated IL-12, which we believe would have potential as a monotherapy and in combination with other therapies.

The design of our masked IL-12 cytokine molecule is closely related to that of our masked IL-2 cytokine molecule, described below, which illustrates the flexibility and robustness of our cytokine engineering approach. The masking domain is designed to prevent binding to the cell-surface IL-12 receptor, unless the linker containing the protease site is cleaved by proteases preferentially active in the tumor microenvironment. The half-life extension domain is designed to overcome the short circulating half-life of the native cytokine and the overall molecule is designed to enhance the efficiency of manufacturing.

Tumor-Activated Design Components of XTX301



We have undertaken extensive preclinical studies that demonstrated the ability of XTX301 to induce potent anti-tumor activity and PD changes consistent with known IL-12 biology. Importantly, these effects on the tumor were observed without inducing concomitant systemic toxicity, which provides evidence that the masking design was performing as intended in preclinical studies.

Preliminary Phase 1 Dose Escalation Safety Data Reported in January 2024

In January 2024, we reported preliminary safety data into the third dose level in the Phase 1 clinical trial. As of a data cutoff date of January 5, 2024, nine patients had been treated with XTX301 in the outpatient setting in Phase 1 dose escalation at three dose levels ranging from 5 ug/kg to 45 ug/kg administered once every three weeks. XTX301 was generally well-tolerated across all dose levels with no dose-limiting toxicities observed in patients as of the data cutoff date. We anticipate reporting safety, PK and PD data for XTX301 in the fourth quarter of 2024.

XTX202, Our Clinical-Stage, Tumor-Activated IL-2 Product Candidate

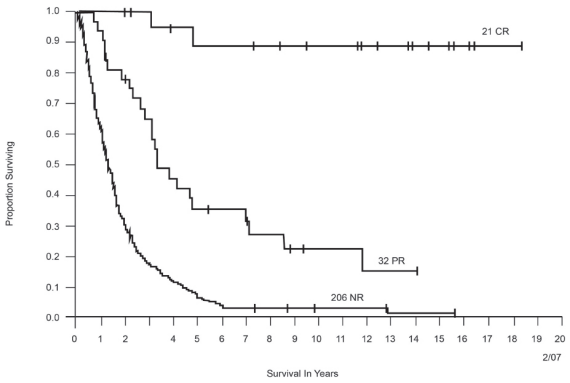
XTX202 is an investigational tumor-activated, beta-gamma biased IL-2 designed to potently stimulate CD8+ effector T cells and NK cells without concomitant stimulation of TREGs when activated (unmasked) in the tumor microenvironment. In March 2024, we announced updated data from our Phase 2 clinal trial evaluating XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic RCC who have progressed on standard-of-care treatment. Together with previously reported data, we believe these additional data further validate our tumor-activated approach and support the broad potential for XTX202 as a combination therapy. In March 2024, we also announced plans to explore strategic opportunities to continue to develop XTX202 in combination with other agents and, as part of a strategic portfolio reprioritization, plans to discontinue further investment in XTX202 as a monotherapy.

Background on IL-2

IL-2: Extensive clinical evidence of the promise and limitations of cytokines

As shown in the figure below, high-dose IL-2 has resulted in long-term survival in a subset of patients who had achieved a CR. We believe that patients who develop a CR when treated with high-dose IL-2 are highly likely to achieve a long-term durable response or cure.

Survival of Patients Who Achieved a CR with High-Dose IL-2



Historical use of IL-2 in cancer has been accompanied by severe toxicity

The power of IL-2 is promising, but it has been greatly reduced due to toxicities. When administered locally, IL-2 has been shown to be clinically active and well-tolerated, shrinking local cancerous lesions and reducing malignant effusions. However, when administered systemically, treatment with IL-2 has been shown to induce severe toxicities, including vascular leak syndrome, or VLS, myocardial infarction, or heart attack, acute renal failure and immune-mediated neuropathy. This toxicity profile greatly limits its current use.

In order to localize IL-2, many groups have tried linking IL-2 to tumor-targeting mAbs, creating fusion proteins. These fusion proteins can accumulate in a tumor and create locally high IL-2 concentrations. However, the use of cytokine fusion proteins has not prevented systemic toxicity because the long circulating half-life of antibody fusions and unexpected cleavage of IL-2 from the antibody domain has contributed to high systemic IL-2 levels in some cases.

The toxicities associated with early IL-2 therapies, such as aldesleukin, are hypothesized to be associated in part with binding and signaling through the high affinity αβγ IL-2receptor on immune cells or vascular endothelial cells. In addition, the αβγ IL-2receptor is expressed at high levels on regulatory T cells, or TREGs, which act to inhibit the immune response, whereas the intermediate affinity βγ IL-2 receptor is expressed on cells that promote immune response including CD8+ effector T cells and NK cells.

Modeling of IL-2 activity in preclinical animal tumor models and evaluation of dosage and dose-frequency data from patients has suggested that IL-2 has a steep dose-activity curve, with reduced exposure impacting both efficacy and toxicity. IL-2 anti-tumor activity and toxicity are both dependent on the amount of IL-2 administered. Therefore, in order to provide the greatest benefit to patients, the goal is to engineer a form of IL-2 that can minimize systemic effects while harnessing and directing activity to the tumor microenvironment.

Rationale for non-alpha IL-2

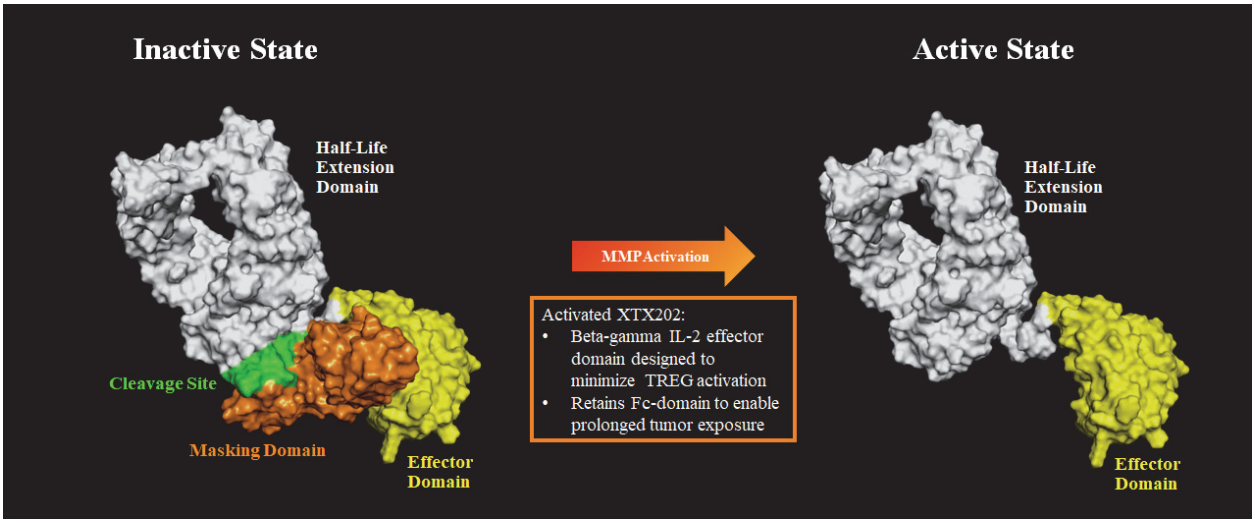
The application of cytokines to treat cancer fits with the role these signaling molecules have evolved to play in the body. Many key cytokines, including IL-2, regulate the immune system, and it is now recognized that there are immune stimulatory cytokines, immune suppressive cytokines and cytokines that have multiple activities on different target cell types. IL-2 is a master regulator of immune responses and has been investigated extensively as a potential anti-cancer immunotherapy. IL-2 supports the function, survival and proliferation of T cells, including the subset of T cells known as CD8+ effector T cells that are most closely linked to anti-tumor immunity.

The activities of IL-2 are driven by two classes of receptor complexes, which are present on different T cell subsets. The high-affinity αβγ receptor present primarily on TREGs, and the intermediate-affinity βγ receptor present primarily on CD8+ effector T cells and NK cells. In contrast to wild-type IL-2, XTX202 does not bind the α-subunit of the IL-2 receptor and therefore does not induce the preferential activity on TREGs that limits the immune activating effect of wild type IL-2. XTX202 is designed to potently stimulate CD8+ effector T cells and NK cells that express the βγ receptor.

Our Solution: XTX202, a Tumor-Activated IL-2

The critical challenge in the development of IL-2 therapies is to improve patient tolerability without reducing efficacy. Deploying the key structural components of our platform technology, we have designed XTX202 with three key features designed to overcome this: (1) avoidance of binding to CD25, the IL-2α receptor subunit, in order to reduce the activation of Treg cells that inhibit immune response, while maintaining effective activation of CD8+ and NK cells that promote an anti-tumor immune response; (2) overcoming the short circulating half-life of the native cytokine using the half-life extension domain; and (3) a removable protease-cleavable protein mask that prevents XTX202 from binding and signaling until the mask is removed by the MMPs that are preferentially active within the tumor microenvironment.

Tumor-Activated Design Components of XTX202



These key features are intended to ensure that XTX202 is released and activated preferentially within the tumor microenvironment, where it has been designed to bind to lymphocytes. In the tumor microenvironment, XTX202 is designed to be unmasked and to bind to the IL-2 βγ receptors that are abundantly expressed on CD8+ effector T cells and NK cells, activating these cells. Locally activated T cells and NK cells have potent anti-tumor cytotoxic activity. The unmasked XTX202 is then rapidly internalized by these lymphocytes, shortening the systemic half-life of the active (unmasked) molecule and localizing its activity to the tumor.

Initial Phase 1/2 Monotherapy Data Presented at Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting in November 2023

In November 2023, we reported initial Phase 1/2 monotherapy data for XTX202 at the SITC Annual Meeting. As of a data cutoff date of October 26, 2023, 62 patients with advanced solid tumors had been administered XTX202 in an outpatient setting. Fifty-four patients were treated in Phase 1 monotherapy dose-escalation and dose-expansion at seven dose levels ranging from 0.27 mg/kg to 4 mg/kg administered on a Q3W dosing schedule. Eight patients were treated in Phase 2 monotherapy at a dose level of 1.4 mg/kg Q3W.

Patients enrolled in Phase 1 were heavily pre-treated, with 74% of patients previously treated with three or more lines of anti-cancer therapy and 69% of patients previously treated with an immunotherapy. All patients in Phase 2 had been previously treated with an immunotherapy. As of the data cutoff date, 20 patients were continuing treatment with XTX202 across the Phase 1/2 trial.

Preliminary Safety Data

Across all dose levels administered in the Phase 1/2 trial, 62 patients were evaluable for safety.

- No signs or symptoms of vascular leak syndrome were reported by investigators through the 4.0 mg/kg dose.

- XTX202 was generally well-tolerated. Treatment-related adverse events, or TRAE, were primarily Grade 1 or 2, and no patients discontinued treatment due to a TRAE. Higher grade TRAEs were primarily asymptomatic laboratory abnormalities, and no Grade 5 TRAEs were reported by investigators.

- The most common TRAEs (≥10% incidence) of any grade reported by investigators across all dose levels were: fatigue (19%, no grade ≥3); pyrexia (18%, no grade ≥3); chills (16%, 2% grade 3); and lymphocyte count decreased (15%, 8% grade 3-4). Grade 3 TRAEs reported in one patient each (2%) were: diarrhea/colitis; myalgia; hypoxia; lymphopenia; and aspartate transferase, or AST/alanine transaminase, or ALT, increased. Investigators reported two Grade 4 TRAEs of lymphocyte count decreased/lymphopenia, which were both transient (<3 days) and resolved without intervention, with both patients able to continue on treatment.

- Across all dose levels, only two patients (3%) had a dose reduction due to a TRAE, and only one dose-limiting toxicity was observed, which was a reversible and transient (<5 days) Grade 3 elevation of AST and ALT at the 1 mg/kg dose.

Preliminary Anti-Tumor Activity

Across all dose levels administered in the Phase 1/2 trial, 42 patients were evaluable for anti-tumor activity. Of these response-evaluable patients, 27 patients were treated at dose levels of 1.4 mg/kg or higher, including six patients treated at the 2.8 mg/kg dose level or higher.

- Data demonstrated evidence of a dose-dependent increase in disease control rate, or DCR. Among the 42 response-evaluable patients treated across all dose levels, investigators reported stable disease, or SD, of at least 9-weeks duration in 13 patients (31% DCR) across a range of solid tumors, including cold tumors: melanoma (n=3); RCC (n=2); NSCLC (n=2); CRC (n=2); and myoepithelial carcinoma, vaginal cancer, testicular cancer and squamous penile cancer (n=1 each). Among the six response-evaluable patients treated at the 2.8 mg/kg dose level or higher, investigators reported SD of at least 9-weeks duration in three patients (50% DCR).

- In addition, two patients were ongoing on treatment for more than one year as of the data cutoff date, including a treatment-refractory MSS CRC patient and an RCC patient, suggesting XTX202 was well-tolerated with repeated, long-term dosing in these patients.

Preliminary PK and PD Data

Preliminary PK analysis demonstrated limited XTX202 activation in peripheral circulation, including:

- Dose-proportional exposure for XTX202 with minimal levels of unmasked XTX202 detected in peripheral circulation that were consistent across dose levels.

- Approximately 15% activated XTX202 in the tumor based on an analysis of an on-treatment patient biopsy for a patient treated with XTX202 at the 2.8 mg/kg dose level as compared to <1% activated XTX202 in plasma across patients treated with XTX202 at the 2.8 mg/kg dose level for whom PK analysis was available. These data along with non-clinical pharmacology data suggest 2.8 mg/kg or higher monotherapy doses of XTX202 are approaching the optimal range to activate CD8+ effector T cells and NK cells in the tumor.

Consistent with IL-2 beta-gamma biology, preliminary PD analysis of four available on-treatment tumor samples showed an average increase >200% of CD8+ effector T cells in the tumor as compared to pre-treatment biopsies.

Additional Phase 2 Monotherapy Data Reported in March 2024

In March 2024, we announced additional data from our Phase 2 clinical trial evaluating XTX202 in patients with metastatic RCC or unresectable or metastatic melanoma. As of a data cutoff date of March 6, 2024:

- A total of 17 RCC patients and 20 melanoma patients were administered XTX202 in the Phase 2 trial in an outpatient setting at dose levels of 1.4 mg/kg Q3W or 4 mg/kg Q3W.

- In 26 patients evaluable for anti-tumor activity in the Phase 2 trial, SD continued to be the best response. Investigators reported SD of at least nine-weeks duration in seven RCC patients (70% disease control rate) and in nine melanoma patients (56% disease control rate). In addition, XTX202 continued to be generally well-tolerated with safety data consistent with previously reported results. We plan to present the full data set at a future medical meeting.

Together with previously reported data, we believe these additional data further validate our tumor-activated approach and support the broad potential for XTX202 as a combination therapy. We plan to explore strategic opportunities to continue to develop XTX202 in combination with other agents. As part of a strategic portfolio reprioritization announced in March 2024, we plan to discontinue further investment in XTX202 as a monotherapy.

Future Opportunities Leveraging Our Proprietary Platform for Tumor-Activated Bispecific Molecules and Immune Cell Engager Molecules (Including Tumor-Activated Cell Engagers and Tumor-Activated Effector-Enhanced Cell Engagers)

To date, we have prioritized efforts to develop XTX101 (anti-CTLA-4), XTX301 (IL-12) and XTX202 (IL-2) based on the therapeutic activity established in other clinical trials, while recognizing that the benefits of anti-CTLA-4, IL-12 and IL2 have been historically hampered by issues of significant toxicity, poor bioavailability and, in the case of cytokines like IL-12 and IL-2, a short half-life. By leveraging the insights and capabilities of our proprietary platform and building on our unique expertise in masking antibodies as well as cytokines, we are focusing our differentiated research platform on developing tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers).

Subject to obtaining sufficient additional capital, we plan to advance XTX501, our tumor-activated PD-1/IL-2 bispecific development candidate, into IND-enabling studies. We also plan to continue to make focused investments in our promising research-stage pipeline for additional tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers). We will continue to evaluate opportunities for better tolerated and more efficacious combination therapies, using product candidates from across our portfolio with other cancer therapies, to increase the potential for curative regimens in oncology.

Competition

We believe our novel and proprietary platform technology and masking approach represent a meaningful competitive advantage in seeking to develop novel and highly effective treatments for cancer. However, the biotechnology and biopharmaceutical industries are characterized by rapid evolution of technologies and sharp competition and emphasis on intellectual property. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions.

Some of our competitors, either independently or with strategic partners, have substantially greater financial, technical and human resources than we do. In addition, our competitors may be more successful than we are in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approval for treatments and achieving widespread market acceptance. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in resources being concentrated among a smaller number of our competitors. These companies also compete with

us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

In addition to competitors specifically targeting anti-CTLA-4, IL-12 and IL-2, we also face competition more broadly across the oncology market. The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy, biologic therapy, such as monoclonal and bispecific antibodies, immunotherapy, cell-based therapy and targeted therapy, or a combination of any such treatments. Beyond these treatments, we may also be subject to competition from additional modalities, including oncolytic viruses and cancer vaccines.

Our commercial opportunity could be substantially limited if our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient, or less expensive than products we may develop. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our products. In addition, our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of other drugs. The key competitive factors affecting the success of any products we may develop are likely to be their efficacy, safety, convenience, price and availability of reimbursement.

Tumor-Activated Anti-CTLA-4 Program

We are aware of a number of companies that are developing anti-CTLA-4 therapies as immunotherapies. With respect to XTX101, if approved, we may face competition from other anti-CTLA-4 based therapies. For example, Yervoy (ipilimumab), an anti-CTLA-4, is approved to treat melanoma, RCC, NSCLC and certain cancers of the large intestine, and Imjudo (tremelimumab) is approved as a combination therapy to treat unresectable hepatocellular carcinoma. In addition, we are aware that several companies have anti-CTLA-4 programs in development, including Adagene, Inc., Agenus Inc., AstraZeneca plc, BioAtla, Inc., CytomX Therapeutics, Inc., MacroGenics, Inc. and OncoC4, Inc.

Tumor Activated Cytokine Programs

With respect to XTX301, there are no approved IL-12 therapies currently on the market for the treatment of cancer; however, we are aware of several other companies that have modified IL-12 or intra-tumoral IL-12 delivery programs for the treatment of cancer in development, including Amunix Pharmaceuticals, Inc., AstraZeneca plc / Moderna, Inc., Cullinan Management Inc., Dragonfly Therapeutics, Inc., ImmunityBio, Inc., PDS Biotechnology Corporation, Philogen S.p.A., Sonnet BioTherapeutics, Werewolf Therapeutics, Inc., Xencor Inc. and Zymeworks Inc.

With respect to XTX202, if approved, it may face competition from other IL-2 based cancer therapies. For example, Proleukin (aldesleukin), a human recombinant interleukin-2 product, is approved and marketed for the treatment of metastatic RCC and melanoma. In addition, we are aware that a number of other companies have modified or low-dose IL-2 programs in development for the treatment of cancer, including Alkermes plc, Anaveon AG, Ascendis Pharma A/S, Asher Biotherapeutics, Inc., Aulos Bioscience, Inc., Bright Peak Therapeutics, Cue Biopharma, Inc., Cugene Inc., Cullinan Management Inc., Egle Therapeutics SAS, GI Innovation, Iovance Biotherapeutics, Inc., Kymab Ltd., Medicenna Therapeutics Corp., Medikine, Inc., Modulate Therapeutics, Inc., Neoleukin Therapeutics, Inc., Philogen S.p.A., Proviva Therapeutics, Inc., Roche AG, Sanofi, Selecxine, Synthekine, Inc., Trutino Biosciences Inc., Werewolf Therapeutics, Inc., XOMA Corporation and Zydus Cadila.

Intellectual Property

We strive to protect our proprietary technology, inventions, improvements, and platforms, including composition of matter for product candidates, methods of use and processes for their manufacture that we believe are important to our business, including by obtaining, maintaining, defending and enforcing patent and other intellectual property rights for the foregoing in the United States and in certain foreign jurisdictions. We also rely on trade secrets and confidentiality agreements to

protect our confidential information and know-how and other aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success depends in part on our ability to:

- obtain, maintain, enforce and defend patent and other intellectual property rights for our commercially important technology, inventions and improvements;
- preserve the confidentiality of our trade secrets and other confidential information;
- obtain and maintain licenses to use and exploit intellectual property owned or controlled by third parties;
- operate without infringing, misappropriating or otherwise violating any valid and enforceable patents and other intellectual property rights of third parties; and
- defend against challenges and assertions by third parties challenging the validity or enforceability of our intellectual property rights, or our rights in our intellectual property, or asserting that the operation of our business infringes, misappropriates or otherwise violates their intellectual property rights.

Patent portfolio

As of March 31, 2024, we own, co-own or exclusively license 18 patent application families related to our business, including four pending Patent Cooperation Treaty, or PCT, patent applications, 14 pending U.S. non-provisional applications, seven issued U.S. patents, 19 issued patents in Armenia, Azerbaijan, Belarus, China, India, Indonesia, Japan, Kazakhstan, Kyrgyzstan, Malaysia, Mexico, South Korea, Russia, Saudi Arabia, Taiwan, Tajikistan, and Turkmenistan and 169 pending foreign applications in Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Saudi Arabia, Singapore, South Africa and Taiwan. In addition, we own four U.S. provisional patent applications within the priority year. Our owned, co-owned or exclusively in-licensed patent applications cover various aspects of our programs and technology, including composition of matter and method of use as further described below. Any U.S. or foreign patents issued from national stage filings of our owned, co-owned, or exclusively in-licensed PCT patent applications and any U.S. patents issued from non-provisional applications we may file in connection with our provisional patent applications will have a statutory expiration date ranging between 2037 and 2045, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

Xilio's Platform for Tumor-Activated I-O Molecules

Our proprietary engineering platform technology enables tumor-activated I-O molecules that can effect tumor-activated immunotherapy while minimizing systemic toxicity. By masking biological agents such as cytokines, antibodies and multi-functional molecules, our platform technology can be used to decouple therapeutic effects from toxicity for treating different cancers. As of March 31, 2024, we own four patent families covering the platform in the cytokine space: a first patent family, including one pending U.S. patent application and corresponding foreign applications in Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, Indonesia, Israel, India, South Korea, Mexico, Malaysia, New Zealand, the Philippines, Saudi Arabia, Singapore and South Africa; and three additional patent families covering our multi-functional, including bispecific, platform technology in the cytokine space, include two pending U.S. and Taiwan applications, two pending PCT applications, and one provisional application within the priority year. We exclusively license two patent families relating to the platform technology and our cytokine and antibody programs. One of the two patent families is exclusively in-licensed in the oncology field from AskGene Pharma, Inc., or AskGene, and covers certain aspects of the platform technology for cytokines. These owned and exclusively licensed patent families will have a statutory expiration date ranging between 2039 and 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

In addition, we own two patent families covering various linker designs that are used or can be used in our technology, including one pending PCT application, and pending patent applications in the United States, Canada, Europe, Japan, South Korea and Taiwan.

Cytokine Programs

Our cytokine pipeline includes our clinical-stage, tumor-activated product candidates, XTX202 (IL-2) and XTX301 (IL-12), and our preclinical bispecific product candidate XTX501 (PD-1/IL-2).

- ***IL-12 Program.*** As of March 31, 2024, we own two patent families directed to different masked IL-12 constructs and sequences, including XTX301, with composition of matter and methods of use claims. These patent families include one issued U.S. patent, one pending U.S. application, and corresponding foreign applications in Australia, Brazil, Canada, China, Eurasia, Europe, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Philippines, Saudi Arabia, Singapore, South Africa and Taiwan. These patent families will have a statutory expiration date in 2039 and 2041, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

- ***IL-2 Program.*** As of March 31, 2024, we own two patent families relating to masked IL-2 cytokines, including XTX202, and seven families related to multi-functional, including bispecific, IL-2 cytokines, including XTX501, with composition of matter and methods of use claims. The masked IL-2 cytokine patent families include one pending U.S. application, five issued U.S. patents, one issued patent in India and corresponding foreign applications pending in Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, Indonesia, Israel, India, Japan, South Korea, Mexico, Malaysia, New Zealand, Philippines, Saudi Arabia, Singapore, South Africa and Taiwan. The multi-functional/bispecific IL-2 cytokine patent families include three pending PCT applications and four provisional applications within the priority year. The patent family exclusively in-licensed in the oncology field from AskGene also relates to the IL-2 program. These owned and exclusively in-licensed patent families will have a statutory expiration date ranging between 2039 and 2045, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

Antibody Program

As of March 31, 2024, we own, co-own or exclusively in-license three patent families relating to masked anti-CTLA-4 antibody constructs and sequences, including XTX101, with composition of matter and methods of use claims. A first patent family is exclusively in-licensed from WuXi Biologics (Shanghai) Co., Ltd. and directed to anti-CTLA-4 antibodies. This family includes two issued U.S. patents covering certain complementarity-determining regions and variable region sequences of anti-CTLA-4 antibodies, including XTX101. Corresponding foreign applications are issued in Armenia, Azerbaijan, Belarus, China, Indonesia, Japan, Kazakhstan, Kyrgyzstan, Malaysia, Mexico, Russia, South Korea, Saudi Arabia, Taiwan, Tajikistan, and Turkmenistan and pending in Australia, Brazil, Canada, China, European Patent Office, Hong Kong, India, Indonesia, Israel, Japan, South Korea, Mexico, New Zealand, Philippines, Singapore, South Africa and Taiwan. A second patent family is owned and directed to anti-CTLA-4 antibodies with modifications that improve antibody-dependent cellular cytotoxicity and includes one pending U.S. application. Corresponding foreign applications are pending in Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, India, Indonesia, Israel, Japan, South Korea, Mexico, Malaysia, New Zealand, Philippines, Saudi Arabia, Singapore, and South Africa. A third patent family is co-owned and directed to masked anti-CTLA-4 antibodies, which includes one pending U.S. application. Corresponding foreign applications are pending in Australia, Brazil, Canada, Eurasia, Europe, Hong Kong, India, Indonesia, Israel, Japan, South Korea, Mexico, Malaysia, New Zealand, Philippines, Saudi Arabia, Singapore, South Africa and Taiwan. In addition, we own two patent applications directed to combination therapies using masked or unmasked anti-CTLA-4 antibodies, including XTX101 and PD-1/PD-L1 antibodies. These families include two pending U.S. applications. Corresponding foreign applications are pending in Australia, Canada, Eurasia, Europe, Japan, South Africa and Taiwan. These owned, co-owned and licensed patent families will have a statutory expiration date ranging between 2037 and 2042, without taking into account any possible patent term adjustments or extensions and assuming payment of all appropriate maintenance, renewal, annuity and other governmental fees.

Trademark portfolio

As of March 15, 2024, we own two federal trademark registrations for XILIO and XILIO THERAPEUTICS (Class 42) in the United States and a pending federal trademark application for XILIO (Class 5) in the United States that has been approved and published for opposition.

Patent prosecution

A PCT patent application is not eligible to become an issued patent until, among other things, we file one or more national stage patent applications within 30 months, 31 months or 32 months of the PCT application's priority date, depending on the jurisdiction, in the countries in which we seek patent protection. If we do not timely file any national stage patent applications, we may lose our priority date with respect to our PCT patent application and any potential patent protection on the inventions disclosed in such PCT patent application. Moreover, a provisional patent application is not eligible to become an issued patent. A provisional patent application may serve as a priority filing for a non-provisional patent application, we file within 12 months of such provisional patent application. If we do not timely file non-provisional patent applications, we may lose our priority date with respect to our existing provisional patent applications and any potential patent protection on the inventions disclosed in our provisional patent applications.

While we intend to timely file additional provisional patent applications and national stage and non-provisional patent applications relating to our PCT patent applications, we cannot predict whether any of our patent applications will result in the issuance of patents. If we do not successfully obtain patent protection, or if the scope of the patent protection we or our licensors obtain with respect to our product candidates, platform or technology is not sufficiently broad, we will be unable to prevent others from using our technology or from developing or commercializing technology and products similar or identical to ours or other similar competing products and technologies. Our ability to stop third parties from making, using, selling, offering to sell, importing or otherwise commercializing any of our technology, inventions and improvements, either directly or indirectly, will depend in part on our success in obtaining, maintaining, defending and enforcing patent claims that cover our technology, inventions and improvements.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. The protection afforded by a patent varies on a product-by-product basis, from jurisdiction-to-jurisdiction, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of patent term adjustments and regulatory-related patent term extensions, the availability of legal remedies in a particular jurisdiction and the validity and enforceability of the patent. Moreover, patent laws and related enforcement in various jurisdictions outside of the United States are uncertain and may not protect our rights to the same extent as the laws of the United States. Changes in the patent laws and rules, whether by legislation, judicial decisions or regulatory interpretation, in the United States and other jurisdictions may diminish our ability to protect our inventions and obtain, maintain, defend and enforce our patent rights, and could therefore affect the value of our business.

The area of patent and other intellectual property rights in biotechnology is evolving and has many risks and uncertainties, and third parties may have blocking patents and other intellectual property that could be used to prevent us from commercializing our platforms and product candidates and practicing our proprietary technology. Our patent rights may be challenged, narrowed, circumvented, invalidated or ruled unenforceable, which could limit our ability to stop third parties from marketing and commercializing related platforms or product candidates or limit the term of patents that cover our platforms and product candidates. In addition, the rights granted under any issued patents may not provide us with protection or competitive advantages against third parties with similar technology, and third parties may independently develop similar technologies. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any competitive advantage provided by the patent. For this and other risks related to our proprietary technology, inventions, improvements, platforms and product candidates and intellectual property rights related to the foregoing, please see the section entitled "Risk Factors—Risks Related to our Intellectual Property."

Patent term extensions

The term of individual patents depends upon the laws of the jurisdictions in which they are obtained. In most jurisdictions in which we file, the patent term is 20 years from the earliest date of filing of the first non-provisional patent application to which the patent claims priority. However, the term of U.S. patents may be extended or adjusted for delays incurred due to compliance with FDA requirements or by delays encountered during prosecution that are caused by the U.S. Patent and Trademark Office, or the USPTO. For example, in the United States, a patent claiming a new biologic product, its method of use or its method of manufacture may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, for up to five years beyond the normal expiration date of the patent. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date in the United States. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent for which extension is sought. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. For more information on patent term extensions, see "Business—Government Regulation and Product Approval—Patent Term Restoration and Extension." In the future, if and when any product candidates we may develop receive FDA approval, we expect to apply for patent term extensions on issued patents covering those product candidates. Moreover, we intend to seek patent term adjustments and extensions for any of our issued patents in any jurisdiction where such adjustments and extensions are available. However, there is no guarantee that the applicable authorities, including the USPTO and FDA, will agree with our assessment of whether such adjustments and extensions should be granted, and even if granted, the length of such adjustments and extensions.

Trade secrets

In addition to patent protection, we also rely on trade secrets, know-how, unpatented technology and other proprietary information to strengthen our competitive position. We take steps to protect and preserve our trade secrets and other confidential and proprietary information and prevent the unauthorized disclosure of the foregoing, including by entering into non-disclosure and invention assignment agreements with parties who have access to our trade secrets or other confidential and proprietary information, such as employees, consultants, outside scientific collaborators, contract research and manufacturing organizations, sponsored researchers and other advisors, at the commencement of their employment, consulting or other relationships with us. In addition, we take other appropriate precautions, such as maintaining physical security of our premises and physical and electronic security of our information technology systems, to guard against any misappropriation or unauthorized disclosure of our trade secrets and other confidential and proprietary information by third parties.

Despite these efforts, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or other confidential or proprietary information. In addition, we cannot provide any assurances that all of the foregoing non-disclosure and invention assignment agreements have been duly executed, and any of the counterparties to such agreements may breach them and disclose our trade secrets and other confidential and proprietary information. Although we have confidence in the measures we take to protect and preserve our trade secrets and other confidential and proprietary information, they may be inadequate, our agreements or security measures may be breached, and we may not have adequate remedies for such breaches. Moreover, 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 our rights in any know-how or inventions arising out of such work. For more information, please see the section entitled "Risk Factors—Risks Related to our Intellectual Property."

License and Collaboration Agreements

Exclusive License Agreement with Gilead

In March 2024, Xilio Development entered into an exclusive license agreement with Gilead pursuant to which it granted Gilead an exclusive global license to develop and commercialize our clinical-stage product candidate XTX301, a tumor-activated IL-12, and specified other molecules directed to IL-12.

Xilio Development will be responsible for conducting clinical development for XTX301 in the ongoing Phase 1 clinical trial through an initial planned Phase 2 dose expansion. Following the delivery by Xilio Development of a specified clinical data package for XTX301 related to the Phase 1 clinical trial and planned Phase 2 clinical trial, Gilead can elect to transition responsibilities for the development and commercialization of XTX301 to Gilead, subject to the terms of the agreement and payment by Gilead of a $75.0 million transition fee.

Under the license agreement, we are eligible to receive approximately $43.5 million in upfront payments, including a cash payment of $30.0 million and an initial equity investment by Gilead of approximately $13.5 million of our common stock at a purchase price of $1.97 per share. The initial equity investment closed on March 28, 2024, and the $30.0 million upfront cash payment is payable by Gilead within a specified time period promptly following signing of the license agreement. We are eligible to receive up to $604.0 million in additional contingent payments, which include (i) the proceeds from up to three additional private placements of common stock, (ii) the $75.0 million transition fee and (iii) specified development, regulatory and sales-based milestones. Prior to the potential transition fee, up to $29.0 million of the total contingent payments are related to the potential additional private placements of common stock and a near-term development milestone. In addition, we are eligible to receive tiered royalties ranging from high single digits to mid-teens on annual global net product sales.

Unless earlier terminated in accordance with its terms, the license agreement will expire upon expiration of the last royalty term for the last licensed product. Gilead may terminate the license agreement for convenience upon specified time periods. If Gilead elects not to transition responsibilities for development and commercialization of the licensed products and pay the transition fee, then the license agreement will automatically terminate. Either party may terminate the license agreement for the other party's uncured material breach or insolvency. Subject to the terms of the license agreement, effective upon termination of the license agreement, the licenses to Gilead terminate and Xilio Development is entitled to continue to exploit the licensed products.

During the term of the license agreement, Xilio Development and its affiliates have agreed not to directly or indirectly conduct specified development, manufacturing or commercialization activities with respect to any molecule that contains, comprises or incorporates IL-12, except for the performance of Xilio Development's activities under and in accordance with the license agreement.

In connection with the execution of the license agreement, on March 27, 2024, we entered into a stock purchase agreement with Gilead. In addition to the initial equity investment by Gilead of approximately $13.5 million of our common stock, through March 27, 2025, we may, at our election and subject to the terms and conditions of the stock purchase agreement, cause Gilead to purchase up to approximately $11.5 million of additional shares of common stock (including, at Gilead's sole election, prefunded warrants in lieu of shares of common stock) in up to three additional private placements at a predetermined price per share specified therein, at all times subject to Gilead not being deemed the beneficial owner of greater than 19.9% of our common stock upon the closing of the applicable additional private placement with Gilead. If Gilead elects to purchase prefunded warrants, each prefunded warrant will have an exercise price of $0.0001 per share of common stock, be immediately exercisable and remain exercisable until exercised in full. Gilead may not exercise its prefunded warrants to the extent that it would beneficially own more than 19.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. Any prefunded warrants that may be issued to Gilead in an additional private placement with Gilead will be in substantially the same form as the prefunded warrants issued to investors in the March 2024 private placement.

In-License Agreements

We are a party to license agreements under which we license patents, patent applications and other intellectual property from third parties. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future. We consider the following license agreements to be material to our business.

Cross-License Agreement with AskGene

In December 2020, Xilio Development entered into a cross-license agreement with AskGene Pharma, Inc., or AskGene, pursuant to which AskGene granted us certain exclusive licenses for AskGene patent rights related to non-antigen binding IL-2 products in the field of oncology and certain co-exclusive licenses for AskGene patent rights related to antigen binding IL-2 products in all fields. Under the agreement, AskGene retains rights to the AskGene patent rights in Singapore, Thailand, Malaysia, Vietnam, the People's Republic of China, Taiwan, Macau, Hong Kong, Korea and India, which we refer to as the AskGene territory, and granted licenses to us for the AskGene patent rights worldwide, excluding the AskGene territory, which we refer to as the Xilio territory.

Under the agreement, we paid AskGene an upfront payment of $6.0 million, and for any licensed IL-2 product, we are obligated to pay AskGene up to $13.0 million in the aggregate upon the achievement of specified regulatory milestones. In addition, subject to specified conditions, for any IL-2 licensed product, we are obligated to pay AskGene percentage royalties in the mid-single digits on aggregate annual net sales of IL-2 licensed products in the Xilio territory during the applicable royalty term.

In addition, we granted a non-exclusive, royalty-free, non-transferable, worldwide license to AskGene for specified Xilio patent rights related to non-antigen binding IL-2 products in the field of immunology and for specified Xilio patent rights related to antigen binding IL-2 products in all fields. Subject to the terms of the agreement and during the time period specified, we also granted AskGene an option to obtain a license in the AskGene territory to develop and commercialize our IL-2 licensed products. If AskGene exercises its option to develop and commercialize our IL-2 licensed products in the AskGene territory, then the parties will negotiate and enter into a license agreement for AskGene's exclusive development and commercialization of such products in the AskGene territory, and AskGene would be obligated to pay us percentage royalties in the mid-single digits on aggregate annual net sales of such licensed products in the AskGene territory.

During the term of the agreement, AskGene has agreed not to exploit any non-antigen binding IL-2 product comprised of specified masking technology in the field of oncology in the Xilio territory.

Subject to the terms of the agreement, each party's obligation to make royalty payments is subject to adjustment in specified circumstances and extends with respect to a licensed product in a country upon the first commercial sale of such licensed product in such country and ending upon the latest of (i) the expiration of the last valid claim of any licensed patent rights in such country that cover such licensed product, (ii) the expiration of regulatory exclusivity, if any, for such licensed product in such country, and (iii) for a specified time period following first commercial sale of such licensed product in such country.

The agreement continues on a product-by-product and country-by-country basis until the expiration of the applicable royalty term in each country, at which time the agreement expires with respect to such product in such country, and the licensed party receives a perpetual, irrevocable, fully-paid and royalty-free license to the licensed patent rights in such country. Either party has the right to terminate the agreement if the other party materially breaches the agreement and fails to cure such breach within specified cure periods or in the event the other party becomes insolvent or files for bankruptcy. Upon any termination, other than the expiration of the agreement with respect to a particular product in a particular country, the licenses granted by each party will terminate and neither party will have the right to practice the other party's patent rights.

Amended and Restated Exclusive License Agreement with City of Hope

In August 2016, Xilio Development entered into an amended and restated exclusive license agreement with City of Hope pursuant to which City of Hope granted us an exclusive worldwide license to specified patent rights related to our anti-CTLA-4 monoclonal antibody program.

For the first three licensed products or licensed services to achieve specified development and regulatory milestones, we are obligated to pay City of Hope up to $10.3 million in the aggregate per licensed product or licensed service. Subject to specified conditions, we are obligated to pay City of Hope tiered royalties in the low single digits on aggregate annual net

sales of licensed products or licensed services on a country-by-country basis until the expiration of the last-to-expire patent or patent application licensed from City of Hope covering the applicable licensed product or licensed service in such country. We are also obligated to pay City of Hope a portion of any consideration we receive for the grant of sublicenses under the agreement ranging from a low to mid double-digit percentage of such consideration, subject to specified conditions under that agreement at the time that we grant any such sublicense. In addition, we paid $0.5 million to City of Hope in connection with the closing of our initial public offering.

The agreement continues on a country-by-country basis until the expiration of the last to expire licensed patent right in such country. We have the right to terminate the agreement for convenience at any time on 30 days' prior written notice to City of Hope. Either party has the right to terminate the agreement if the other party materially breaches the agreement and fails to cure such breach within specified cure periods. City of Hope may terminate the agreement if we or any of our affiliates or sublicensees bring specified patent challenges with respect to the licensed patents against City of Hope or if we assist others in bringing a patent challenge against City of Hope. However, instead of terminating as a result of a patent challenge, City of Hope may elect to increase our payment obligations by a specified percentage amount retroactive to the commencement of such patent challenge.

CTLA-4 Monoclonal Antibody License Agreement with WuXi Biologics

In September 2016, we entered into a license agreement with WuXi Biologics (Hong Kong) Limited, or WuXi Biologics, as amended in December 2017, pursuant to which WuXi Biologics granted us an exclusive worldwide license, including the rights to grant sublicenses through multiple tiers, to specified monoclonal antibodies and patent rights and know-how controlled by WuXi Biologics, including certain patent rights related to our anti-CTLA-4 mAb program.

For each product that incorporates a licensed antibody that has been modified using the rights licensed under the agreement, we are obligated to pay WuXi Biologics up to approximately $25.8 million in the aggregate for specified development and regulatory milestones. In addition, subject to specified conditions, we are obligated to pay WuXi Biologics tiered royalties in the low to mid-single digits on aggregate annual worldwide net sales of licensed products during the applicable royalty term and subject to early expiration or adjustment in specified circumstances. Our obligation to make royalty payments extends with respect to a licensed product in a country until the later of the expiration of the last-to-expire patent or patent application licensed from WuXi Biologics covering the applicable licensed product in such country or for a specified time period following the first commercial sale of such licensed product. Subject to specified conditions under the agreement, we also have certain obligations to contract with WuXi Biologics for specified services related to the development or manufacture of licensed products.

Unless terminated earlier in accordance with its terms, the agreement will continue until the expiration of the last to expire royalty term for a licensed product. We have the right to terminate the agreement for convenience at any time upon at least 90 days' prior written notice to WuXi Biologics. Either party may terminate the agreement for the other party's uncured material breach. Other than following our termination for convenience or termination by WuXi Biologics for our material breach, upon the expiration of the applicable royalty term for a licensed product in a country, we will receive a paid-up and royalty free license to exploit such licensed product in such country.

Manufacturing

We currently contract with a third-party contract development and manufacturing organization, or CDMO, to manufacture our product candidates for preclinical studies and our ongoing clinical trials, and we intend to continue to do so with one or more third parties for future preclinical studies and clinical trials. We do not own or operate manufacturing facilities for the production of our product candidates, and we currently do not have plans to build our own clinical or commercial scale manufacturing capabilities. To date, our CDMO has met our production requirements. Our CDMO is under contract to provide clinical material meeting FDA current good manufacturing practice, or cGMP, requirements and in sufficient quantities to meet anticipated clinical-trial demands. To meet our projected needs for commercial manufacturing, our current third-party manufacturer will need to increase its scale of production, or we will need to secure one or more alternate suppliers. We believe that there are alternate manufacturers that could satisfy our anticipated clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such manufacturers, if necessary, would not result in significant delay or material additional costs.

Although we expect to rely on one or more third-party contract manufacturers for the production of our current and future product candidates, we have personnel with extensive technical, manufacturing, analytical and quality experience in biotherapeutic protein manufacturing to oversee our contract manufacturer relationships. In collaboration with our third-party manufacturer, we have manufactured cGMP clinical supply for our clinical trials for our tumor-activated, clinical-stage product candidates, XTX101 (anti-CTLA-4), XTX301 (IL-12), and XTX202 (IL-2). As we scale clinical and develop commercial manufacturing capability for each of our product candidates, we intend to develop the network of contract manufacturing sites operated by our CDMO to include EU- or U.S.-based sites.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and foreign jurisdictions, including the European Union, or EU, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, post-approval monitoring and reporting, and import and export of pharmaceutical products. 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.

Review and Approval of Drugs and Biologics in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Biological products, or biologics, are licensed for marketing under the Public Health Service Act, or PHSA, and subject to regulation under the FDCA and related regulations. A company, institution, or organization that takes responsibility for the initiation and management of a clinical development program for such products is generally referred to as a sponsor. A sponsor seeking approval to market and distribute a new drug or biological product in the United States must typically secure the following:

- completion of preclinical laboratory tests in compliance with the FDA's good laboratory practice, or GLP, regulations and standards;
- design of a clinical protocol and submission to the FDA of an investigational new drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug product, and with respect to biologics, the purity, potency and safety of such drug product, for each proposed indication;
- submission to the FDA of a new drug application, or NDA, for a drug candidate product and a biologics license application, or BLA, for a biological product requesting marketing for one or more proposed indications;
- review of the request for approval by an FDA advisory committee, where appropriate or if applicable;
- completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current good manufacturing practices, or cGMPs, to assure the product's identity, strength, quality and purity;
- completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA or BLA; and

- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before a sponsor begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured substance or active pharmaceutical ingredient and the formulated product, as well as *in vitro* and animal studies to assess the safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. These studies are typically referred to as IND-enabling studies. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations and standards and the U.S. Department of Agriculture's Animal Welfare Act, if applicable. Some long-term preclinical testing, such as animal tests of reproductive AEs and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is a request for FDA authorization to administer an investigational product candidate to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biologic that is not the subject of an approved NDA or BLA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. 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. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects and patients will be exposed to unreasonable health risks or whether there are any issues surrounding chemistry, manufacturing and controls, or CMC, for the proposed product. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. The FDA's primary objectives in reviewing an IND are to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or CMC. 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 a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval in the United States. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, or IEC, and seeking and receiving informed consent from subjects. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, 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.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial 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 trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to trial subjects. An IRB must operate in compliance with FDA regulations. 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 product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring committee, or DMC. This group provides authorization for whether a trial may move forward at designated check points based on access that only the group maintains to available data from the trial. 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 or for other reasons, including evolving business objectives and/or competitive climate.

Human Clinical Studies in Support of an NDA or BLA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written trial protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

The clinical investigation of an investigational drug or biological product is generally divided into four phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The four phases of an investigation are as follows:

- Phase 1. Phase 1 studies include the initial introduction of an investigational new drug or biological product into humans. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational drug or biological product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.

- Phase 2. Phase 2 includes the controlled clinical trials conducted to preliminarily or further evaluate the effectiveness of the investigational drug or biological product for a particular indication(s) in patients with the disease or condition under trial, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug or biological product. Phase 2 trials are typically well-controlled, closely monitored, and conducted in a limited patient population.

- Phase 3. Phase 3 trials are generally controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug or biological product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug or biological product, and to provide an adequate basis for product approval.

- Phase 4. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 1 or Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans. In January 2024, the FDA issued draft guidance setting out its policies for the collection of race and ethnicity data in clinical trials.

In March 2022, the FDA released a final guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology biological product development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to biological product development and reduce developmental costs and time.

In June 2023, the FDA issued draft guidance with updated recommendations for GCPs aimed at modernizing the design and conduct of clinical trials. The updates are intended to help pave the way for more efficient clinical trials to facilitate the development of medical products. The draft guidance is adopted from the International Council for Harmonisation's recently updated E6(R3) draft guideline that was developed to enable the incorporation of rapidly developing technological and methodological innovations into the clinical trial enterprise. In addition, the FDA issued draft guidance outlining recommendations for the implementation of decentralized clinical trials.

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

Sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017. Although the FDA has historically not enforced these reporting requirements due to the long delay by the Department of Health and Human Services, or HHS, in issuing final implementing regulations, the FDA has issued several pre-notices for voluntary corrective action and several notices of non-compliance during the past two years. While these notices of non-compliance did not result in civil monetary penalties, the failure to submit clinical trial information to clinicaltrials.gov is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues.

Interactions with FDA During the Clinical Development Program

Following the clearance of an IND and the commencement of clinical trials, the sponsor will continue to have interactions with the FDA. An annual report on the progress of the study must be submitted to the FDA and more frequently if serious AEs 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 product; and any clinically important increase in the occurrence 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In addition, sponsors are given opportunities to meet with the FDA at certain points in the clinical development program. Specifically, sponsors may meet with the FDA prior to the submission of an IND, or Pre-IND meeting, at the end of Phase 1 clinical trial, or EOP1 meeting, at the end of Phase 2 clinical trial, or EOP2 meeting, and before an NDA or BLA is submitted, or Pre-NDA or Pre-BLA meeting. Meetings at other times may also be requested. There are five types of meetings that occur between sponsors and the FDA. Type A meetings are those that are necessary for an otherwise stalled product development program to proceed or to address an important safety issue. Type B meetings include pre-IND and pre-NDA/pre-BLA meetings, as well as end of phase meetings such as EOP2 meetings. A Type C meeting is any meeting other than a Type A or Type B meeting regarding the development and review of a product, including, for example, meetings to facilitate early consultations on the use of a biomarker as a new surrogate endpoint that has never been previously used as the primary basis for product approval in the proposed context of use. A Type D meeting is focused on a narrow set of issues and does not require input from more than three disciplines or divisions. Finally, INTERACT meetings are intended for novel products and development programs that present unique challenges in the early development of an investigational product.

The FDA has indicated that its responses, as conveyed in meeting minutes and advice letters, only constitute mere recommendations and/or advice made to a sponsor and, as such, sponsors are not bound by such recommendations and/or advice. Nonetheless, from a practical perspective, a sponsor's failure to follow the FDA's recommendations for design of a clinical program may put the program at significant risk of failure. In September 2023, the FDA issued draft guidance outlining the terms of such meetings in more detail.

Expanded Access

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

There is no requirement for a sponsor to provide expanded access to an investigational product. However, if a sponsor decides to make its investigational product available for expanded access, the FDA reviews requests for expanded access and determines if treatment may proceed. Expanded access may be appropriate when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with initiation, conduct or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

Sponsors of one or more investigational products for the treatment of a serious disease(s) or condition(s) must make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 trial; or 15 days after the investigational drug or biologic receives designation as a Breakthrough Therapy, fast track product or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides an additional mechanism for patients with a life-threatening condition who have exhausted approved treatments and are unable to participate in clinical trials to access certain investigational products that have completed a Phase 1 trial, are the subject of an active IND and are undergoing investigation for FDA approval. Unlike the expanded access framework described above, the Right to Try Pathway does not require FDA to review or approve requests for use of the investigational product. There is no obligation for a manufacturer to make its investigational products available to eligible patients under the Right to Try Act.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, an application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time. In May 2023, the FDA issued new draft guidance that further describes the pediatric study requirements under PREA.

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

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

In 2017, with the passage of the FDA Reauthorization Act of 2017, or FDARA, Congress established new requirements to govern certain molecularly targeted cancer indications. Section 505B of the FDCA, as amended by FDARA, requires that any original NDA or BLA submitted on or after August 18, 2020, for a new active ingredient, must contain reports on the molecularly targeted pediatric cancer investigation, unless the requirement is waived or deferred, if the drug that is the subject of the application is: (i) intended for the treatment of an adult cancer, and (ii) directed at a molecular target that the Secretary of HHS determines to be substantially relevant to the growth or progression of a pediatric cancer in accordance with FDA guidance. The FDA maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Submission and Review of an NDA or BLA by the FDA

In order to obtain approval to market a drug or biological product in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the proposed drug product for the proposed indication, and the safety, purity and potency of the biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product and the safety, purity and potency of the biological product to the satisfaction of the FDA.

The application is the vehicle through which sponsors formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new product candidate must be the subject of an approved

NDA or BLA before it may be commercialized in the United States. Under federal law, the submission of most applications is subject to an application user fee. The sponsor of an approved application is also subject to an annual program fee. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses. If an application is withdrawn prior to the FDA acceptance for filing, 75% of these fees may be refunded to the sponsor. If an application is withdrawn after filing, a lower portion of these fees may be refunded in certain circumstances. Currently, the fee required for the submission and review of an application for federal fiscal year 2024 is approximately $4.05 million, and the sponsor of an approved application is also subject to an annual program fee, currently more than $416,000 for federal fiscal year 2024.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. The FDA's regulations state that an application "shall not be considered as filed until all pertinent information and data have been received" by the FDA. In the event that the FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the applicant. Typically, an RTF will be based on administrative incompleteness, such as clear omission of information or sections of required information; scientific incompleteness, such as omission of critical data, information or analyses needed to evaluate safety and efficacy or provide adequate directions for use; or inadequate content, presentation, or organization of information such that substantive and meaningful review is precluded. The FDA may request additional information rather than accept an application 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. The FDA has agreed to specified performance goals in the review process of NDAs and BLAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission.

In connection with its review of an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA or BLA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted to the FDA. With the passage of FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process.

In addition, as a condition of approval, the FDA may require a sponsor to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential AEs, and whether the product is a new molecular entity. Under FDARA, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on an NDA or BLA

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term "substantial evidence" is defined under the FDCA as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof." The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. In December 2019, the FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. Although the FDA has not yet finalized that guidance, it did issue additional draft guidance in September 2023 that outlines considerations for relying on confirmatory evidence in lieu of a second clinical study.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either an approval letter or a Complete Response Letter, or CRL. To issue an approval letter, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six-month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications described in the FDA-approved labeling. Depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a 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-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs and biologics within 30 days of approval of such products. To date, CRLs are not publicly available documents.

Fast Track, Breakthrough Therapy and Priority Review Designations

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 include fast track designation, Breakthrough Therapy designation and priority review designation. None of these expedited programs changes the standards for approval but they may help expedite the development or approval process governing product candidates.

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

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

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

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on 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. 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, 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 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 product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of phase 4 or post-approval 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 initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

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

In March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The agency indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. While this guidance is currently only in draft form and will ultimately not be legally binding even when finalized, sponsors typically observe the FDA's guidance closely to ensure that their investigational products qualify for accelerated approval.

Post-Approval Regulation

Drugs and biologics 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 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, 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 AEs 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, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, 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. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. In September 2021, the FDA published final regulations that describe the types of evidence the FDA will consider in determining the intended use of a drug or biologic.

It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Moreover, with the passage of the Pre-Approval Information Exchange Act in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance, but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products. In addition, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws. The Prescription Drug Marketing Act, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. In November 2013, the federal Drug Supply Chain Security Act, or DSCSA, became effective in the United States, mandating an industry-wide, electronic, interoperable system to trace prescription drugs through the pharmaceutical distribution supply chain with a ten-year phase-in process. Manufacturers were required by November 2023 to have such systems and processes in place but, in August 2023, the FDA set a one-year period in which it would exercise its enforcement discretion with respect to these requirements.

Biosimilars and Regulatory Exclusivity

The 2010 Patient Protection and Affordable Care Act, or ACA, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, the FDA has approved a number of biosimilar products and several interchangeable biosimilar products. The FDA has also issued numerous guidance documents outlining its approach to reviewing and licensing biosimilars and interchangeable biosimilars under the PHSA.

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

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

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA or BLA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the Prescription Drug User Fee Act, or PDUFA, goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. If a drug or biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a company with orphan drug exclusivity is not able to meet market demand and in cases where a subsequent product with the same drug or biologic for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a subsequent product to show clinical superiority in order to break the previous product's orphan drug exclusivity applies to drugs and biologics that

received orphan drug designation before enactment of FDARA in 2017 but have not yet been approved or licensed by FDA.

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

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of existing regulatory exclusivity. For drug products, the six-month exclusivity may be attached to the term of any existing patent or regulatory exclusivity. For biologic products, the six-month period may be attached to any existing regulatory exclusivities but not to any patent terms. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of non-patent exclusivity for drugs and biologics, or patent protection that covers a drug 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.

Patent Term Restoration and Extension

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

Pharmaceutical Coverage, Pricing and Reimbursement

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

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

Healthcare Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements.

Restrictions under applicable federal and state health care laws and regulations, include the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid; the federal civil and criminal false claims laws, false statements, and civil monetary penalties laws, including the civil False Claims Act, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; the Health Insurance Portability and Accountability Act, or HIPAA, which, in addition to privacy protections applicable to healthcare providers and other entities, prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs; analogous state laws and regulations, including state anti-kickback and false claims laws; and the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these federal transparency reporting obligations will extend to include transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives. In addition, HIPAA as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, among other things, imposes limitations on certain covered healthcare providers, health plans, and healthcare clearinghouses and their respective business associates and their covered subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures or restrict financial interactions between pharmaceutical companies and healthcare providers. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. In particular, numerous federal and state laws and regulations, including state data breach notification laws, state health

information privacy laws, and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of health-related and other personal information.

In addition, we may be subject to laws and regulations prohibiting bribery and corruption such as the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment as well as federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Violation of the laws described above or any other governmental laws and regulations may result in significant penalties, including civil, criminal, and administrative penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment, and additional reporting requirements and oversight if a manufacturer becomes subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly.

Similar healthcare laws and regulations exist in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of personal information

Health Care Reform in the United States and Potential Changes to Health Care Laws

Sales of any biopharmaceutical products, if and when approved by the FDA or analogous authorities outside the United States, will depend in significant part on the availability of third-party coverage and adequate reimbursement for the products.

Health care reform has been a significant trend in the U.S. health care industry and elsewhere. In particular, government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services. Under the former Trump administration, there were efforts to repeal or modify prior health care reform legislation and regulation and also to implement new health care reform measures, including measures related to payment for drugs under government health care programs. However, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate'' was repealed by Congress. Thus, the ACA will remain in effect in its current form. The nature and scope of health care reform in the new Biden administration remains uncertain but early actions including additional health care reform, its expressed intent to pursue certain policy initiatives to reduce drug prices, as well as challenges to actions taken under the Trump administration have been taken and are likely to continue.

There has been heightened governmental scrutiny in recent years over the manner in which manufacturers set prices for their marketed products, which has resulted in proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing and reform government program reimbursement methodologies for pharmaceutical and biologic products. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or the IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B, to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and

beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the Pharmaceutical Research and Manufacturers of America, or PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results.

In addition, the HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program to import certain prescription drugs from Canada into the United States. That regulation was challenged in a lawsuit by PhRMA but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue the HHS. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2024, the FDA approved Florida's plan for Canadian drug importation.

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, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

We 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. We expect that additional federal and state health care reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for health care products and services.

Data Privacy Regulation

U.S. Privacy Law

There are multiple privacy and data security laws that may impact our business activities in the United States and in other countries where we may conduct trials or do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, for example, under HIPAA, the U.S. Department of Health and Human Services has issued regulations to protect the privacy and security of protected health information used or disclosed by specific covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Federal Policy for the Protection of Human Subjects, also known as the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number

of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. Moreover, new laws and regulations governing privacy and security may be adopted in the future as well.

There have been several developments in recent years with respect to U.S. state data privacy laws. In 2018, California passed into law the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In addition, the California Privacy Rights Act, or the CPRA, went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created the California Privacy Protection Agency, a new enforcement agency whose sole responsibility is to enforce the CPRA, which will further increase compliance risk.

In addition to California, 11 other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data, which includes health data in some cases. Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2024 legislative sessions that will go into effect in 2025 and beyond. Other states will be considering similar laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, the State of Washington passed the My Health My Data Act in 2023 which specifically regulated health information that is not otherwise regulated by the HIPAA rules, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data, and more states are considering such legislation in 2024, including New York and New Jersey. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

General data protection regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or EEA, and the processing of personal data that takes place in the EEA, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from

violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Following the Court of Justice of the European Union, or the CJEU, decision, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022, and the European Commission, or EC, adopted the adequacy decision in July 2023. The adequacy decision permits U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the United States. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business.

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, commonly referred to as Brexit. As with other issues related to Brexit, there are open questions about how personal data will be protected in the United Kingdom and whether personal information can transfer from the EU to the United Kingdom. Following the withdrawal of the United Kingdom from the EU, the United Kingdom Data Protection Act 2018 applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR. While the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is unclear whether transfer of data from the EEA to the United Kingdom will remain lawful under the GDPR, although these transfers currently are permitted by an adequacy decision from the EC. The United Kingdom government has already determined that it considers all EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the United Kingdom as being "essentially adequate" for purposes of data transfer from the EU to the United Kingdom, although this decision may be re-evaluated in the future. The United Kingdom and the United States have also agreed to a U.S.-UK "Data Bridge," which functions similarly to the EU-U.S. Data Privacy Framework and provides an additional legal mechanism for companies to transfer data from the United Kingdom to the United States. In addition to the United Kingdom, Switzerland is also in the process of approving an adequacy decision in relation to the Swiss-U.S. Data Privacy Framework (which would function similarly to the EU-U.S. Data Privacy Framework and the U.S.-UK Data Bridge in relation to data transfers from Switzerland to the United States). Any changes or updates to these developments have the potential to impact our business.

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

Employees and Human Capital Resources

As of March 25, 2024, we had 73 full-time employees, including 32 employees with M.D., Pharm.D. or Ph.D. degrees. Of these full-time employees, 53 were engaged in research and development activities and 20 were engaged in general and administrative activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good. In March 2024, as part of a strategic portfolio reprioritization, we announced plans to undergo a workforce reduction to further reduce our expenses and streamline our operations, including a reduction in headcount of 15 employees, representing approximately 21% of our workforce prior to the workforce reduction. We anticipate that the workforce reduction will be substantially completed in the first half of 2024.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and developing our existing and additional employees. We are committed to diversity, equity and inclusion across all aspects of our organization, including in our recruitment, advancement and development practices. Each year, we review employee demographic information to evaluate our diversity efforts across all functions and levels of the company. We conduct

annual performance and development reviews for each of our employees to discuss the individual's strengths and development opportunities, career development goals and performance goals. We also regularly survey employees to assess employee engagement and satisfaction. In addition, each regular full-time employee is provided an allowance and time to attend appropriate job-related trainings and other professional development courses, seminars, meetings, and similar sessions.

The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards. We value our employees and regularly benchmark total rewards we provide, such as short- and long-term compensation, 401(k) contributions, tuition reimbursement, health, welfare and quality of life benefits, paid time off and personal leave, against our industry peers to ensure we remain competitive and attractive to potential new hires.

Corporate Information

We are a Delaware corporation that was incorporated on June 18, 2020 under the name Xilio Therapeutics, Inc. We maintain a website at the following address: www.xiliotx.com. The information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or in any other report or document we have filed or may file with the Securities and Exchange Commission, or SEC, and any reference to our website address is intended to be an inactive textual reference only.

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Securities Exchange Act of 1934, as amended, or the Exchange Act. These include our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. We make this information available on our website (free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. In addition, we routinely post on the "Investors & Media" page of our website investor and scientific presentations, SEC filings, press releases, public conference calls and webcasts and other statements about our business and results of operations, some of which may contain information that may be deemed material to investors. Accordingly, investors should monitor these portions of our website, in addition to following our press releases, SEC filings, public conference calls and webcasts, as well as current or future social media channels (including LinkedIn). This list of channels may be updated from time to time on our investor relations website and may include other social media channels than the one described above. The contents of our website or these channels, or any other website that may be accessed from our website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at the following address: http://www.sec.gov.

Item 1A. Risk Factors

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and our other public filings. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Risks Related to Our Limited Operating History, Financial Position and Capital Requirements

Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern. If we are unable to raise sufficient additional capital in the near term, we may in the future need to implement additional cost reduction strategies, which could include delaying, limiting, reducing or eliminating both internal and external costs related to our operations and research and development programs.

As of December 31, 2023, we had cash and cash equivalents of $44.7 million. Based on our current operating plans, we anticipate that our cash and cash equivalents as of December 31, 2023, together with (i) the $30.0 million upfront payment under the license agreement with Gilead Sciences, Inc., or Gilead, (ii) the approximately $13.5 million in proceeds from the initial private placement with Gilead, which closed on March 28, 2024, and (iii) the approximately $11.3 million in gross proceeds from our private placement, which is expected to close on April 2, 2024 (subject to customary closing conditions), and after giving effect to (a) one-time costs and anticipated future cost savings associated with our strategic portfolio reprioritization and workforce reduction announced in March 2024 and (b) the repayment in the first quarter of 2024 of the outstanding loan balance under our loan and security agreement with Pacific Western Bank, will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2025. However, since these amounts may not be sufficient to fund our operations for at least twelve months from the date of issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K, the report from our independent registered public accounting firm for the year ended December 31, 2023 includes an explanatory paragraph stating that our losses from operations and required additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary from what we expect, and we may not achieve the expected savings that we anticipate as a result of our recent portfolio reprioritization and workforce reduction. Our management has developed plans to continue to fund our operations, which primarily consist of raising additional capital through one or more of the following: additional equity or debt financings; additional collaborations, partnerships or licensing transactions; or other sources. However, there can be no assurance that we will be able to complete any such transaction on acceptable terms or otherwise, and we may be unable to obtain sufficient additional capital in the near term. If we are not able to secure sufficient additional capital, we may in the future need to implement additional cost reduction strategies, which could include delaying, limiting, further reducing or eliminating both internal and external costs related to our operations and research and development programs. For example, in March 2024, we announced that we would discontinue further investment in the development of XTX202 as a monotherapy and would undergo a workforce reduction to further reduce our expenses and streamline our operations, which workforce reduction we estimate will be substantially completed in the first half of 2024. Furthermore, our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources earlier than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may exhaust our available capital sooner than planned. Please see Note 1 to our consolidated financial statements appearing elsewhere in our Annual Report on Form 10-K for additional information on our assessment.

We expect to continue to incur operating losses in connection with our ongoing research and development activities, particularly as we advance our product candidates through clinical trials, maintain the infrastructure necessary to support these activities and incur costs associated with operating as a public company. Our revenue, if any, will be derived from sales of products that we do not expect to be commercially available for a number of years, if at all. If we obtain marketing approval for any current or future product candidates that we develop, we expect to incur significant commercialization

expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval and could be substantial.

Our future capital requirements, both short-term and long-term, will depend on many factors, including:

- our ability to implement and maintain further cost reduction strategies, as well as the timing of such cost reductions;
- the scope, progress, results and costs of research and development for our current and future product candidates, including our ongoing and planned clinical trials for our clinical-stage product candidates;
- the scope, prioritization and number of our research and development programs;
- the progress of the development efforts of parties with whom we have entered or may in the future enter into collaboration agreements;
- the timing and amount of payments we may receive or are obligated to pay under our collaboration agreements and license agreements;
- the scope, costs, timing and outcome of regulatory review of our product candidates;
- the costs of expanding manufacturing capacity through third-party manufacturers and securing manufacturing materials for use in preclinical studies, clinical trials and, for any product candidates for which we receive regulatory approval, if any, use as commercial supply;
- the costs and timing of future commercialization activities for any of our product candidates for which we receive regulatory approval;
- the amount and timing of revenue, if any, received from commercial sales of any product candidates for which we receive regulatory approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims;
- the extent to which we may acquire or in-license other products, product candidates, technologies or intellectual property, as well as the terms of any such arrangements;
- our ability to maintain our current collaborations, including our clinical collaboration to further develop XTX101, our tumor-activated, Fc-enhanced anti-CTLA-4, in combination with atezolizumab, including the cost-sharing arrangements of such collaboration, and our partnership with Gilead for XTX301;
- the timing and amount of milestones, equity investments and other contingent payments under our partnership with Gilead for XTX301;
- the costs of maintaining our operations and continuing to operate as a public company; and
- whether we are able to overcome the substantial doubt about our ability to continue as a going concern.

We will require additional capital to sustain our operations. We currently do not have any committed external sources of funds and adequate additional capital may not be available to us on acceptable terms, or at all. In addition, our ability to raise additional capital may be adversely impacted by potential worsening economic conditions, both inside and outside the United States, including without limitation heightened inflation, capital market volatility, interest rate and currency rate fluctuations, any potential economic slowdown or recession, future pandemics, geopolitical tensions, including trade

wars or civil or political unrest, or wars or other armed conflicts. We can give no assurance that we will be able to secure additional capital to support our operations, or if such funds are available to us, that such additional funding will be sufficient to meet our needs. These factors raise substantial doubt about our ability to continue as a going concern, and our failure to raise capital, on attractive terms or at all, would have a material adverse effect on our business, results of operations and financial condition.

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

Unless and until we can generate a substantial amount of product revenue, we expect to seek additional capital through a combination of public or private equity offerings, debt, collaborations, licensing arrangements or other sources. Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our common stock to decline, and our stockholders may not agree with our plans for additional capital or the terms of such capital. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. For example, (i) when we issue shares of common stock in connection with the March 2024 private placement, which private placement is expected to close on April 2, 2024 (subject to customary closing conditions), or if we issue shares of common stock upon the exercise of the prefunded warrants to be issued in connection with the March 2024 private placement, or (ii) if we issue shares of common stock in connection with the sale of additional shares of our common stock or prefunded warrants to Gilead in up to three potential private placements, our existing stockholders will suffer dilution. In addition, as a condition to providing additional funds to us, Gilead received, and future investors may receive, rights superior to those of existing stockholders. To the extent that we incur additional indebtedness, we would become obligated to make payments to repay the loan balance with interest. The incurrence of any additional indebtedness would result in additional payment obligations and is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, would be repaid before holders of our equity securities received any distribution of our corporate assets. Additionally, in raising funds through our collaborations and licensing arrangements with third parties, we have had to, and may in the future need to, relinquish valuable rights, partially or fully, to our technologies, future revenue streams, research programs or product candidates and grant licenses on terms unfavorable to us. In addition, securing additional capital would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we fail to regain compliance with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

On January 19, 2024, we received a deficiency letter from the Listing Qualifications Department, or the Nasdaq Staff, of the Nasdaq Stock Market LLC, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below $1.00 per share, which is the minimum bid price required to maintain continued listing on the Nasdaq Global Market, referred to as the minimum bid price requirement. In accordance with Nasdaq Listing Rules, we have an initial period of 180 calendar days, or until July 17, 2024, to regain compliance with the minimum bid price requirement. If, at any time before July 17, 2024, the closing bid price for our common stock is at least $1.00 per share for a minimum of 10 consecutive business days, the Nasdaq Staff will provide written notification to us that we are in compliance with the minimum bid price requirement, unless the Nasdaq Staff exercises its discretion to extend this 10-day period pursuant to the Nasdaq Listing Rules.

If we do not regain compliance with the minimum bid price requirement by July 17, 2024, we may be eligible for an additional 180 calendar day compliance period. To qualify, we would need to transfer the listing of our common stock to the Nasdaq Capital Market, provided that we meet the continued listing requirement for the market value of publicly held shares and all other initial listing standards, with the exception of the minimum bid price requirement. To effect such a transfer, we would also need to pay an application fee to Nasdaq and would need to provide written notice to the Nasdaq Staff of our intention to cure the deficiency during the additional compliance period.

If it appears to the Nasdaq Staff that we will not be able to cure the deficiency during the second compliance period or if we do not meet the other listing standards, the Nasdaq Staff will provide us with notice that our common stock may be delisted. At that time, we may appeal the Nasdaq Staff's delisting determination to a Nasdaq Listing Qualifications Panel. We expect that our common stock would remain listed pending the panel's decision. However, there can be no assurance that, even if we appeal the Nasdaq Staff's delisting determination to the panel, such appeal would be successful.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the minimum bid price requirement, which could include seeking to effect a reverse stock split. However, there can be no assurance that we will be able to regain compliance with the minimum bid price requirement, secure a second period of 180 days to regain compliance, or maintain compliance with any of the other Nasdaq continued listing requirements.

If we are unable to comply with applicable Nasdaq listing standards, shares of our common stock would be subject to delisting, which could have a material adverse effect on the market for, and liquidity and price of, our common stock and would adversely affect our ability to raise capital on terms acceptable to us, or at all. Delisting from Nasdaq could also have other negative results, including, without limitation, the potential loss of confidence by investors, customers and employees and fewer business development opportunities. Any delisting of our common stock from Nasdaq would also make it more difficult for our stockholders to sell their shares of our common stock in the public market.

We have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future.

We have incurred significant operating losses since our inception and have not yet generated any revenue. If our product candidates are not successfully developed and approved, we may never generate any revenue. Our net losses were $76.4 million and $88.2 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $325.5 million. To date, we have funded our operations primarily through proceeds from our initial public offering, or IPO, the sale of preferred units and convertible preferred stock and a debt financing. We have devoted substantially all of our financial resources and efforts to research and development. We are still in the early stages of development of our product candidates, and we have not completed clinical development for our clinical-stage, tumor-activated product candidates, XTX101 (anti-CTLA-4), XTX301 (IL-12) and XTX202 (IL-2), and we have not commenced clinical development for any of our other product candidates. We have not generated any revenue from product sales to date. We expect to continue to incur significant expenses and operating losses for the foreseeable future, particularly to the extent we:

- continue to advance our current research programs and conduct additional research programs;
- advance our current product candidates and any future product candidates we may develop into preclinical and clinical development;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- obtain, expand, maintain, defend and enforce our intellectual property;
- hire additional research, clinical, regulatory, quality, manufacturing and general and administrative personnel;
- establish a commercial and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- continue to discover, validate and develop additional product candidates;
- continue to expand manufacturing capacity through third-party manufacturers and manufacture increasing quantities of our current or future product candidates for use in preclinical studies, clinical trials and for any potential commercialization;

- acquire or in-license other product candidates, technologies or intellectual property; and

- incur additional costs associated with current and future research, development and commercialization efforts and operations as a public company.

Even if we successfully complete clinical trials and obtain regulatory approval for one or more of our product candidates, our product candidates may not be commercially successful. In addition, we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate revenue, we will not become profitable and may be unable to continue operations without continued funding.

We have no products approved for commercial sale and have not generated any revenue from product sales. We may never generate any revenue or become profitable and, if we achieve profitability, we may not be able to sustain it.

To date, we have not generated any revenue from our product candidates or product sales, we do not expect to generate any revenue from the sale of products for a number of years, and we may never generate revenue from the sale of products. Our ability to generate product revenue depends on a number of factors, including our ability to:

- successfully complete our ongoing and planned preclinical studies and clinical trials for any current or future product candidates;

- successfully receive U.S. Food and Drug Administration, or FDA, clearance for any investigational new drug application, or IND, for any current or future product candidates;

- successfully initiate and complete clinical trials for our clinical-stage product candidates and any other current or future product candidates, including all safety and efficacy studies necessary to obtain U.S. and foreign regulatory approval for our product candidates;

- establish and maintain clinical and commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;

- launch commercial sales of our products, if and when approved, whether alone or in collaboration with others;

- obtain and maintain acceptance of the products, if and when approved, by patients, the medical community and third-party payors;

- effectively compete with other therapies;

- obtain and maintain healthcare coverage and adequate reimbursement for our products, if and when approved;

- maintain a continued acceptable safety profile of our products following approval; and

- enforce and defend intellectual property rights and claims.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of expenses we may incur in connection with these activities prior to generating product revenue. In addition, we may never succeed in these activities, and, even if we do, we may never generate revenues that are significant enough 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 candidates or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

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

We are a clinical-stage biotechnology company with a limited operating history upon which investors can evaluate our business and prospects. Since inception, we have devoted substantially all of our financial resources and efforts to performing research and development activities. Our approach to the discovery and development of tumor-activated product candidates using our proprietary platform technology for tumor-activated molecules is unproven, and we do not know whether we will be able to develop any approved products of commercial value. In addition, each of our product candidates is either in early clinical or preclinical development, and all of our other development programs are still in discovery stages. We have not yet demonstrated an ability to successfully complete any clinical trials, obtain regulatory approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct the sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing biopharmaceutical products.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history. As of December 31, 2023, we had federal and state net operating loss, or NOL, carryforwards of $209.3 million and $180.9 million, respectively. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we do not know whether or when we will generate taxable income necessary to utilize our NOLs.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity by certain stockholders over a three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income is subject to limitations. We have not yet completed a detailed study of our inception to date ownership change activity under Sections 382 and 383 of the Code. As a result of our prior private placements for preferred units and convertible preferred stock, our IPO or other transactions, we may have experienced such ownership changes in the past, and we may experience such ownership changes in the future as a result of changes 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 net operating loss carryforwards and other pre-change tax attributes to offset such taxable income may be subject to limitations, which could result in increased future tax liability to us and could have an adverse effect on our future results of operations.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. As described below in "Risks Related to Ownership of Our Common Stock—Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the Tax Cuts and Jobs Act of 2017, or the Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. In addition, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Risks Related to the Discovery and Development of Our Product Candidates

Our business is highly dependent on the success of our current product candidates, which are in the early stages of development and will require significant additional preclinical and clinical development before we can seek regulatory approval for and commercially launch a product.

Our business and future success is highly dependent on our ability to obtain regulatory approval for, and if approved, successfully launch and commercialize, our current product candidates, including our clinical-stage, tumor-activated product candidates: XTX101 (anti-CTLA-4), XTX301 (IL-12) and XTX202 (IL-2). We are currently evaluating XTX101 in combination with atezolizumab (Tecentriq®) in Phase 1 combination dose escalation and XTX301 in a Phase 1 clinical

trial. Additionally, we have been evaluating XTX202 in a Phase 2 clinical trial; however, as announced in March 2024, we plan to discontinue further investment in XTX202 as a monotherapy and plan to explore strategic opportunities to continue to develop XTX202 in combination with other agents. We also have a portfolio of programs that are in even earlier stages of preclinical development and may never advance to clinical-stage development.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies, or we are required to satisfy other FDA requests prior to commencing clinical trials, the start of our clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union, or EU.

To date, we have only had limited interactions with the FDA regarding our clinical development plans. We may experience issues surrounding preliminary trial execution, such as delays in FDA acceptance of any future INDs, revisions in trial design and finalization of trial protocols, difficulties with patient recruitment and enrollment, quality and provision of clinical supplies, or early safety signals.

We are not permitted to market any biological product in the United States until we receive approval of a Biologics License Application, or BLA, from the FDA. We have not previously submitted a BLA to the FDA, or similar marketing application to comparable foreign regulatory authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, pure and potent for each desired indication. A BLA must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-license inspection.

FDA approval of a BLA is not guaranteed, and the review and approval process is expensive, uncertain and may take several years. The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for BLA approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage.

The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidate that we develop based on the completed clinical trials.

Generally, public concern regarding the safety of biopharmaceutical products could delay or limit our ability to obtain regulatory approval, result in the inclusion of unfavorable information in our labeling or require us to undertake other activities that may entail additional costs. We have not obtained FDA approval for any product. This lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for any current or future product candidates.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of our current and any future product candidates, which may never occur. However, given our early stage of development, it will be years before we are able to demonstrate the safety and efficacy of a treatment sufficient to warrant approval for commercialization, and we may never be able to do so. If we are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize our current or any future product candidates, we may not be able to generate sufficient revenue to continue our business.

Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

All our product candidates are still in the early clinical stage or preclinical stage of development, and their risk of failure is high. Before we can commence clinical trials for a product 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 we cannot predict if the FDA or other regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our current or future preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Preclinical studies and clinical trials are expensive, time-consuming and difficult to design and implement, and involve uncertain outcomes. Furthermore, results of earlier preclinical studies and clinical trials may not be predictive of results of future preclinical studies or clinical trials.

The risk of failure for our current and any future product candidates is high. It is impossible to predict when or if any of our product candidates will successfully complete preclinical studies or clinical trials evaluating their safety and effectiveness in humans or will ultimately receive regulatory approval. To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans for use in each target indication. Preclinical and clinical testing is expensive and can take many years to complete, and the outcome is inherently uncertain. Failure can occur at any time during the preclinical or clinical trial process. The outcome of preclinical testing and early clinical trials may not be predictive of the results of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In particular, while we have conducted certain preclinical studies for each of our clinical stage product candidates, we do not know whether these product candidates will perform in our clinical trials as they have performed in these prior preclinical studies. For example, in preclinical mouse models, we observed XTX101 had tumor-selective activity and tumor growth inhibition superior to that of an ipilimumab analog, and that XTX202 had comparable tumor growth inhibition to aldesleukin and non-masked IL-2, with both XTX101 and XTX202 avoiding mortality and body weight loss. However, there is no guarantee these preclinical results will be replicated in clinical trials. Similarly, there can be no assurance that early, interim or preliminary clinical data or results will be predictive of or replicated in future clinical data or results, including without limitation, the preliminary Phase 1 data reported for XTX101, including the partial response observed in one patient treated with XTX101, the preliminary safety data into the third dose level reported for XTX301, or the Phase 1/2 monotherapy data reported for XTX202. Many companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events, or AEs. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants. If we fail to produce positive results in our planned and ongoing preclinical studies or clinical trials, or if we experience material changes in clinical data or results from those we have previously reported, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business, financial condition and results of operations would be materially and adversely affected.

We may encounter substantial delays in the commencement or completion, or termination or suspension, of our clinical trials, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate for its intended indications. We cannot guarantee that any clinical trials, including our Phase 1 combination dose escalation portion of our Phase 1/2 clinical trial for XTX101 in combination with atezolizumab or our Phase 1 clinical trial for XTX301, will be conducted as planned or completed on schedule, if at all. For example, in March 2024, we announced that we plan to discontinue further investment in XTX202 as a monotherapy. We may experience numerous unforeseen events leading up to, during or as a result of clinical trials that could delay or prevent the initiation or completion of a clinical trial or our ability to receive marketing approval or commercialize our product candidates, including:

- we may be unable to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to obtain regulatory authorizations to commence a clinical trial;
- we may experience issues in reaching a consensus with regulatory authorities on trial design;
- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trial sites may deviate from a trial protocol or drop out of a trial or fail to conduct the trial in accordance with regulatory requirements;
- the number of subjects required for clinical trials of our product candidates may be larger than we anticipate, or subjects may fail to enroll or remain in clinical trials at the rate we expect;
- subjects that enroll in our studies may misrepresent their eligibility or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the subject from the trial, increase the needed enrollment size for the clinical trial or extend its duration;
- subjects may choose an alternative treatment for the indication for which we are developing our product candidates, or participate in competing clinical trials;
- subjects may experience severe or unexpected treatment-related adverse effects;
- clinical trials of our product candidates may produce unfavorable, inconclusive, or clinically insignificant results;
- we may decide to, or regulators, or IRBs, or ethics committees may require us to, make changes to a clinical trial protocol or conduct additional preclinical studies or clinical trials, or we may decide to abandon product development programs;
- we may need to add new or additional clinical trial sites;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we may experience manufacturing delays, and any changes to manufacturing processes or third-party contractors that may be necessary or desired could result in other delays;

- we or our third-party contractors may experience delays due to complications resulting from the impact of public health crises, including epidemics and pandemics;

- the cost of preclinical testing and studies and clinical trials of any product candidates may be greater than we anticipate or greater than our available financial resources;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate or we may not be able to obtain sufficient quantities of combination therapies for use in current or future clinical trials;

- reports may arise from preclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our product candidates; and

- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond the clinical trials and testing that we contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these clinical trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with any of product candidates, we may:

- incur additional unplanned costs;

- be required to suspend or terminate ongoing clinical trials;

- be delayed in obtaining marketing approval, if 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 or other requirements;

- be required to perform additional clinical trials to support approval;

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

- be subject to the addition of labeling statements, such as warnings or contraindications;

- have the product removed from the market after obtaining marketing approval;

- be subject to lawsuits; or

- experience damage to our reputation.

Conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocols as a result of differences in healthcare services or cultural customs, managing additional administrative

burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authorities, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

In addition to the factors above, we may make formulation or manufacturing changes to our product candidates, in which case we may need to conduct additional preclinical studies or clinical trials to bridge our modified product candidates to earlier versions, which may be costly, time consuming and may not be successful at all.

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business. We cannot guarantee that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our clinical trials. Significant preclinical study or clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. The enrollment of patients depends on many factors, including:

- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- the severity of the disease under investigation;
- the patient eligibility and the inclusion and exclusion criteria defined in the protocol;
- AEs in our clinical trials and in third-party clinical trials of agents similar to our product candidates;
- the size and health of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;

- our ability to monitor patients adequately during and after treatment;

- the risk that patients enrolled in clinical trials will drop out of the trials before completion; and

- factors we may not be able to control that may limit the availability of patients, principal investigators or staff or clinical sites, such as public health crises, including epidemics and pandemics.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial site.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, slow down or halt our product candidate development and approval process and jeopardize our ability to seek and obtain the marketing approval required to commence product sales and generate revenue, which would cause the value of our company to decline and limit our ability to obtain sufficient additional capital.

Our product candidates may cause undesirable or unexpectedly severe side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable or unexpectedly severe side effects caused by our product candidates could cause us to interrupt, delay or halt preclinical studies or could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Traditional cytokine therapies and checkpoint inhibitors have long been associated with severe toxicities, which can be life-threatening or fatal, that have resulted in the need to dose-reduce, dose-interrupt and discontinue many patients from treatment. As has been the case with traditional immuno-oncology, or I-O, treatments for cancer, it is possible that there may be side effects associated with the use of our current or future product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our clinical trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, clinical trials rely on a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered when a significantly larger number of patients is exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;

- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;

- regulatory authorities may require a REMS plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;

- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;

- we may be subject to regulatory investigations and government enforcement actions;

- regulatory authorities may withdraw or limit their approval of such product candidates;

- we may decide to remove such product candidates from the marketplace;

- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and

- we may suffer reputational harm.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

Interim top-line and preliminary data from our 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 clinical trials. For example, in 2023, we reported preliminary monotherapy data from our Phase 1 clinical trial for XTX101 and from our Phase 1/2 clinical trial for XTX202, and in January 2024, we reported preliminary Phase 1 safety data into the third dose level for XTX301. Preliminary and 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 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 business prospects.

We expect to develop certain of our product candidates in combination with third-party drugs and we will have limited or no control over the safety, supply, regulatory status or regulatory approval of such third-party drugs.

We intend to develop our clinical-stage product candidates, and likely other future product candidates, in combination with third-party cancer drugs, which may be either approved or unapproved. For example, we are evaluating XTX101 in combination with atezolizumab (Tecentriq®) in Phase 1 combination dose escalation and plan to evaluate the combination in Phase 2 in patients with microsatellite stable colorectal cancer. Our ability to develop and ultimately commercialize our current product candidates, and any future product candidates, used in combination with third-party drugs will depend on our ability to access such drugs on commercially reasonable terms for clinical trials and their availability for use with our commercialized product, if approved. We cannot be certain that current or potential future commercial relationships will provide us with a steady supply of such drugs on commercially reasonable terms or at all. Any failure to maintain or enter into new successful commercial relationships, or the expense of purchasing such third-party drugs in the market, may delay our development timelines, increase our costs and jeopardize our ability to develop our current product candidates and any future product candidates as commercially viable therapies. If any of these occur, our business, financial condition, operating results or prospects may be materially harmed.

Moreover, the development of product candidates for use in combination with another product or product candidate may present challenges that are not faced for single agent product candidates. For example, our plans to evaluate current or future product candidates in combination with other agents may result in AEs based on the combination therapy that may negatively impact the reported safety profile of the monotherapy in clinical trials. In addition, the FDA or comparable foreign regulatory authorities may require us to use more complex clinical trial designs in order to evaluate the contribution of each product and product candidate to any observed effects. It is possible that the results of such trials could show that

any positive previous trial results are attributable to the third-party drug and not our product candidate. Developments related to the third-party drug may also impact our clinical trials for the combination therapy as well as our commercial prospects should we receive regulatory approval. Such developments may include changes to the third-party drug's safety or efficacy profile, changes to the availability of the third-party drug, quality, and manufacturing and supply issues with respect to the third-party drug.

If we are able to obtain marketing approval, the FDA or comparable foreign regulatory authorities may require that products used in conjunction with each other be cross labeled for combined use. To the extent that we do not have rights to the third-party drug, this may require us to work with such third party to satisfy such a requirement. We would also continue to be subject to the risks that the FDA or comparable foreign regulatory authorities could revoke approval of the third-party drug used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with such drug. Similarly, if the third-party drugs we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

We may not be successful in our efforts to use our platform technology to enable the development of a pipeline of tumor-activated product candidates.

A key element of our strategy is to use our novel platform technology to engineer and develop tumor-activated molecules with the potential to trigger anti-tumor immunity with minimal systemic toxicity in order to build a pipeline of product candidates. We may not be able to continue to identify and develop novel I-O therapies. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, potential product candidates may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to or will not be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our platform approach or take longer to do so than anticipated, we will not or may not be able to obtain drug revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

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

Although we intend to explore other therapeutic opportunities in addition to the product candidates that we are currently developing, we may fail to identify or discover viable new product candidates for clinical development for a number of reasons. If we fail to identify additional potential product candidates, our business could be materially harmed.

Research programs to pursue the development of our existing and planned product candidates for additional indications and to identify new product candidates and disease targets require substantial technical, financial and human resources whether or not they are ultimately successful. We may in the future rely on third parties for certain research, and we will not have complete control over their performance and ability to successfully develop product candidates. Our research programs may initially show promise in identifying potential indications and/or product candidates, yet fail to yield results for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;

- potential product candidates may, after further study, be shown to have harmful adverse effects or other characteristics that indicate they are unlikely to be effective drugs; and

- it may take greater human and financial resources than we will possess to identify and advance additional therapeutic opportunities for our product candidates or to develop suitable potential product candidates through internal research programs, thereby limiting our ability to develop, diversify and expand our product portfolio.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our current product candidates or to develop suitable additional product candidates through internal research programs, which could materially adversely affect our future growth and prospects.

Our approach to the discovery and development of product candidates based on our technological approaches is unproven, and we do not know whether we will be able to develop any products of commercial value.

The success of our business depends primarily upon our ability to discover, develop and commercialize products based on our technological approaches. While we have had favorable preclinical study results related to our clinical stage product candidates, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidates in current or future clinical trials or in obtaining marketing approval thereafter. We rely on matrix metalloproteases, or MMPs, to activate our molecules within the tumor microenvironment. If MMP activity in human tumors is not sufficient to cleave the masking protein domain, the potential efficacy of our product candidates would be limited. We have no assurance that our product candidates will successfully progress through clinical development and ultimately marketing approval. We have invested substantially all of our efforts and financial resources in developing our initial product candidates and our future success is highly dependent on the outcome of our ongoing clinical trials and the successful development of our technology and product candidates.

In addition, the clinical trial requirements of the FDA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate may vary according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. As a result, we may face a greater regulatory burden to initiate clinical trials or to obtain regulatory approval of our product candidates as compared to product candidates based on more established technology. In addition, any product candidates for which we may be able to obtain marketing approval may be subject to extensive post-approval regulatory requirements, including requirements pertaining to manufacturing, distribution and promotion. We may need to devote significant time and resources to comply with these requirements.

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

We have chosen to initially develop each of our clinical-stage product candidates for the treatment of various solid tumor types. Nevertheless, our development efforts will be limited to a small number of cancer types, and we may forego or delay pursuit of opportunities in other cancer types that may prove to have greater potential. Likewise, we may forego or delay the pursuit of opportunities with other potential product candidates that may prove to have greater commercial potential.

In addition, 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 product candidates for specific indications may not yield any viable product candidates. Similarly, if we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or following commercial sale, and any product liability insurance we may obtain may not cover all damages from such claims.

We are exposed to potential product liability risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. The use of product candidates by us in clinical trials, and any sale of approved products in the future, may expose us to liability claims. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to

warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval thereof, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the development or commercialization of our product candidates or any products for which we may have received marketing approval. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- delay or termination of clinical trials;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media and social media attention;
- withdrawal of clinical trial participants or difficulties in recruiting new trial participants;
- initiation of investigations by regulators;
- costs to defend or settle the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant negative financial impact; and
- the inability to commercialize any of our product candidates, if approved.

Although we will seek to procure and maintain sufficient product liability insurance coverage, our current insurance coverage and any insurance coverage we obtain in the future may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. As the expense of insurance coverage is increasing, we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be materially harmed.

Risks Relating to Manufacturing and Supply

Manufacturing biologics is complex, and we may experience manufacturing problems that result in delays in our development or commercialization programs.

The manufacturing of biologics is complex and difficult and we may experience production issues or interruptions in supply for our product candidates, including variability of raw material, consumable or starting material quality, cell line viability, productivity or stability issues, shortages of any kind, shipping, distribution, storage and supply chain failures, media contamination, equipment malfunctions or failures, operator errors, facility contamination, labor problems, quality system and regulatory inspection failures, natural disasters, disruption in utility services, terrorist activities, or acts of god

that are beyond our control or the control of our third-party contract development and manufacturing organizations, or CDMOs.

Given the nature of biologics manufacturing, there is a risk of contamination during manufacturing. Any contamination could materially harm our ability to produce product candidates on schedule and could harm our results of operations and cause reputational damage. In the event that raw materials required in our manufacturing process need to be derived from biologic sources, they may be difficult to procure and may be subject to contamination or recall.

Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects, out-of-specification analytical results or manufacturing failures that result in lot failures, product recalls, product liability claims, insufficient inventory or potentially delay progression of our preclinical or clinical development of any product candidates we may develop. If we successfully develop product candidates, we may encounter problems achieving adequate quantities and quality that meet FDA, European Medicines Agency, or EMA, or other comparable applicable foreign standards or specifications with consistent and acceptable production yields and costs. The ability to scale our manufacturing and maintain the manufacturing process at the same levels of quality and efficiency that we are currently manufacturing is yet to be tested. If we or our third-party CDMO is unable to scale our manufacturing and meet the same levels of quality and efficiency, or provide sufficient manufacturing campaign slots to generate materials, we may not be able to supply the required number of doses for clinical trials or commercial supply. A material shortage, contamination event or manufacturing failure in the manufacture of any product candidate we may develop or other adverse impact or disruption in the commercial manufacturing or the production of clinical material could materially harm our development timelines and our business, financial condition, results of operations and prospects.

We face risks related to our reliance on our current and any future CDMOs. For example, we and our CDMO are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities of the CDMO on which we rely may not continue to meet regulatory requirements, may have limited capacity or may experience interruptions in supply, any of which could adversely affect our development and commercialization plans for our product candidates. All entities involved in the preparation and storage of therapeutics for clinical trials or commercial sale, including any CDMOs of any product candidates we may develop, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured in accordance with current Good Manufacturing Practices, or cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We, in partnership with our CDMO, must supply all necessary documentation in support of an IND for clinical product, and later in support of a BLA for any potential commercial product, on a timely basis and must adhere to the FDA's and EMA's current Good Laboratory Practices and cGMP regulations enforced through the applicable regulatory authority's facilities inspection program. Our facilities and quality systems and the facilities and quality systems of our CDMO must pass a pre-approval inspection, or PAI, to confirm validity of the information presented in the BLA and to confirm the capability of the facility to manufacture our product in compliance with the applicable regulations. The PAI is a condition of regulatory approval of any product candidates we may develop or any of our other potential products. If our or our CDMO's quality systems or facilities involved with the preparation of our product candidates do not pass the PAI, FDA approval of such product candidates will not be granted.

In addition, the regulatory authorities may, at any time, conduct a routine or for-cause inspection of a manufacturing facility involved with the preparation of our product candidates, which inspection is related to other products manufactured at the site or the associated quality systems, for compliance with the regulations applicable to the activities being conducted. The regulatory authorities also may, at any time following approval of a product for sale, inspect our facilities or the manufacturing facilities of our CDMOs. If any such inspection identifies a failure to comply with applicable regulations, or if a violation of our product specifications or applicable regulations occurs independent of such an inspection, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales, the temporary or permanent closure of a facility, or other remedial measures that may delay or disrupt the manufacture or release of our product candidates or other potential products. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any CDMO with which we contract for manufacturing and supply fails to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, a clinical hold, refusal to approve a pending application for a new drug product or biologic product, revocation of a pre-existing approval, or an import alert. As a result, our business, financial condition and results of operations may be materially harmed.

Currently, we depend on a single manufacturer for developing the manufacturing processes required to supply our product candidates. We cannot ensure that this manufacturer will remain in business or have sufficient capacity or supply to meet our needs. Our use of a single manufacturer exposes us to several risks, including price increases or manufacturing delays beyond our control. This CDMO is based in and has significant operations in China, where our product candidates are manufactured, which subjects us to additional risks including those related to U.S. export control laws, potential sanctions or other trade restrictions imposed by the U.S. government. Moreover, reliance on third-party manufacturers generally entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms or at all, particularly if they are affiliated with our competitors;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities, particularly if they are under contract with our competitors;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including geopolitical tensions or restrictions, such as export controls or sanctions, or the bankruptcy of the manufacturer or supplier;
- the inability to import or obtain components or materials from alternate sources at acceptable prices or with acceptable quality in a timely manner; and
- substantial delays or difficulties related to the establishment of replacement manufacturers who meet regulatory requirements.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure, import alert, or total or partial suspension of production.

Additionally, if supply from one approved manufacturer is interrupted, such as could be the case with our current CDMO, there could be a significant disruption in supply. While we believe there are alternate manufacturers who can provide the manufacturing processes required to develop and manufacture our product candidates, if we have to switch to a replacement manufacturer, the manufacture and delivery of our product candidates could be interrupted for an extended period, which could adversely affect our business. Furthermore, an alternative manufacturer must be able to demonstrate successful technology transfer of the manufacturing process and associated assays, and, to do so, may need to modify the manufacturing process required to develop our product candidates, and the alternative manufacturer would need to be qualified through additional regulatory filings, all of which could result in further delay and significant costs. The regulatory agencies may also require additional studies or trials if a new manufacturer is relied upon for clinical or commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed, or we could lose potential revenue or market share with respect to any product that has received marketing approval.

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

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

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

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws, regulations and permitting requirements. These current or future laws, regulations and permitting requirements may impair our research, development or production efforts. Failure to comply with these laws, regulations and permitting requirements also may result in substantial fines, penalties or other sanctions or business disruption, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Risks Related to our Dependence on Third Parties

We expect to rely on third parties to conduct, supervise and monitor IND-enabling studies and clinical trials, and if these third parties perform in an unsatisfactory manner, it may harm our business, reputation and results of operations.

We expect to rely on CROs and research and clinical trial sites to ensure our IND-enabling studies and clinical trials are conducted properly and on time, and we expect to rely in the future on CROs for additional research programs. While we will have agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of these studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs will be required to comply with the FDA's Good Clinical Practices, or GCPs, for conducting, recording and reporting the results of IND-enabling studies and clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these GCPs through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we or our

CROs fail to comply with applicable GCPs, the preclinical and clinical data generated in our studies may be deemed unreliable and the FDA may require us to perform additional studies before approving any marketing applications. Upon inspection, the FDA may determine that our studies did not comply with GCPs.

Our CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols or regulatory requirements, or for any other reasons, our studies may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidates we may develop. As a result, our financial results and commercial prospects would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We have entered into, and may in the future seek to enter into, licenses, collaborations or similar arrangements with third parties for the research, development and commercialization of certain of our current or future product candidates. If any such arrangements are not successful, we may not be able to capitalize on the market potential of those product candidates.

In March 2024, our wholly-owned subsidiary, Xilio Development, Inc., or Xilio Development, entered into the license agreement with Gilead, pursuant to which Gilead was granted an exclusive global license to develop and commercialize XTX301, our tumor activated IL-12, and other specified molecules directed toward IL-12, which we refer to as our IL-12 program. We may in the future seek third-party collaborators or licensors for the research, development and commercialization of other current or future product candidates. With respect to our license agreement with Gilead, and what we expect will be the case with any future collaboration agreements we enter into, we have and would likely have limited control over whether such collaborators pursue the development of our product candidates or the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates that we seek to develop with them. For example, under the license agreement with Gilead, if Gilead exercises its right to transition responsibilities for the development and commercialization of XTX301 and the rest of our IL-12 program, it will have sole decision making authority with respect to the continued development and future commercialization of our IL-12 program and may elect to prioritize other assets that it believes are more competitive, or it may exercise its right to terminate the license and return the licensed IL-12 program assets to us. As a result, there can be no assurances that any of the programs covered by our existing or future collaborations or licenses will be developed further or reach commercialization. Further, our ability to generate revenues from these existing and future 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, licenses or similar arrangements involving our research programs or any product candidates currently pose, and will continue to pose, numerous risks to us, including the following:

- collaborators or licensors have significant discretion in determining the efforts and resources that they will apply to these arrangements;

- collaborators or licensors may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in such third party's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;

- collaborators or licensors may delay programs, preclinical studies or clinical trials, provide insufficient funding for programs, preclinical studies or clinical trials, stop a preclinical study or clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

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

- collaborators or licenses may be acquired by a third party having competitive products or different priorities;

- collaborators or licensors with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidate(s);

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

- disputes may arise between the collaborators or licensors and us that result in the delay or termination of the research, development, or commercialization of our product candidates or any of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources or that jeopardize or invalidate our intellectual property or proprietary information;

- we may lose certain valuable rights under certain circumstances, including if we undergo a change of control;

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

- collaborations or license agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator or licensor 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 current or future collaborations, licenses or similar transactions do not result in the successful development and commercialization of product candidates, or if one of our collaborators or licensors terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under such agreement, we may lose valuable rights to our intellectual property, or we may incur significant costs in reestablishing the development and manufacturing of such product candidates. If we do not receive the funding we expect under these agreements, our development of product candidates could be delayed, and we may need additional resources to develop product candidates. In addition, if one of our collaborators terminates its agreement with us, we may find it more difficult to find a suitable replacement collaborator or licensor or for us to attract new collaborators or licensors, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K apply to the activities of our collaborators or licensors.

These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute 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 or license agreement with future partners will depend, among other things, upon our assessment of the resources and expertise of such third-party collaborator or licensor and the terms and conditions of the proposed collaboration or license. Further, if we license rights for use in any product 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.

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

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

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

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate future collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidates for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay their potential commercialization, reduce the scope of any sales or marketing activities, or increase our own expenditures on the development of the applicable product candidate.

Certain of our research and development and manufacturing activities take place in China through a third-party CDMO. A significant disruption in our ability to rely on this CDMO could materially adversely affect our business, financial condition and results of operations.

We have relied on a third party located in China to manufacture and supply certain raw materials used in our product candidates, and we expect to continue to use such third-party CDMO for such purposes. A natural disaster, epidemic or pandemic, such as the COVID-19 pandemic, trade war, political unrest, economic conditions, changes in legislation, including the passage of the People's Republic of China Biosecurity law, which became effective on April 15, 2021, and subsequent legislation that China or the United States may adopt in the future, or other events in China could disrupt our ability to continue to rely upon CROs, collaborators, manufacturers or other third parties with whom we conduct business now or in the future. Any disruption in China or the United States that significantly impacts such third parties, including services provided by CROs for our research and development programs, or our manufacturers' ability to produce and export raw or manufactured materials in adequate quantities to meet our needs, could impair our ability to operate our business on a day-to-day basis and impede, delay, limit or prevent the research, development or commercialization of our current and future products or product candidates. In addition, for any activities conducted in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the policies of the U.S. or Chinese governments, political unrest or unstable economic or geopolitical conditions, including sanctions in China or against certain Chinese companies; changes in U.S. export laws or the imposition by the United States of trade barriers; sanctions; limitations on uses of U.S. government executive agency contract, grant or loan funds; or other restrictions on doing business with certain Chinese companies, including our CDMO, which could have a material adverse effect on our business. Additionally, we may be exposed to fluctuations in the value of the local currency in China for goods and services. Our costs for any of these services or activities could also increase as a result of future appreciation of the local currency in China or increased labor costs if the demand for skilled laborers increases and/or the availability of skilled labor declines in China.

Risks Related to Commercialization

We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any products that receive regulatory approval, either on our own or together with collaborators.

We have never commercialized a product candidate. We currently have no sales force or marketing or distribution capabilities. To achieve commercial success of our product candidates, if any are approved, we will have to develop our own sales, marketing and supply capabilities or outsource these activities to one or more third parties. Factors that may affect our ability to commercialize our product candidates on our own include our ability to recruit and retain adequate numbers of effective sales and marketing personnel and obtain access to or persuade adequate numbers of physicians to prescribe our product candidates, as well as any unforeseen costs we may incur in connection with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment and substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization in the United States, the EU or other key global markets. To the extent we need to rely upon one or more third parties, we may have little or no control over the marketing and sales efforts of those third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We will also face competition in any search for third parties to assist us with sales and marketing efforts for our product candidates. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may have difficulties generating revenue from them.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical, specialty pharmaceutical and biotechnology companies among others. We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop immunotherapies for the treatment of cancer. There are other companies working to develop immunotherapies for the treatment of cancer including divisions of pharmaceutical and biotechnology companies of various sizes. Some of these competitive therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are developing our current product candidates for the treatment of cancer and have not completed clinical development for our clinical-stage, tumor-activated product candidates, XTX101 (anti-CTLA-4), XTX301 (IL-12) or XTX202 (IL-2), and we have not commenced clinical development for any of our other product candidates or received marketing approval for any of our product candidates. There are already a variety of available therapies marketed for cancer and some of the currently approved therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved therapies are well-established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates. Competition may further increase with advances in the commercial applicability of technologies and greater availability of capital for investment in these industries.

XTX101, if approved, may face competition from other anti-CTLA-4 based therapies. For example, Yervoy (ipilimumab), an anti-CTLA-4, is approved to treat melanoma, renal cell carcinoma and certain cancers of the large intestine, and Imjudo (tremelimumab) is approved as a combination therapy to treat unresectable hepatocellular carcinoma. In addition, we are aware that several companies have anti-CTLA-4 programs in development, including Adagene, Inc., Agenus Inc., AstraZeneca plc, BioAtla, Inc., CytomX Therapeutics, Inc., MacroGenics, Inc. and OncoC4, Inc.

With respect to XTX301, there are no approved IL-12 therapies currently on the market for the treatment of cancer; however, we are aware of several other companies that have modified IL-12 or intra-tumoral IL-12 delivery programs for the treatment of cancer in development, including Amunix Pharmaceuticals, Inc., AstraZeneca plc / Moderna, Inc., Cullinan Management Inc., Dragonfly Therapeutics, Inc., ImmunityBio, Inc., PDS Biotechnology Corporation, Philogen S.p.A., Sonnet BioTherapeutics, Werewolf Therapeutics, Inc., Xencor Inc. and Zymeworks Inc.

XTX202, if approved, may face competition from other IL-2-based cancer therapies. For example, Proleukin (aldesleukin), a human recombinant interleukin-2 product, is approved and marketed for the treatment of metastatic renal cell carcinoma and melanoma. In addition, we are aware that a number of other companies have modified or low-dose IL-2 programs in development for the treatment of cancer, including Alkermes plc, Anaveon AG, Ascendis Pharma A/S, Asher Biotherapeutics, Inc., Aulos Bioscience, Inc., Bright Peak Therapeutics, Cue Biopharma, Inc., Cugene Inc., Cullinan Management Inc., Egle Therapeutics SAS, GI Innovation, Iovance Biotherapeutics, Inc., Kymab Ltd., Medicenna Therapeutics Corp., Medikine, Inc., Modulate Therapeutics, Inc., Neoleukin Therapeutics, Inc., Philogen S.p.A., Proviva Therapeutics, Inc., Roche AG, Sanofi, Selecxine, Synthekine, Inc., Trutino Biosciences Inc., Werewolf Therapeutics, Inc., XOMA Corporation and Zydus Cadila.

Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, 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. We also compete with these organizations in establishing clinical trial sites and patient registration for clinical trials, as well as in recruiting and retaining qualified scientific and management personnel, which could negatively affect our level of expertise and our ability to execute our business plan.

Many of our competitors, either alone or with their collaborators, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel product candidates or to in-license novel product candidates that could make our product candidates less competitive or obsolete. Smaller or early-stage companies may also prove to be significant competitors, including through collaborative arrangements with large and established companies. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. The availability of competing products could limit the demand and the price we are able to charge for product candidates we commercialize, if any. The inability to compete with existing or subsequently introduced products would harm our business, financial condition and results of operations.

If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the commercialization of any of our product candidates may be delayed, and our business could be harmed.

For planning purposes, we sometimes estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies and clinical trials, the submission of regulatory filings or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the release of clinical trial data, the completion of an ongoing clinical trial, the initiation of other clinical trials, receipt of regulatory approval or the commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions which may cause the timing of achievement of the milestones to vary considerably from our estimates, including:

- our available capital resources or capital constraints we experience;
- the rate of progress, costs and results of our clinical trials and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators;
- our ability to identify and enroll patients who meet clinical trial eligibility criteria;

- our receipt of approvals by the FDA, EMA and comparable regulatory authorities in other jurisdictions, and the timing thereof;

- other actions, decisions or rules issued by regulators;

- our ability to access sufficient, reliable and affordable supplies of materials used in the manufacture of our product candidates;

- our ability to manufacture and supply clinical trial materials to our clinical trial sites on a timely basis;

- the efforts of our collaborators with respect to the development of our product candidates or the potential commercialization of any of our product candidates, if approved; and

- the securing of, costs related to, and timing issues associated with, commercial product manufacturing as well as sales and marketing activities.

If we fail to achieve announced milestones in the timeframes we expect, the commercialization of any of our product candidates may be delayed, and our business, results of operations, financial condition and prospects may be adversely affected.

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

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, was enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, to establish an abbreviated pathway for the approval of biosimilar and interchangeable with an FDA-licensed reference biologic product. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic.

Under the BPCIA, reference biological product is granted 12 years of non-patent data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the licensure of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still develop and receive licensure of a competing biologic, so long as their BLA does not rely on the reference product or sponsor's data or submit the application as a biosimilar application.

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

If competitors are able to obtain regulatory approval for biosimilars referencing our product candidates, our product candidates may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

The sizes of the potential markets for our product candidates are difficult to estimate and, if any of our assumptions are inaccurate, the actual markets for our product candidates may be smaller than our estimates.

The potential market opportunities for our product candidates are difficult to estimate and, if our product candidates are approved, will ultimately depend on, among other things, the indications for which our product candidates are approved for sale, any products with which our product candidates are co-administered, the success of competing therapies and therapeutic approaches, acceptance by the medical community, patient access, product pricing, reimbursement and our ability to create meaningful value propositions for patients, prescribers and payors. Our estimates of the potential market opportunities for our product candidates are predicated on many assumptions, which may include industry knowledge and publications, third-party research reports and other surveys. Although we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain, and their reasonableness has not been assessed by an independent source. If any of the assumptions prove to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities.

The successful commercialization of our product candidates will depend in part on the extent to which we obtain and maintain favorable insurance coverage, adequate reimbursement levels and cost-effective pricing policies with third-party payors.

The availability and adequacy of coverage and reimbursement by third-party payors, including governmental healthcare programs such as Medicare and Medicaid, managed care organizations, and private health insurers, are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by third-party payors will have an effect on our ability to successfully commercialize our product candidates. We cannot be sure that coverage and reimbursement in the United States, the EU or elsewhere will be available for our product candidates, if approved, or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates, if approved. Even if our product candidates are approved and we obtain coverage for our product candidates by a third-party payor, such products may not be considered cost-effective and/or the resulting reimbursement payment rates may be insufficient or may require co-payments that patients find unacceptably high. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, if approved, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. The regulations that govern marketing approvals, pricing and reimbursement for new medicines vary widely from country to country. In the United States, third-party payors play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how third-party payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates, if approved.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States and coverage and reimbursement for products can therefore differ significantly from payor to payor and coverage and reimbursement by one payor does not guarantee coverage and reimbursement by another payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Our ability to demonstrate to these third-party payors that any of our approved product candidates creates a meaningful value proposition for patients, prescribers and payors will be important to gaining market access and reimbursement and there is no guarantee that we will be successful in doing so. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Even if a product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, hospitals, cancer treatment centers, third-party payors and others in the medical community necessary for commercial success.

If any product candidate we develop receives marketing approval, whether as a single agent or in combination with other therapies, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, hospitals, cancer treatment centers, third-party payors, and others in the medical community. For example, cancer treatments like chemotherapy, radiation therapy and certain existing immunotherapies are well established in the medical community, and doctors may continue to rely on these therapies. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of any product, if approved for commercial sale, will depend on a number of factors, including:

- the product's efficacy, safety and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects;
- the product's convenience and ease of administration compared to alternative treatments;
- the clinical indications for which the product is approved;
- the willingness of the target patient population to try a novel treatment and of physicians to prescribe such treatments;
- the recommendations with respect to the product in guidelines published by scientific organizations;
- the ability to obtain sufficient third-party insurance coverage and adequate reimbursement, including, if applicable, with respect to the use of the product as a combination therapy;
- the strength of marketing, sales and distribution support;
- the effectiveness of our sales and marketing efforts;
- the approval of other new products for the same indications; and
- our ability to offer the product for sale at competitive prices.

If we obtain marketing approval for a product but such product does not achieve an adequate level of market acceptance, we may not generate or derive significant revenue from that product and our business, financial condition and results of operations may be adversely affected.

Risks Related to Our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment and development that are important to our business. If we do not adequately protect our intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our product candidates that are important to our business; we also license and may in the future license or purchase additional patents and patent applications filed by others. If we are unable to secure or maintain patent protection with respect to our product candidates and any proprietary products and technology we develop, our business, financial condition, results of operations and prospects could be materially harmed.

We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. Specifically, our patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our product candidates but that uses a different masking moiety that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or have licensed with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business.

The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. The U.S. Patent and Trademark Office, or the USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. Our or our licensor's failure to comply with all such provisions during the patent process could result in abandonment or lapse of a patent or patent application that we own or license, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market and compete with us earlier than would otherwise have been the case. Moreover, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. In addition, to the extent that we license intellectual property in the future, we cannot guarantee that those licenses will remain in force.

Patent positions of life sciences companies can be uncertain and involve complex factual and legal questions and have in recent years been the subject of much litigation. No consistent policy governing the scope of claims allowable in the field of engineered therapeutic proteins has emerged in the United States. The scope of patent protection in jurisdictions outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in any jurisdiction that we seek patent protection may diminish our ability to protect our inventions, maintain and enforce our intellectual property rights; and, more generally, may affect the value of our intellectual property, including the narrowing of the scope of our patents and any that we may license. Under the Leahy-Smith America Invents Act enacted in 2011, or the AIA, the United States moved to a first-to-file system in early 2013 (whereby, assuming the other requirements for patentability are met, the first to file a patent application is entitled to the patent), from the previous system under which the first to make a claimed invention was entitled to the patent. Publications of discoveries in the scientific and academic literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to file for patent protection on the inventions claimed in our patents or pending patent applications. Furthermore, for U.S.

applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications.

The patent prosecution process is complex, expensive, time-consuming and inconsistent across jurisdictions. We may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent rights at a commercially reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is possible that we will fail to identify important patentable aspects of our research and development efforts in time to obtain appropriate or any patent protection. While we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development efforts, including for example, our employees, external academic scientific collaborators, CROs, CDMOs, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose our confidential or proprietary information before a patent application is filed, thereby endangering our ability to seek patent protection.

The issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Pending patent applications cannot be enforced against third parties unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or any patent applications that we may license in the future will result in patents being issued. Further, the scope of the invention claimed in a patent application can be significantly reduced before the patent is issued, and this scope can be reinterpreted after issuance. Even if patent applications we currently own or that we may license in the future issue as patents, they may not issue in a form that will provide us with adequate protection to prevent competitors or other third parties from competing with us, or otherwise provide us with a competitive advantage. Any patents that eventually issue may be challenged, narrowed or invalidated by third parties. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by valid and enforceable patent rights. Our competitors or other third parties may be able to evade our patent rights by developing new products that are similar to our product candidates, biosimilars of our product candidates, or alternative technologies or products in a non-infringing manner.

The issuance or grant of a patent is not irrefutable as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. We may in the future, become subject to a third-party pre-issuance submission of prior art, pre- or post-issuance opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceeding and other similar proceedings challenging our patent rights or the patent rights of others in the USPTO or other foreign patent office. An unfavorable determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us.

Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, third parties may have certain ownership interest in some of our owned and in-licensed patents and patent applications. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we or our licensors may need the cooperation of any such co-owners of our owned and in-licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

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

Some of our patent applications have been granted or may be granted or allowed in the future. We cannot be certain that an allowed patent application will become an issued patent. There may be events that can cause the allowance of a patent application to be withdrawn. For example, after a patent application has been allowed, but prior to being issued, material that could be relevant to patentability may be identified. In such circumstances, the sponsor may pull the application from allowance in order for the USPTO to review the application in view of the new material. We cannot be certain that the USPTO will re-allow the application in view of the new material. Further, periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and following the issuance of a patent. We rely on our outside counsel and other professionals or our licensing partners to pay these fees due to the USPTO and non-U.S. government patent agencies and to help us comply with other procedural, documentary and other similar requirements and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, 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 might be able to enter the market, which would have a material adverse effect on our business.

Issued patents covering our product candidates or technology could be found invalid or unenforceable if challenged in court or the USPTO.

Despite the measures we take to obtain and maintain patent and other intellectual property rights with respect to our product candidates, our intellectual property rights could be challenged or invalidated. If we or one of our licensors initiate legal proceedings against a third party to enforce a patent covering one of our product candidates or our technology, the defendant could counterclaim that the patent covering our product candidate or technology, as applicable, is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post-grant review and equivalent proceedings in foreign jurisdictions (such as opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates or technology. 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 we, our patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates or technology. Such a loss of patent protection could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates.

Changes to patent law in the United States and in foreign jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States continues to adapt to wide-ranging patent reform legislation that became effective starting in 2012. Moreover, 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 regarding 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 new

legislation and decisions by the federal courts, and the USPTO, 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. For example, the U.S. Supreme Court, in the case *Amgen v. Sanofi*, held that broad functional antibody claims are invalid for lack of enablement. In addition, in *Juno v. Kite*, the Federal Circuit held claims reciting broad antibody genus based on function invalid for lack of written description. Recently, the Federal Circuit issued a precedential decision in *In re Cellect* (No. 22-1293) that could shorten or eliminate an extended patent term awarded under patent term adjustment if challenged on the basis of obviousness-type double patenting. While we do not believe that any of the patents owned or licensed by us will be found invalid based on these decisions, we cannot predict how future decisions by the courts, Congress or the USPTO may impact the value of our patents. Similarly, changes in the patent laws of other jurisdictions could adversely affect our ability to obtain and effectively enforce our patent rights, which would have a material adverse effect on our business and financial condition.

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

We have obtained allowed patents in the United States that we consider to be important for certain of our product candidates, however, we may have less robust intellectual property rights outside the United States, and, in particular, we may not be able to pursue generic coverage of our product candidates outside of the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in 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. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Most of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents 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.

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

We rely on in-license agreements for patent rights with respect to our product candidates and may in the future acquire or in-license additional third-party intellectual property rights on which we may similarly rely. We face risks with respect to such reliance, including the risk that we could lose these rights that are important to our business if we fail to comply with our obligations under these licenses or that we may be unable to acquire or in-license third-party intellectual property that may be necessary or important to our business operations.

We rely on third-party license agreements pursuant to which we have non-exclusive and exclusive rights to technology that is incorporated into our development programs and product candidates. For example, under our cross-license agreement with AskGene, we have exclusively in-licensed patent rights relating to our IL-2 program. In addition, under our license agreement with City of Hope, we have exclusively in-licensed certain patent rights that cover our anti-CTLA-4 antibody. We also have a license agreement with WuXi Biologics (Hong Kong) Limited, or WuXi Biologics, pursuant to which we received an exclusive worldwide license to specified monoclonal antibodies, or mAbs, and patent rights and know-how controlled by WuXi Biologics, including certain patent rights related to our anti-CTLA-4 mAb program. These license agreements impose diligence, milestone payment, royalty payment and other obligations on us.

Moreover, the growth of our business may depend in part on our ability to acquire, in-license or use additional third-party intellectual property rights. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Licenses to additional third-party intellectual property, technology, processes, and materials that may be required for the development and commercialization of our product candidates or technology may not be available at all or on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our product candidates or manufacturing processes, or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize our future product candidates or technologies, which could materially harm our business, financial condition, results of operations and growth prospects.

In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, in the event we do in-license third-party intellectual property rights, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

Under our agreement with City of Hope, we are responsible for the achievement of certain diligence milestones, and our failure to timely achieve such milestones could result in City of Hope's termination of the agreement or conversion of our exclusive licenses under the licensed patents to non-exclusive licenses. If City of Hope terminates the agreement or converts our licenses to non-exclusive licenses as a result of our failure to meet these diligence milestones, then our ability to commercialize products comprising our anti-CTLA-4 antibody may be impaired or we may face increased competition in the commercialization of anti-CTLA-4 antibody products. Furthermore, our agreement with City of Hope is subject to, and we expect our future license agreements may also be subject to, a reservation of rights by one or more third parties, including the licensor.

Under our agreement with AskGene, AskGene retained co-exclusive rights to exploit antigen-binding IL-2 products. Therefore, AskGene could develop and commercialize one or more antigen-binding IL-2 products on a more timely basis than us, if we ever develop such a product, or that are more effective or have more commercial success than products that we may develop. Additionally, AskGene is responsible for prosecution and maintenance of the licensed patents under the agreement and any future third party from whom we may license patent rights may similarly be responsible for prosecution and maintenance of such patents. We have limited control over the activities that are the responsibility of AskGene and would have limited control over the activities that are the responsibility of any future licensor, and it is possible that prosecution and maintenance of licensed patents by AskGene or any future licensor may be less vigorous than had we conducted such activities ourselves.

Disputes may arise regarding intellectual property subject to our current or any future license agreements, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the amount and timing of payments owed under the license agreements;
- our or our licensor's ability to defend intellectual property and to enforce intellectual property rights against third parties;
- the extent to which our technology, product candidates and processes infringe, misappropriate or otherwise violate any intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under the license agreement;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and any partners of ours; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. We are generally also subject to all of the same risks described in this Annual Report on Form 10-K with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately obtain or protect this intellectual property, our ability to commercialize products could suffer.

Our current and any potential future licensors might conclude that we have materially breached our license agreements and might therefore terminate the relevant license agreements, thereby removing our ability to develop and commercialize products and technology covered by such license agreements. If any of our current or future inbound license agreements are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products that are covered by such license agreements and underlying patents, which might be identical or similar to our products or product candidates. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and growth prospects. Our business also would suffer if any current or future licensors fail to abide by the terms of the license or fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights.

Any licensor of ours may have relied on third-party consultants or collaborators or on funds from third parties, such as the United States government, such that such licensor is not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

If our efforts to protect the proprietary nature of the intellectual property related to our technologies and product candidates are not adequate, we may not be able to compete effectively in our market.

Biotechnology and pharmaceutical companies generally, and we in particular, compete in a crowded competitive space characterized by rapidly evolving technologies and aggressive development of intellectual property.

We rely upon a combination of patents, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our technologies and our product candidates. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate

or surpass our technological achievements and product candidates, thus eroding our competitive position in our market. We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position.

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, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, licensees or licensors fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees or licensors 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. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. We cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries. Third parties may challenge the validity, enforceability or scope thereof. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe our patents. Various post-grant review proceedings, such as *inter partes* review, post-grant review and derivation proceedings, are available and may be pursued by any interested third party in the USPTO to challenge the patentability of claims issued in patents to us or our licensors. No assurance can be given as to the outcome of any such post-grant review proceedings. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates or technology is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced.

We may analyze patents or patent applications of our competitors that we believe are relevant to our activities, and consider that we are free to operate in relation to our product candidates, but our competitors may achieve issued claims, including in patents we consider to be unrelated, which block our efforts or may potentially result in our product candidates or our activities infringing such claims. On the other hand, the possibility exists that others will develop products which have the same effect as our products on an independent basis which do not infringe our patents or other intellectual property rights, or will design around the claims of patents that we have had issued that cover our products.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. For example, the AIA implemented in March 2013, moved the United States from a "first to invent" to a "first-to-file" system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The AIA includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a USPTO-administered post-grant review system that has affected patent litigation. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to make or use polypeptides or nucleic acids that are similar to our product candidates or components of our product candidates but that are not covered by the claims of our patents;

- the active biological ingredients in our current product candidates will eventually become commercially available in biosimilar drug products, and no patent protection may be available with regard to formulation or method of use;

- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regard to any patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;

- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies;

- it is possible that our pending patent applications will not result in issued patents;

- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;

- it is possible that others may circumvent our owned or in-licensed patents;

- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;

- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;

- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates or technology;

- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;

- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;

- it is possible that our owned or in-licensed patents or patent applications omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable;

- we have engaged in scientific collaborations in the past and will continue to do so in the future, and such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;

- we may not develop additional proprietary technologies for which we can obtain patent protection;

- it is possible that product candidates or technology we develop may be covered by third parties' patents or other exclusive rights; or

- the patents of others may have an adverse effect on our business.

Our proprietary position depends upon patents that are manufacturing, formulation or method-of-use patents, which may not prevent a competitor or other third party from designing around or using the same product candidate for another use.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of making or method of use. We cannot be certain, however, that the claims in our pending patent applications, including those claims covering the composition of matter of our product candidates, will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any of our patents that have issued or may issue will be considered valid and enforceable by courts in the United States or foreign countries. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions of matter relating to our product candidates, and instead may need to rely on secondary intellectual property, including patents or patent applications with claims covering formulations, methods of use and/or methods of manufacture. Method of use patents protect a specified method of using a product, such as a method of treating a particular medical indication. This type of patent may only be enforced against a competitor through indirect infringement, *i.e.*, inducement or contributory infringement, which is more difficult to prove than direct infringement. A competitor may be able to circumvent this type of patent by skinny labelling. Furthermore, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their products for our targeted indications, physicians may prescribe these products "off-label" for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent by enforcing patent rights or otherwise.

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

In addition to the protection afforded by patents, we seek to rely on trade secret protection, confidentiality agreements, and license and other agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. For example, significant elements of our product candidates, including aspects of sample preparation, methods of manufacturing, cell culturing conditions and related processes are based on unpatented trade secrets that are not publicly disclosed. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties. We have also adopted policies and conduct training that provides guidance on our expectations, and our advice for best practices, in protecting our trade secrets. However, we cannot provide assurance that these agreements and policies will not be breached by our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors and that our trade secrets and other proprietary and confidential information will not be disclosed to publicly or to competitors. We cannot be certain that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our trade secrets and other confidential proprietary know-how, information, or technology both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our trade secrets and other confidential information to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful.

Third-party claims of intellectual property infringement or violations may prevent or delay our discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the patents and violation of other proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination, and post-grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. We may be exposed to, or threatened with, future litigation or other adversarial proceedings by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents may ultimately issue because many patent filings cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

If a third party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims, which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;

- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us, which it is not required to do;

- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products; and

- redesigning our product candidates or processes so they do not infringe third-party intellectual property rights, which may not be possible or may require substantial monetary expenditures and time.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Third parties may assert that we are employing their proprietary technology without authorization. Generally, conducting preclinical and clinical trials and other development activities in the United States is not considered an act of infringement. If any of our product candidates is approved by the FDA, a third party may then seek to enforce its patent by filing a patent infringement lawsuit against us. While we do not believe that any claims that could otherwise have a materially adverse effect on the commercialization of our product candidates are valid and enforceable, we may be incorrect in this belief, or we may not be able to prove it in litigation. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods

of manufacture or methods for treatment related to the use or manufacture of our product candidates. Patent applications can take many years to issue.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents or patent applications, the scope of pending or issued patent claims, or the expiration of relevant patents are complete, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary to commercialization of our product candidates in any jurisdiction. There may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant third-party patents or incorrectly interpret the relevance, scope, or expiration of a third-party patent or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of any such patent may be able to block our ability to develop and commercialize the product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. In either case, such a license may not be available on commercially reasonable terms or at all. If we are unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and would be a substantial diversion of resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available on commercially reasonable terms or at all. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

Currently, we have certain intellectual property rights under patents and patent applications that we own or have rights to under our inbound license agreements related to our product candidates. Our development of additional product candidates may require the use of proprietary rights held by third parties, and the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights.

Our product candidates may also require specific formulations to work effectively and efficiently, and rights to such formulation technology may be held by others. Similarly, efficient production or delivery of our product candidates may also require specific compositions or methods, and the rights to these may be owned by third parties. Moreover, the specific components, such as linkers and antibody fragments, that will be used with our product candidates may be covered by the intellectual property rights of others. We may be unable to acquire or in-license any compositions, methods of use, formulations, processes or other third-party intellectual property rights from third parties that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by

such third-party intellectual property rights and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Additionally, we may collaborate with or sponsor research at academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration or sponsorship. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer.

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

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file lawsuits with infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

Third parties may initiate post-grant proceedings and the Patent Trial and Appeal Board of the USPTO may institute such proceedings to determine the validity or priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, or at all. Litigation or post-grant proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, infringement of our patents or misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

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 this type of litigation. 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.

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

We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances, where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time consuming. If we were unsuccessful, we could lose valuable rights in intellectual property that we regard as our own.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed confidential information of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

Many of our employees, consultants and advisers were previously employed at other pharmaceutical companies, including our competitors or potential competitors, in some cases until recently. Some of these employees, consultants, advisers, and members of management executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we take steps to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, advisers, and members of management have inadvertently or otherwise used or disclosed trade secrets or other confidential information of these former employers or competitors. In addition, we may in the future be subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defense to those claims fails, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Any litigation or the threat thereof may adversely affect our ability to hire employees. A loss of key personnel or their work product could hamper or prevent our ability to commercialize product candidates, which could have an adverse effect on our business, results of operations and financial condition.

In the future, we may in-license intellectual property that may have been discovered through government funded programs and thus may be subject to federal regulations and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

Any of the intellectual property rights that we have licensed or may license in the future and that have been generated through the use of U.S. government funding are subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our product candidates pursuant to the Bayh-Dole Act of 1980, or the Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose, generally referred to as "march-in rights." To our knowledge, none of our current product candidates are subject to march-in rights. However, intellectual property rights that we license in the future could be subject to such limitations. The U.S. government also has the right to take title to such intellectual property rights if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. We cannot be certain that our current or future licensors will comply with the disclosure or reporting requirements of the Bayh-Dole Act at all times or be able to rectify any lapse in compliance with these requirements.

In addition, the U.S. government requires that any products embodying the subject invention or produced using the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that, under the circumstances, domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit

our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

If we do not obtain patent term extension for any of our current or future product candidates, our business may be materially harmed.

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

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our marks of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The factors that may limit any potential competitive advantage provided by our intellectual property rights include:

- pending patent applications that we own or license may not lead to issued patents;
- patents, should they issue, that we own or license, may not provide us with any competitive advantages, or may be challenged and held invalid or unenforceable;
- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of any of our owned or in-licensed patents, should any such patents issue;

- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we (or our licensors) might not have been the first to make the inventions covered by a pending patent application that we own or license;
- we (or our licensors) might not have been the first to file patent applications covering a particular invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- we may not be able to obtain and/or maintain necessary licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights, or any rights at all, over that intellectual property;
- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operation.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drug and biologic products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We are not permitted to market our product candidates in the United States or in other countries until we receive approval of an NDA or BLA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Our product candidates are in various stages of development and are subject to the risks of failure inherent in development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have no experience as a company in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. The FDA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use.

Further, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA, or NDA or supplement to an NDA, for certain biological products and drug products, respectively, must contain data to assess the safety and effectiveness of the biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a deferral or waiver from the FDA. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate

is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. The applicable legislation in the EU also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the EMA or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the United States or the EU, we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

For example, in December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Further, in January 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the EU and replaced the prior Clinical Trials Directive 2001/20/EC. This regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the EU. Under the coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one EU Member State will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

Accordingly, any delay in obtaining or failure to obtain required approvals could negatively affect our ability or that of any future collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Disruptions in the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA, EMA and other agencies may also slow the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the Securities and Exchange Commission, or the SEC, had to furlough critical employees and stop critical activities.

In addition, disruptions may result from events similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. In the event of a similar public health emergency in the future, the FDA may not be able to continue its current pace and review timelines could be extended. Regulatory authorities outside the United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

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

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad. Any approval we may be granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions and any of our product candidates that may be approved for marketing in a foreign jurisdiction will be subject to risks associated with foreign operations.

In order to market and sell our products in the EU and other foreign jurisdictions, 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 approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive necessary approvals to commercialize our products in any market.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we fail to obtain the non-U.S. approvals required to market our product candidates outside the United States or if we fail to comply with applicable non-U.S. regulatory requirements, our target markets will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, we could face heightened risks with respect to obtaining marketing authorization in the United Kingdom as a result of the withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and EU Customs Union.

As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas under the terms of the Northern Ireland Protocol, Northern Ireland is currently subject to EU rules. The United Kingdom and EU have however agreed to the Windsor Framework which fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the United Kingdom Once implemented, the changes introduced by the Windsor Framework will see the MHRA be responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. Any delay in obtaining, or an inability to obtain, any marketing authorizations, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term

Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business. We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

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

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in the EU. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

We may seek orphan drug designations for our product candidates and may be unable to obtain such designations. Even if we do secure such designations and orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Further, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, to be more effective or to make a major contribution to patient care. Finally, orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

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

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

Any product candidate for which we obtain marketing approval will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, the approval may be subject to limitations on the

indicated uses for which the product may be marketed or to the conditions of approval or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy. Accordingly, if we receive marketing approval for one or more of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability.

Failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- 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;
- damage to relationships with collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions. Further, the marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and are also subject to EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Accordingly, assuming we, or our collaborators, receive marketing approval for one or more of our product candidates, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all

areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we, and our collaborators, are not able to comply with post-approval regulatory requirements, our or our 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 operating results and financial condition.

Any regulatory approval to market any of our products candidates for which we obtain approval will be limited by indication. If we fail to comply or are found to be in violation of FDA regulations restricting the promotion of any of our product candidates for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA, EMA, MHRA and other government agencies. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. Physicians may nevertheless prescribe products off-label to their patients in a manner that is inconsistent with the approved label. Prior to the approval of any of our product candidates, we intend to implement compliance and training programs designed to ensure that any future sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our products for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. In addition, under some relatively recent guidance from the FDA and the Pre-Approval Information Exchange Act, or PIE Act, signed into law as part of the Consolidated Appropriations Act of 2023, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

In recent years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission, or the FTC, and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the False Claims Act, the Prescription Drug Marketing Act and anti-kickback laws and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim or caused a false claim to be submitted to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and

corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

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

We may seek certain designations for one or more of our product candidates that could expedite review and approval by the FDA. A Breakthrough Therapy product is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens.

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

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

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

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

conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

Accelerated approval by the FDA, even if granted for any of our current or future product candidates, may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek approval of any of our current and future product candidates using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition, generally provides a meaningful advantage over available therapies, and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA or other applicable regulatory agency makes the determination regarding whether a surrogate endpoint is reasonably likely to predict long-term clinical benefit.

Prior to seeking such accelerated approval, we will seek feedback from the FDA and otherwise evaluate our ability to seek and receive such accelerated approval. As a condition of approval, the FDA requires that a sponsor of a product receiving accelerated approval perform an adequate and well-controlled post-marketing confirmatory clinical trial or trials. These confirmatory trials must be completed with due diligence and we may be required to evaluate different or additional endpoints in these post-marketing confirmatory trials. These confirmatory trials may require enrollment of more patients than we currently anticipate and will result in additional costs, which may be greater than the estimated costs we currently anticipate. In addition, the FDA currently requires as a condition for accelerated approval preapproval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

There can be no assurance that the FDA will agree with any proposed surrogate endpoints or that we will decide to pursue or submit a BLA for accelerated approval or any other form of expedited development, review or approval for any of our current or future product candidates. Similarly, there can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all.

The FDA may withdraw approval of a product candidate approved under the accelerated approval pathway if, for example, the trial required to verify the predicted clinical benefit of our product candidate fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period for commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

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

More recently, in March 2023, the FDA issued draft guidance that outlines its current thinking and approach to accelerated approval. The FDA indicated that the accelerated approval pathway is commonly used for approval of oncology drugs due to the serious and life-threatening nature of cancer. Although single-arm trials have been commonly used to support accelerated approval, a randomized controlled trial is the preferred approach as it provides a more robust efficacy and safety assessment and allows for direct comparisons to an available therapy. To that end, the FDA outlined considerations

for designing, conducting, and analyzing data for trials intended to support accelerated approvals of oncology therapeutics. While this guidance is currently only in draft form and will not be legally binding even when finalized, we will need to consider the FDA's guidance closely if we seek accelerated approval for any of our products. Accordingly, even if we do receive accelerated approval, we may not experience a faster development or regulatory review or approval process, and receiving accelerated approval does not provide assurance of ultimate full FDA approval.

In the EU, a "conditional" marketing authorization may be granted in cases where all the required safety and efficacy data are not yet available. A conditional marketing authorization is subject to conditions to be fulfilled for generating missing data or ensuring increased safety measures. A conditional marketing authorization is valid for one year and has to be renewed annually until fulfillment of all relevant conditions. Once the applicable pending studies are provided, a conditional marketing authorization can become a "standard" marketing authorization. However, if the conditions are not fulfilled within the timeframe set by the EMA, the marketing authorization will cease to be renewed.

Current and future legislation may increase the difficulty and cost for us to obtain reimbursement for any of our candidate products that do receive marketing approval.

In the United States and 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 product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

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

Under current legislation, the actual reductions in Medicare payments may vary up to 4%. The Consolidated Appropriations Act, which was signed into law by President Biden in December 2022, made several changes to sequestration of the Medicare program. Section 1001 of the Consolidated Appropriations Act delays the 4% Statutory Pay-As-You-Go Act of 2010, or PAYGO, sequester for two years, through the end of calendar year 2024. Triggered by enactment of the American Rescue Plan Act of 2021, the 4% cut to the Medicare program would have taken effect in January 2023. The Consolidated Appropriation Act's health care offset title includes Section 4163, which extends the 2% Budget Control Act of 2011 Medicare sequester for six months into fiscal year 2032 and lowers the payment reduction percentages in fiscal years 2030 and 2031.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Act, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace, which began on February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such other challenges to repeal or replace the ACA or the health reform measures of the Biden administration will impact the ACA or our business.

In the EU, on December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. While the Regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once applicable, it will have a phased implementation depending on the concerned products. The Regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products as well as certain high-risk medical devices, and provide the basis for cooperation at the EU level for joint clinical assessments in these areas. It will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the highest potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional 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. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

Current and future legislative efforts may limit the prices for our products, if and when they are licensed for marketing, and that could materially impact our ability to generate revenues.

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

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. That

regulation was challenged in a lawsuit by the Pharmaceutical Research and Manufacturers of America, or PhRMA, but the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Nine states (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and Wisconsin) have passed laws allowing for the importation of drugs from Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting approval. On January 5, 2023, the FDA approved Florida's plan for Canadian drug importation. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration until January 1, 2026 by the Infrastructure Investment and Jobs Act. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with the passage of the Inflation Reduction Act of 2022, or the IRA, has been delayed by Congress to January 1, 2032.

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

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

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period must pay 100% of the cost of their prescriptions until they reach

the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

We expect that current or future litigation involving provisions of the IRA will have unpredictable and uncertain results on the implementation and impact of the IRA on biotechnology industry generally, as well as our business and current or future products. For example, on June 6, 2023, Merck & Co., or Merck, filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits in various courts with similar constitutional claims against the HHS and CMS. We expect that litigation involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

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

Finally, outside the United States, in some nations, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished future profits and earnings, if any.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our current and future arrangements with healthcare providers and third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research as well as market, sell and distribute any products for which we obtain marketing approval. Potentially applicable U.S. federal and state healthcare laws and regulations include the following:

- *Anti-Kickback Statute*. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid.

- *False Claims Laws*. The federal false claims laws and civil monetary penalties laws, including the civil False Claims Act and the Civil Monetary Penalty Law, impose criminal and civil penalties, including those from civil

whistleblower or qui tam actions against individuals or entities for knowingly presenting, or causing to be presented to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government.

- *HIPAA*. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program.

- *HIPAA and HITECH*. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- *False Statements Statute*. The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

- *Transparency Requirements*. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Department of Health and Human Services information related to payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), other healthcare providers, and ownership and investment interests by physicians and their immediate family members. As of January 1, 2022, applicable manufacturers are also required to report such information regarding its payments and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

- *Analogous State and Foreign Laws*. Analogous state laws and regulations, such as state anti-kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the EU. Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business arrangements with third parties, and our business generally, 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 products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do

business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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

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

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

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

There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission, or FTC, and state attorneys general all are aggressive in reviewing privacy and data security protections for consumers. In addition, new laws have been enacted or are considered at both the federal and state levels. As a result, we will need to seek to ensure our business practices comply with evolving rules and guidance at the federal and state level related to privacy and data security in order to mitigate our risk for any potential enforcement action, which may be costly. In addition, if we are subject to an enforcement action and settlement order, we may be required to adhere to very specific privacy and data security practices or pay fines and adhere to specified compliance requirements, all of which could be costly and adversely impact our business.

For example, the FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be "unfair" under Section 5 of the FTC Act, as well as the types of activities it views to trigger the Health Breach Notification Rule, which the FTC also has the authority to enforce, and is in the process of developing rules related to commercial surveillance and data security.

Similarly, in 2018, California passed into law the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020 and imposed many requirements on businesses that process the personal information of California

residents. Many of the CCPA's requirements are similar to those found in the General Data Protection Regulation, or the GDPR, including requiring businesses to provide notice to data subjects regarding the information collected about them and how such information is used and shared, and providing data subjects the right to request access to such personal information and, in certain cases, request the erasure of such personal information. The CCPA also affords California residents the right to opt-out of "sales" of their personal information. The CCPA contains significant penalties for companies that violate its requirements. In addition, the California Privacy Rights Act, or the CPRA, went into effect on January 1, 2023 and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created the California Privacy Protection Agency, a new enforcement agency whose sole responsibility is to enforce the CPRA.

In addition to California, at least 11 other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2023 legislative sessions that will go into effect in 2024 and beyond, including New Hampshire and New Jersey. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state recently passed a health privacy law that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

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

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

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the EU-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the EU to the United

States. However, some privacy advocacy groups have already suggested that they will be challenging the EU-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the EU-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact our business at the international level.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the EEA to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like a EU member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

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

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

We are subject to U.S. and certain foreign export control, import, sanctions, anti-corruption, and anti-money laundering laws and regulations with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 202, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. In addition, we may engage third-party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with the laws and regulations described above could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage and other collateral consequences. If any subpoenas, investigations or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

Changes in U.S. and international trade policies, particularly with respect to China, may adversely impact our business and operating results.

The U.S. government has recently made statements and taken certain actions that may lead to potential changes to U.S. and international trade policies, including imposing several rounds of tariffs and export control restrictions affecting certain products manufactured in China, and, most recently, proposing legislation that, if passed, would restrict trade with certain Chinese companies that provide biopharmaceutical research, development and manufacturing services. Recently, both China and the United States have each imposed tariffs indicating the potential for further trade barriers. It is unknown whether and to what extent new tariffs, export controls, trade restrictions, or other new laws or regulations will be adopted, or the effect that any such actions would have on us or our industry. Sustained uncertainty about, or the further escalation of, trade and political tensions between the United States and China could result in a disadvantageous research and manufacturing environment in China, particularly for U.S.-based companies, including retaliatory restrictions that hinder or potentially inhibit our ability to rely on our CDMO and other service providers that operate in China. For example, proposed legislation has been introduced in Congress that could prohibit, among other things, the use of U.S. government executive agency contract, grant, or loan funding to provide or to enter into, extend or renew contracts involving the use of certain equipment or services produced or provided by certain Chinese companies, which could cause us to reevaluate our relationship with our current CDMO, which is located in China. While we have not started commercialization of drug candidates, any unfavorable government policies on international trade, such as export controls, capital controls, tariffs or other trade restrictions, may affect the demand for our drug products, the competitive position of our product candidates, and import or export of raw materials and finished product candidate used in our preclinical studies and clinical trials, particularly with respect to our manufactured product candidates that we import from China, including pursuant to our manufacturing arrangements and license agreement with WuXi Biologics. If any new tariffs, export controls, legislation and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if the U.S. government takes retaliatory trade actions due to the recent U.S.-China trade tension, such changes could have an adverse effect on our business, financial condition and results of operations.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. 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 also produce hazardous waste products. Even if 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 us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, however 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. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

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

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, CROs, consultants, commercial partners, vendors and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU and other jurisdictions, provide accurate information to the FDA, the EC and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. Even with appropriate policies and procedures, it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent such activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

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

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

We are highly dependent on the management, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our scientific and clinical teams. Although we have employment offer letters which outline the terms of employment with each of our executive officers, each of them may terminate their employment with us at any time. As such, these employment offer letters do not guarantee our retention of our executive officers for any period of time. In addition, insurance coverage is increasingly expensive, including with respect to directors' and officers' liability insurance, or D&O insurance. We may not be able to maintain D&O insurance at a reasonable cost or in an amount adequate to satisfy any liability that may arise. An inability to secure and maintain D&O insurance may make it difficult for us to retain and attract talented and skilled directors and officers to serve our company, which could adversely affect our business. We do not maintain "key person" insurance for any of our employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we are successful in obtaining marketing approval for our product candidates, sales and marketing personnel, is and will be critical to our success. The loss of the services of our executive officers or other key employees could impede, delay or prevent the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval for and commercialize products in the life sciences industry, and specifically our product candidates. We are based in Massachusetts, a state that is home to many other biopharmaceutical companies as well as many academic and research institutions, resulting in fierce competition for qualified personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their

former employers own their research output. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Additionally, the United States is experiencing a workforce shortage, which in turn has created a competitive wage environment, which is likely to further exacerbate the foregoing risks and may impact our ability to retain our executive officers or other key employees. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited and could adversely affect our business, prospects, financial condition and results of operations.

Our cost savings plan and the associated workforce reduction implemented in March 2024 may not result in anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.

In connection with our strategic portfolio reprioritization in March 2024, we implemented a workforce reduction, representing approximately 21% of our workforce prior to the reduction in headcount. We may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from our restructuring efforts due to unforeseen difficulties, delays or unexpected costs. We expect to incur one-time costs of approximately $1.0 million primarily related to cash expenditures for severance and benefits continuation, and we estimate the workforce reduction will be substantially completed in the first half of 2024. If we are unable to realize the expected operational efficiencies and cost savings from the restructuring, our operating results and financial condition could be adversely affected. We also cannot guarantee that we will not have to undertake additional workforce reductions or restructuring activities in the future. Furthermore, our workforce reduction may be disruptive to our operations, or could yield unanticipated consequences, such as attrition beyond planned staff reductions, or disruptions in our day-to-day operations. Our workforce reductions could also harm our ability to attract and retain qualified management, scientific, clinical, and manufacturing personnel who are critical to our business. Any failure to attract or retain qualified personnel could prevent us from successfully developing and commercializing our product candidates in the future, if approved.

We depend on our information technology systems and those of our third-party service providers, and any failure of these systems could harm our business. Security breaches, loss of data, inability to access systems, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability or competitive or reputational harm, which could adversely affect our business, results of operations and financial condition.

We collect and maintain information in digital and other forms that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the privacy, security, confidentiality, availability and integrity of such confidential information. Our internal information technology systems and infrastructure, and those of our contractors, consultants, vendors, service providers and other third parties on which we rely, are vulnerable to damage or unauthorized access or use resulting from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, denial or degradation of service attacks, ransomware, hacking, phishing and other social engineering attacks, attachments to emails, intentional or accidental actions or inactions by persons inside our organization or by persons with access to systems inside our organization.

The risk of a security breach or disruption or data loss, particularly through cyber-attacks or cyber intrusion, including by computer hackers, supply chain attacks, 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. Additionally, attackers may use artificial intelligence and machine learning to launch more automated, targeted and coordinated attacks against targets. In addition, the prevalent use of mobile devices that access confidential information increases the risk of lost or stolen devices, security incidents and data security breaches, which could lead to the loss of confidential information or other intellectual property. We also may face increased risks of a security breach or disruption due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. The costs to us to mitigate network security problems, bugs,

viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures 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, negative publicity and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs.

Any security compromise affecting us, our partners, our service providers or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures and lead to regulatory scrutiny. If such an event were to occur and cause interruptions in our operations or result in the unauthorized acquisition of or access to personally identifiable information or individually identifiable health information (violating certain privacy laws, as applicable, such as HIPAA, CCPA, HITECH and GDPR), it could result in a material disruption of our discovery and development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. Some of the federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Notifications and follow-up actions related to a security breach could impact our reputation, cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We would also be exposed to a risk of loss, governmental investigations or enforcement, or litigation and potential liability, any of which could materially adversely affect our business, results of operations and financial condition. While we do maintain cyber liability insurance, our insurance coverages may not be sufficient in type or amount to cover us against any such losses, claims, or liabilities related to security breaches, cyber-attacks, cyber intrusion, or other related breaches or disruptions.

A variety of risks associated with marketing our product candidates internationally, if approved, could materially adversely affect our business.

We also plan to seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating, including conducting marketing and sales activities, in international jurisdictions if we obtain the necessary approvals, including:

- regulatory requirements in foreign countries that differ from those in the United States;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or other comparable foreign regulations;

- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

- business interruptions resulting from geopolitical actions, including war, armed conflicts and terrorism or natural disasters, including pandemics or other outbreaks of infectious disease, earthquakes, typhoons, floods and fires.

Any of these factors, along with other risks associated with international operations, could materially adversely affect our future international expansion and operations and, consequently, our results of operations.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future acquisitions may also require us to obtain sufficient additional capital, which may not be available on favorable terms or at all. These transactions may not be successful and may require significant time and attention of management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize any or all potential benefits of the acquisition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

Our operations or those of the third parties upon whom we depend might be affected by the occurrence of a catastrophic event, such as a terrorist attack, war or other armed conflict, geopolitical tensions or trade wars, pandemic or natural disaster.

We depend on our employees, consultants, CDMOs, CROs, as well as regulatory agencies and other parties, for the continued operation of our business. While we maintain disaster recovery plans, they might not adequately protect us. Despite any precautions that we or any third parties on whom we depend take for catastrophic events, including terrorist attacks, wars or other armed conflicts, geopolitical tensions or trade wars, pandemics or natural disasters, these events could result in significant disruptions to our research and development, manufacturing, preclinical studies, clinical trials, and, ultimately, if approved, the commercialization of our products. Long-term disruptions in the infrastructure caused by these types of events, such as natural disasters, which are increasing in frequency due to the impacts of climate change, the outbreak of wars or other armed conflicts, the escalation of hostilities, geopolitical tensions or trade wars, acts of terrorism or "acts of God," particularly involving geographies in which we or third parties on whom we depend have offices, manufacturing or clinical trial sites, could adversely affect our businesses. Although we carry business interruption insurance policies and typically have provisions in our contracts that protect us in certain events, our coverage might not include or be adequate to compensate us for all losses that may occur. Any catastrophic event affecting us, our CDMOs, our CROs, regulatory agencies or other parties with which we are engaged could have a material adverse effect on our operations and financial performance.

Risks Related to Ownership of Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may never develop or be sustained.

Although our common stock is listed on the Nasdaq Global Select Market, an active trading market for our shares may never develop or be sustained. As a result, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares, or at all.

The price of our common stock has been, and could continue to be, subject to volatility related or unrelated to our operations and purchasers of our common stock could suffer a decline in value.

The market price of our common stock has been, and may continue to be, subject to significant fluctuations in response to numerous factors, many of which are beyond our control. The stock market in general and the market for biotechnology and pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the results from our preclinical studies and clinical trials;
- the commencement, enrollment or results of any current or future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results from, delays in initiating or completing, or termination of clinical trials;
- unanticipated serious safety concerns related to the use of our product candidates;
- clinical trial results from, or regulatory developments regarding, a competitor's product candidate;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- regulatory or legal developments in the United States and foreign countries;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- the public's response to press releases or other public announcements by us or third parties, including our filings with the SEC, and announcements relating to acquisitions, strategic transactions, licenses, joint ventures, collaborations, capital commitments, intellectual property, litigation or other disputes impacting us or our business;
- lower than expected market acceptance of our product candidates, if approved;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- variations in the level of expenses related to our preclinical and clinical development programs, including relating to the timing of invoices from, and other billing practices of, our CROs and clinical trial sites;
- variations in the level of expenses related to our commercialization activities, if any product candidates are approved;

- the clinical results of our competitors or potential competitors;
- introduction of new products or services by our competitors;
- changes in financial estimates by us or by any securities analysts who might cover our common stock;
- conditions or trends in our industry;
- our cash position;
- sales of our common stock by us or our stockholders in the future;
- adoption of new, or changes to current accounting standards;
- ineffectiveness of our internal controls;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biotechnology and pharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- changes in the structure of healthcare payment systems;
- investors' general perception of our company and our business;
- overall performance of the equity markets;
- trading volume of our common stock;
- potential inclusion or exclusion of our common stock in exchange, industry, or other tracking indices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies and product candidates;
- significant lawsuits, including patent or stockholder litigation;
- proposed changes to healthcare laws, intellectual property laws or pharmaceutical pricing in the United States or foreign jurisdictions, or speculation regarding such changes;
- future sales of our common stock by our officers, directors and significant stockholders;
- recruitment or departure of key personnel;
- public health epidemics or pandemics, such as the COVID-19 pandemic, and any recession, depression, or other sustained adverse market event or economic impact resulting from such epidemics or pandemics;

- general political, economic, industry and market conditions; and

- other events or factors described in this "Risk Factors" section, many of which are beyond our control.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. This risk is especially relevant for us, because biopharmaceutical companies have experienced significant stock price volatility in recent years. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

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

The trading market for our common stock relies, in part, on the research and reports that securities or industry analysts publish about us or our business. A limited number of securities and industry analysts currently publish research on our company. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. Although we have obtained analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

Unstable global economic and political conditions, including economic uncertainty tied to interest rates and heightened inflation, credit and financial market instability, and uncertainty related to ongoing geopolitical conflicts, could adversely affect our business, financial condition, stock price and ability to raise capital.

Unstable global economic and political conditions, including economic uncertainty tied to interest rates and heightened inflation, credit and financial market instability, and uncertainty related to ongoing geopolitical conflicts, could adversely affect our business, financial condition, stock price and ability to raise capital. The global economy, in particular the financial markets, have recently experienced significant disruption and volatility, including without limitation, as a result of heightened inflation, capital market volatility, interest rate and currency rate fluctuations, volatility in commodity prices, decline in consumer confidence and economic growth, supply chain disruptions, banking disruptions, and uncertainty resulting from geopolitical events, including trade wars, civil and political unrest, wars and other armed conflicts. In addition, market volatility, high levels of inflation and high interest rates may increase our cost of financing or restrict our access to potential sources of future capital. Furthermore, our stock price may further decline due in part to the volatility of the stock market and any general economic downturn. If the disruption and volatility persist or deepen, we may be unable to raise sufficient additional capital on acceptable terms, or at all. If we are unable to raise sufficient additional capital, our business, financial condition, stock price and results of operations could be adversely affected, and we will need to implement cost reduction strategies, which could include delaying, reducing or altogether terminating both internal and external costs related to our operations and research and development programs. In addition, political developments impacting government spending and international trade, including changes in trade agreements, trade disputes, tariffs and investment restrictions, such as the ongoing trade dispute between the United States and China, may negatively impact markets and cause weaker macroeconomic conditions. These global economic and political factors could also strain certain of our suppliers and manufacturers, including our primary CDMO, possibly resulting in supply disruptions or increased raw material or manufacturing costs, or adversely impacting their ability to manufacture clinical trial materials for our product candidates. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic and geopolitical climate and financial market conditions could adversely impact our business.

Our principal stockholders and management own a significant percentage of our common stock and exert significant control over matters subject to stockholder approval.

As of March 25, 2024, our executive officers, directors, holders of 5% or more of our common stock and their respective affiliates beneficially owned shares in the aggregate representing a majority of our outstanding common stock. As a result

of their share ownership, these stockholders, if they act together, would have the ability to influence our management and policies and would be able to significantly affect the outcome of matters requiring stockholder approval, such as elections of directors, amendments of our organizational documents or approvals of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that our stockholders may feel are in their best interest.

Some of these persons or entities may have interests different than our unaffiliated stockholders, or they may want us to pursue strategies that deviate from the interests of other stockholders. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- entrench our management and board of directors;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

We have broad discretion regarding use of our cash and cash equivalents, and we may not use them effectively.

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

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any determination to pay dividends in the future will be at the sole discretion of our board of directors. In addition, the terms of any future debt agreements may preclude us from paying dividends. Any return to stockholders will therefore be limited in the foreseeable future to the appreciation of their stock.

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

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until December 31, 2026, although if the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have annual gross revenues of $1.235 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1.0 billion of non-convertible debt over a three-year period. For so long as we remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

- reduced disclosure obligations regarding executive compensation; and

- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Even after we no longer qualify as an emerging growth company, we may continue to qualify as a smaller reporting company, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation. In addition, if we are a smaller reporting company with less than $100 million in annual revenue, we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404.

We cannot predict whether investors will find our common stock less attractive if we 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.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we can adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an EGC or a smaller reporting company. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

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

As a public company, we have incurred and will continue to incur substantial legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, Nasdaq listing requirements, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

We evaluate developments in these rules and regulations as they are promulgated and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often 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. We intend to continue to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be materially adversely effected.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC or a smaller reporting company with less than $100 million in annual revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our

independent registered public accounting firm. To comply with Section 404, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also subject us to regulatory scrutiny and sanctions, impair our ability to raise revenue and cause investors to lose confidence in our reported financial information, which could harm our business and have a negative effect on the trading price of our common stock and adversely affect our results of operations and financial condition.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an EGC or a smaller reporting company with less than $100 million in annual revenue, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an EGC for up to five years. An independent assessment of the effectiveness of our internal control over financial reporting could detect problems that our management's assessment might not. 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, which could have a negative effect on the trading price of our common stock and adversely affect our results of operations and financial condition.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

As a public company, we are subject to certain reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal control over financial reporting, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. The Tax Act, enacted on December 22, 2017, as amended by the CARES Act, enacted on March 27, 2020, significantly revises the Code. The Tax Act contains, among other things, significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21% and the limitation of the deduction for net operating losses to 80% of current-year taxable income for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). In addition, beginning in 2022, the Tax Act eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over five years or fifteen years (for expenditures attributable to foreign research).

In addition to the CARES Act, as part of Congress's response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021 containing tax provisions. The IRA was also signed into law in August 2022. The IRA introduced new tax provisions, including a 1% excise tax imposed on certain stock repurchases by publicly traded corporations. The 1% excise tax generally applies to any acquisition by the publicly traded corporation (or certain of its affiliates) of stock of the publicly traded corporation in exchange for money or other property (other than stock of the corporation itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases. Regulatory guidance under the Tax Act, the CARES Act, the IRA, and such additional legislation is and continues to be forthcoming. Such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, the IRA, and additional tax legislation.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our restated certificate of incorporation and our second amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

- require the approval of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware and the federal district courts of the United States of America as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers and employees and increase the costs to our stockholders of bringing such claims.

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;

- any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders;

- any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or

- any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine.

These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, and increase the costs to such stockholders of bringing such a claim, either of which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find the either exclusive forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could materially adversely affect our business, financial condition and operating results.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Cybersecurity Risk Management and Strategy

We have established processes for assessing, identifying and managing cybersecurity risks, which are built into our overall information technology, or IT, function. These processes are designed to help protect our operations and information assets from unauthorized access or attack, as well as secure our networks and information systems. Such processes include technical, procedural, and organizational safeguards, including, without limitation: detection and response platforms on all endpoints within the organization; various additional security tools designed to help protect, identify, escalate, investigate, resolve and recover from security incidents in a timely manner; monitoring and regular testing of our data controls and provenance for vulnerabilities; incident simulations; incident response plans; employee training, including bimonthly phishing simulations to provide "experiential learning" on how to recognize phishing attempts; integrated and easily accessible mechanisms available to all employees that encourage proactive reporting of any perceived or actual vulnerabilities across the organization; and routine review of our policies and procedures to identify risks and refine our practices.

As part of these processes, we engage a third-party penetration testing firm to conduct annual penetration testing from both internal and external perspectives to identify and mitigate potential vulnerabilities. We also consider the internal risk oversight programs of third-party service providers, and our IT department uses an audit review process to evaluate the internal controls of third-party vendors who will have access to personally identifiable information or our confidential financial data.

We do not believe there are currently any known risks from cybersecurity threats, including as a result of any previous cybersecurity incident of which we are aware, that are reasonably likely to materially affect our business strategy, results of operations or financial condition. For more information regarding cybersecurity risks and the potential related impacts on our Company, please see the risk factor beginning with the caption "*We depend on our information technology systems and those of our third-party service providers, and any failure of these systems could harm our business*" in Part I, Item 1A. "Risk Factors" in this Annual Report on Form 10-K.

Governance

Our board of directors is responsible for monitoring and assessing strategic risk exposures, including reviewing our policies and practices with respect to risk assessment and risk management. The audit committee of our board of directors assists the board of directors with this responsibility by discussing our risk assessment and risk management policies, including the guidelines and policies that govern the process by which we manage our exposure to cybersecurity risks, with members of management on a periodic basis, and the audit committee is notified between such updates regarding significant new cybersecurity threats or incidents. The audit committee, in turn, periodically reports on its review to the board of directors.

Management is responsible for the day-to-day assessment and management of cybersecurity risks. Our senior vice president of information technology, or our SVP, IT, has primary oversight of material risks from cybersecurity threats and leads the operational oversight of company-wide cybersecurity strategy, policy, standards and processes, including through his management of, and participation in, the cybersecurity risk management and strategy processes described above, and his oversight of our incident response plans and escalation procedures described below. Our SVP, IT reports to our chief operating officer, or COO, and is an experienced information technology leader with over 25 years of expertise in cybersecurity defense, both in academic and corporate environments. This experience includes, but is not limited to, data defense, perimeter and infrastructure defense, corporate risk awareness, compliance adherence, and cybersecurity training and leadership.

We have also established a cross-functional information security counsel, or ISC, led by our SVP, IT, that brings together representatives from across the organization, including from our IT, finance, clinical, human resources, research and

development, program leadership, facilities, and legal functions, that is responsible for reviewing, responding, mitigating and reporting all cybersecurity incidents. The ISC meets quarterly and on an ad hoc basis, as necessary. In the event of a cybersecurity incident, our ISC is promptly convened and follows a standardized review and mitigation process and incident response plan, which includes escalation to our data protection committee, or DPC. Our DPC is composed of our SVP, IT, our COO, our senior vice president, finance and accounting, and senior members of our legal and IT teams and is responsible for assessing, among other factors, the actual or potential operational, business, financial, legal or reputational impact of a cybersecurity incident on the Company. The DPC is also responsible for notifying the audit committee of the board of directors in the event of a significant cybersecurity threat or incident.

Item 2. Properties

We occupy approximately 28,000 square feet of office and laboratory space in Waltham, Massachusetts under a lease that expires in March 2030 with an option to renew for an additional five years. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are currently not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our common stock is traded on the Nasdaq Global Select Market under the symbol "XLO." Trading of our common stock commenced on October 22, 2021, following the completion of our initial public offering, or IPO. Prior to that date, there was no public market for our common stock.

Holders

As of March 25, 2024, there were 35 holders of record of our common stock. This number does not include beneficial owners whose shares are held in street name.

Dividend Policy

We have never paid cash dividends and we do not anticipate paying any cash dividends on our shares of common stock in the foreseeable future. We intend to retain any future earnings for reinvestment in our business. Any future determination to pay cash dividends will be at the discretion of our board of directors, and will be dependent upon our financial condition, results of operations, capital requirements and such other factors as our board of directors deems relevant.

Item 6. [Reserved]

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

The following discussion and analysis is meant to provide material information relevant to an assessment of the financial condition and results of operations of our company, including an evaluation of the amounts and uncertainties of cash flows from operations and from outside resources, so as to allow investors to better view our company from management's perspective. You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K.

Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the section entitled "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. You should carefully read the section entitled "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements.

Overview

We are a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology, or I-O, therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. We are leveraging our proprietary platform to build a pipeline of novel, tumor-activated I-O molecules that are designed to optimize the therapeutic index by localizing anti-tumor activity within the tumor microenvironment, including tumor-activated cytokines and antibodies (including bispecifics) and immune cell engagers (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers). Current I-O therapies have curative potential for patients with cancer; however, their potential is significantly curtailed by systemic toxicity that results from activity of the therapeutic molecule outside the tumor microenvironment. Our molecules are engineered to localize activity within the tumor microenvironment with minimal systemic effects, resulting in the potential to achieve enhanced anti-tumor activity and increasing the population of patients who may be eligible to receive our medicines. Our most advanced tumor-activated, clinical-stage product candidates are XTX101, an Fc-enhanced, anti-CTLA-4 monoclonal antibody, or mAb, XTX301, an interleukin 12, or IL-12, therapy, and XTX202, an interleukin 2, or IL-2, therapy. In 2023, we presented clinical data across these programs showing initial clinical validation for each of these molecules and our tumor-activated approach. In addition to our clinical-stage product candidates, we are continuing to leverage our differentiated research platform and expertise in developing tumor-activated I-O therapies to advance preclinical development for tumor-activated bispecific molecules and immune cell engager molecules (including tumor-activated cell engagers and tumor-activated effector-enhanced cell engagers).

To date, we have financed our operations primarily from proceeds raised through private placements of preferred units and convertible preferred stock, a debt financing and our initial public offering, or IPO, of common stock in October 2021. We have not generated any revenue from product sales and do not expect to generate any revenue from product sales for at least the next several years, if at all. All of our programs are in early clinical or preclinical development. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our product candidates, if approved. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve profitability. Even if we are able to generate revenue from product sales, we may not become profitable.

Recent Developments

Exclusive License Agreement with Gilead

On March 27, 2024, our wholly-owned subsidiary, Xilio Development, Inc., or Xilio Development, entered into an exclusive license agreement with Gilead Sciences, Inc., or Gilead, pursuant to which it granted Gilead an exclusive global

license to develop and commercialize XTX301, our tumor-activated IL-12 product candidate, and specified other molecules directed to IL-12.

Xilio Development will be responsible for conducting clinical development for XTX301 in the ongoing Phase 1 clinical trial through an initial planned Phase 2 dose expansion. Following the delivery by Xilio Development of a specified clinical data package for XTX301 related to the Phase 1 clinical trial and planned Phase 2 clinical trial, Gilead can elect to transition responsibilities for the development and commercialization of XTX301 to Gilead, subject to the terms of the license agreement and payment by Gilead of a $75.0 million transition fee.

Under the license agreement, we are eligible to receive approximately $43.5 million in upfront payments, including a cash payment of $30.0 million and an initial equity investment by Gilead of approximately $13.5 million of our common stock at a purchase price of $1.97 per share. The initial equity investment closed on March 28, 2024, and the $30.0 million upfront cash payment is payable by Gilead within a specified time period promptly following signing of the license agreement. We will be eligible to receive up to $604.0 million in additional contingent payments, which include (i) the proceeds from up to three additional private placements of common stock, (ii) the $75.0 million transition fee and (iii) specified development, regulatory and sales-based milestones. Prior to the potential transition fee, up to $29.0 million of the total contingent payments are related to the potential additional private placements of common stock and a near-term development milestone. In addition, we are eligible to receive tiered royalties ranging from high single digits to mid-teens on annual global net product sales.

In connection with the execution of the license agreement, on March 27, 2024, we entered into a stock purchase agreement with Gilead. In addition to the initial equity investment by Gilead of approximately $13.5 million of our common stock, through March 27, 2025, we may, at our election and subject to the terms and conditions of the stock purchase agreement, cause Gilead to purchase up to approximately $11.5 million of additional shares of common stock (including, at Gilead's sole election, prefunded warrants in lieu of shares of common stock) in up to three additional private placements at a predetermined price per share specified therein, at all times subject to Gilead not being deemed the beneficial owner of greater than 19.9% of our common stock upon the closing of the applicable additional private placement with Gilead. If Gilead elects to purchase prefunded warrants, each prefunded warrant will have an exercise price of $0.0001 per share of common stock, be immediately exercisable and remain exercisable until exercised in full. Gilead may not exercise its prefunded warrants to the extent that it would beneficially own more than 19.99% of the number of shares of common stock outstanding immediately after giving effect to such exercise. Any prefunded warrants that may be issued to Gilead in an additional private placement with Gilead will be in substantially the same form as the prefunded warrants issued to investors in the March 2024 private placement.

March 2024 Private Placement

On March 28, 2024, we entered into a securities purchase agreement with certain existing accredited investors, including Bain Capital Life Sciences and Rock Springs Capital, to issue and sell an aggregate of 1,953,125 shares of our common stock at a price of $0.64 per share and prefunded warrants to purchase up to an aggregate of 15,627,441 shares of our common stock at a purchase price of $0.6399 per prefunded warrant share, through a private investment in public equity financing. The prefunded warrants will have an exercise price of $0.0001 per share of common stock, be immediately exercisable and remain exercisable until exercised in full. We anticipate receiving aggregate gross proceeds from the private placement of approximately $11.3 million, before deducting placement agent fees and expenses payable by us. The private placement is expected to close on April 2, 2024, subject to the satisfaction of customary closing conditions. We expect to use the proceeds from the private placement to fund working capital and other general corporate purposes.

Strategic Portfolio Reprioritization and Workforce Reduction

On March 27, 2024, our board of directors approved a strategic portfolio reprioritization and restructuring. As part of the strategic portfolio reprioritization and restructuring, we plan to:

- focus on rapidly advancing clinical development for XTX301 and XTX101 and leveraging our promising research platform to advance differentiated bispecific and cell-engager molecules;

- discontinue further investment in XTX202 as a monotherapy and explore strategic opportunities to continue to develop XTX202 with other agents; and

- undertake efforts to further reduce our expenses and streamline our operations, including a reduction in headcount of 15 employees, representing approximately 21% of our workforce immediately prior to the workforce reduction.

Repayment of Loan and Security Agreement

In the first quarter of 2024, we repaid all amounts outstanding under the loan and security agreement, as amended, with Pacific Western Bank, or PacWest, and PacWest released all security interests in our and our affiliates' assets.

Liquidity and Going Concern Overview

Since inception, we have incurred significant operating losses, including net losses of $76.4 million and $88.2 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of $325.5 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future, particularly to the extent we:

- continue to advance our current research programs and conduct additional research programs;

- advance our current product candidates and any future product candidates we may develop into preclinical and clinical development;

- seek marketing approvals for product candidates that successfully complete clinical trials, if any;

- obtain, expand, maintain, defend and enforce our intellectual property;

- hire additional research, clinical, regulatory, quality, manufacturing and general and administrative personnel;

- establish a commercial and distribution infrastructure to commercialize products for which we may obtain marketing approval, if any;

- continue to discover, validate and develop additional product candidates;

- continue to manufacture increasing quantities of our current or future product candidates for use in preclinical studies, clinical trials and for any potential commercialization;

- acquire or in-license other product candidates, technologies or intellectual property; and

- incur additional costs associated with current and future research, development and commercialization efforts and operations as a public company.

As a result, we will need substantial additional capital to support our continuing operations and pursue our strategy

As of December 31, 2023, we had cash and cash equivalents of $44.7 million. Based on our current operating plans, we anticipate that our cash and cash equivalents as of December 31, 2023, together with (i) the $30.0 million upfront payment under the license agreement with Gilead, (ii) the approximately $13.5 million in proceeds from the initial private placement with Gilead, which closed on March 28, 2024, and (iii) the approximately $11.3 million in gross proceeds from our private placement, which is expected to close on April 2, 2024 (subject to customary closing conditions), and after giving effect to (a) one-time costs and anticipated future cost savings associated with our strategic portfolio reprioritization and workforce reduction announced in March 2024 and (b) the repayment in the first quarter of 2024 of the outstanding loan balance under our loan and security agreement with Pacific Western Bank, will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2025. However, we have based this estimate on

assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we anticipate. In addition, since these amounts may not be sufficient to fund our operations for at least twelve months from the date of issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K, there is substantial doubt about our ability to continue as a going concern. Our management has developed plans to fund our operations, which primarily consist of raising additional capital through one or more of the following: additional equity or debt financings; additional collaborations, partnerships or licensing transactions; or other sources. However, there can be no assurance that we will be able to complete any such transaction on acceptable terms or otherwise, and we may be unable to obtain sufficient additional capital. If we are not able to secure sufficient additional capital in the near term, we may in the future need to implement additional cost reduction strategies, which could include delaying, limiting, further reducing or eliminating both internal and external costs related to our operations and research and development programs. For more information, refer to "—Liquidity and Capital Resources—Capital Requirements and Going Concern" below and Note 1 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Financial Operations Overview

Revenue

We have not generated any revenue since inception and do not expect to generate any revenue from the sale of products for at least the next several years, if at all. If our development efforts for our current or future product candidates are successful and result in regulatory approval, we may generate revenue in the future from product sales. In March 2024, Xilio Development entered into the license agreement with Gilead pursuant to which we are eligible to receive $43.5 million of upfront payments, including a cash payment of $30.0 million and an initial equity investment by Gilead of approximately $13.5 million of our common stock at a purchase price of $1.97 per share. The initial equity investment closed on March 28, 2024, and the $30.0 million upfront cash payment is payable by Gilead within a specified time period promptly following signing of the license agreement.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our discovery efforts, research activities and development and testing of our programs and product candidates. These expenses include:

- personnel-related expenses, including salaries, bonuses, benefits and stock-based compensation expense for employees engaged in research and development functions;
- costs incurred with third-party contract development and manufacturing organizations, or CDMOs, to acquire, develop and manufacture materials for both preclinical studies and current or future clinical trials;
- costs of funding research performed by third parties that conduct research and development and preclinical activities on our behalf;
- costs incurred with third-party contract research organizations, or CROs, and other third parties in connection with the conduct of our current or future clinical trials;
- costs of sponsored research agreements and outside consultants, including their fees and related expenses;
- costs incurred to maintain compliance with regulatory requirements;
- fees for maintaining licenses and other amounts due under our third-party licensing agreements;
- expenses incurred for the procurement of materials, laboratory supplies and non-capital equipment used in the research and development process; and

- depreciation, amortization and other direct and allocated expenses, including rent, maintenance of facilities and other operating costs, incurred as a result of our research and development activities.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific deliverables using information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated balance sheets as prepaid expenses or accrued research and development expenses. We record cost-sharing payments under our clinical trial collaboration with F. Hoffmann-La Roche Ltd., which we refer to as the Roche clinical collaboration, as a reduction of research and development costs upon the achievement of each study development event specified in the clinical supply agreement. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are capitalized as assets, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

We use our personnel and infrastructure resources for our discovery efforts, including the advancement of our platform technology, developing programs and product candidates and managing external research efforts. A significant portion of our research and development costs have been, and will continue to be, external costs. We track these external costs, such as fees paid to CDMOs, CROs, preclinical study vendors and other third parties in connection with our manufacturing and manufacturing process development, clinical trials, preclinical studies and other research activities by program. Due to the number of ongoing programs and our ability to use resources across several projects, personnel-related expenses and indirect or shared operating costs incurred for our research and development programs are not recorded or maintained on a program-by-program basis.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will remain approximately the same or will continue to increase for the foreseeable future as we advance our programs and our current or future product candidates into and through the development phase. We expect our discovery research efforts and our related personnel costs to remain consistent with historical levels. In addition, as we progress our most advanced product candidates in clinical development, we may incur additional expenses related to milestone and royalty payments payable to third parties with whom we have entered into, or may enter into license, acquisition, option or other agreements to acquire the rights to future products and product candidates. In the event we are unable to raise sufficient additional capital in the near term to fund our operations, we will be required to adopt cost reduction strategies that seek to maintain our ability to continue the development of our most advanced product candidates in clinical development while otherwise reducing our overall research and development expenses.

At this time, we cannot reasonably estimate or know the nature, timing and projected costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, any of our product candidates or programs. This is due to the numerous risks and uncertainties associated with drug development, including the uncertainty of

- the scope, timing, costs and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to implement and maintain cost reduction strategies, as well as the timing of such cost reductions;
- our ability to maintain our current research and development programs;
- our ability to establish an appropriate safety profile for our product candidates with IND-enabling studies;
- our ability to hire and retain key research and development personnel;

- the costs associated with the development of any additional product candidates we develop or acquire through collaborations;
- our successful enrollment in and completion of clinical trials;
- our ability to successfully complete clinical trials with safety, potency and purity profiles that are satisfactory to the U.S. Food and Drug Administration, or the FDA, or any comparable foreign regulatory authority;
- our receipt of regulatory approvals from applicable regulatory authorities;
- our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize, our product candidates;
- our ability to commercialize products, if and when approved, whether alone or in collaboration with others;
- the continued acceptable safety profiles of the product candidates following approval, if any;
- our ability to establish and maintain agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if any of our product candidates are approved;
- the terms and timing of any collaboration, license or other arrangement, including the terms and timing of any milestone payments thereunder, if any;
- our ability to obtain and maintain patent, trade secret and other intellectual property protection and regulatory exclusivity for our product candidates if and when approved; and
- general economic conditions, including inflation.

A change in any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any product candidate we may develop.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel-related costs, including salaries, bonuses, benefits, recruiting and stock-based compensation, for personnel in our executive, finance, legal, business development, human resources and other administrative functions. General and administrative expenses also include legal fees relating to corporate matters; professional and consulting fees for accounting, auditing, tax, human resources and administrative consulting services; board of directors' fees; insurance costs; and facility-related expenses, which include depreciation costs and other allocated expenses for rent, maintenance of facilities, and other general administrative costs. These costs relate to the operation of the business and are in support of but separate from the research and development function and our individual development programs. Costs to secure and defend our intellectual property are expensed as incurred and are classified as general and administrative expenses.

We anticipate that our general and administrative expenses will remain consistent with historical levels as we maintain our infrastructure to support our research and development activities. We also expect to continue to incur significant expenses associated with operating as a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services attributable to maintaining compliance with exchange listing standards and U.S. Securities and Exchange Commission, or SEC, requirements, directors' and officers' liability insurance costs and investor and public relations costs. We also expect to continue to incur additional expenses related to intellectual property as we file patent applications to protect intellectual property arising from our research and development activities. In the event we are unable to obtain sufficient additional capital in the near term, we will need to implement cost reduction strategies that seek to reduce our

general and administrative expenses while maintaining sufficient infrastructure to support our planned research and development activities and operations as a public company.

Other Income, Net

Other income, net consists primarily of interest income earned from our cash and cash equivalents, interest expense principally on the note payable under our debt arrangement with PacWest and amortization of the debt discount related to debt issuance costs.

Income Taxes

Since our inception, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or for our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2023, we had federal and state net operating loss, or NOL, carryforwards of $209.3 million and $180.9 million, respectively, which may be available to offset future taxable income. As of December 31, 2023, federal NOLs of $204.5 million have an indefinite carryforward period. The remaining federal NOL carryforwards and our state NOL carryforward will expire beginning in 2035. These loss carryforwards are available to reduce future federal taxable income, if any. As of December 31, 2023, we also had federal and state research and development credit carryforwards of approximately $7.8 million and $3.1 million, respectively, which may be available to offset any future income tax and which will begin to expire in 2033. These loss and credit carryforwards are subject to review and possible adjustment by the appropriate taxing authorities.

Utilization of our NOL carryforwards and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future in accordance with Section 382 of the Internal Revenue Code of 1986, or Section 382, as well as similar state provisions. These "ownership changes", as defined by Section 382, may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and taxes, respectively. In general, an ownership change as defined by Section 382 results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. Since our formation, we have raised capital through the issuance of units and capital stock on several occasions. These financings may have resulted in an "ownership change". We have not yet completed a detailed study of our inception to date "ownership change" activity.

In addition, we have not yet conducted a study of our research and development credit carryforwards. Such a study may result in an adjustment to our research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amount is being presented as an uncertain tax position. A full valuation allowance has been provided against our research and development credits, and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheet or statement of operations and comprehensive loss if an adjustment were required.

Income taxes are determined at the applicable tax rates adjusted for non-deductible expenses, research and development tax credits and other permanent differences. Our income tax provision may be significantly affected by changes to our estimates.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

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

	Year Ended December 31,		
	2023	2022	Change
Operating expenses			
Research and development	$ 52,136	$ 59,201	$ (7,065)
General and administrative	26,997	29,948	(2,951)
Total operating expenses	79,133	89,149	(10,016)
Loss from operations	(79,133)	(89,149)	10,016
Other income, net			
Other income, net	2,729	927	1,802
Total other income, net	2,729	927	1,802
Net loss	$ (76,404)	$ (88,222)	$ 11,818

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2023 and 2022 (in thousands):

	Year Ended December 31,		
	2023	2022	Change
XTX101	$ 1,787	$ 6,374	$ (4,587)
XTX202	9,864	6,249	3,615
XTX301	6,438	11,475	(5,037)
Other early programs and indirect research and development	14,040	14,037	3
Personnel-related	20,007	21,066	(1,059)
Total research and development expenses	$ 52,136	$ 59,201	$ (7,065)

Research and development expenses decreased by $7.1 million from $59.2 million for the year ended December 31, 2022 to $52.1 million for the year ended December 31, 2023. The decrease in research and development expenses was primarily due to the following:

- XTX101 costs decreased by $4.6 million, primarily driven by a $2.0 million cost-sharing payment that we earned under our Roche clinical collaboration and recorded as a reduction in research and development expenses and a decrease of manufacturing costs of $2.2 million due to costs associated with the production of drug substance and drug product incurred during the year ended December 31, 2022 for which there were no comparable costs during the year ended December 31, 2023;

- XTX202 costs increased by $3.6 million, primarily driven by a $5.3 million increase in clinical development activities related to our Phase 1/2 clinical trial, partially offset by a $1.3 million decrease in manufacturing activities and a $0.2 million decrease in preclinical activities;

- XTX301 costs decreased by $5.0 million, primarily driven by a $4.6 million decrease in manufacturing activities relating to the initial supply of clinical trial material in the comparable period, a $2.4 million decrease in preclinical activities and a $0.2 million decrease in regulatory activities relating to the filing of our investigational

new drug application in the comparable period, partially offset by a $2.3 million increase in clinical development activities related to our Phase 1 clinical trial; and

- personnel-related costs decreased by $1.1 million, primarily driven by a $0.6 million decrease in salaries, bonuses and benefits due to lower research and development headcount, which was partially offset by an increase in average compensation, a $0.3 million decrease in stock-based compensation and a $0.2 million decrease in recruiting costs.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2023 and 2022 (in thousands):

	Year Ended December 31,		
	2023	2022	Change
Personnel-related	$ 15,827	$ 16,701	$ (874)
Professional and consulting fees	6,879	7,926	(1,047)
Facility-related and other general and administrative expenses	4,291	5,321	(1,030)
Total general and administrative expenses	$ 26,997	$ 29,948	$ (2,951)

General and administrative expenses decreased by $3.0 million from $29.9 million for the year ended December 31, 2022 to $27.0 million for the year ended December 31, 2023. The decrease in general and administrative expenses was primarily due to the following:

- personnel-related costs decreased by $0.9 million, primarily driven by a $0.8 million decrease in stock-based compensation, as the prior year period included $0.6 million in non-recurring compensation expense resulting from the modification of previously issued stock options;

- professional and consulting fees decreased by $1.0 million, primarily driven by a decrease in consulting fees; and

- facility-related and other general and administrative expenses decreased by $1.0 million, primarily driven by lower costs related to directors' and officers' liability insurance and a reduction in other general and administrative expenses.

Other Income, Net

Other income, net increased by $1.8 million from $0.9 million for the year ended December 31, 2022 to $2.7 million for the year ended December 31, 2023. The increase in other income, net was primarily due to an increase in interest income earned on our cash and cash equivalents due to higher interest rates and lower interest expense on our note payable under our debt arrangement with PacWest as a result of the commencement of the repayment of principal beginning in January 2023.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant operating losses and negative cash flows from operations. We have not yet commercialized any of our product candidates, which are in preclinical or early clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. To date, we have financed our operations primarily from proceeds raised through private placements of preferred units and convertible preferred stock, a debt financing and our IPO of common stock in October 2021. Through December 31, 2023, we have received an aggregate of

$350.9 million in net proceeds from such transactions, including $116.4 million in net proceeds from our IPO, $224.5 million in net proceeds from the sale and issuance of preferred units and convertible preferred stock, and $10.0 million in net proceeds from our debt financing with PacWest. As of December 31, 2023, we had cash and cash equivalents of $44.7 million.

Under the license agreement with Gilead, we are eligible to receive approximately $43.5 million in upfront payments, including a cash payment of $30.0 million and an initial equity investment by Gilead of approximately $13.5 million of our common stock at a purchase price of $1.97 per share. The initial equity investment closed on March 28, 2024, and the $30.0 million upfront cash payment is payable by Gilead within a specified time period promptly following signing of the license agreement.

On March 28, 2024, we entered into a securities purchase agreement with certain existing accredited investors pursuant to which we expect to receive approximately $11.3 million of gross proceeds upon closing of the March 2024 private placement, which is expected to close on April 2, 2024 (subject to customary closing conditions).

In November 2022, we filed a universal shelf registration statement on Form S-3 with the SEC, or Form S-3, to register for sale up to $250,000,000 of our common stock, preferred stock, debt securities, units and warrants, which we may issue and sell from time to time in one or more offerings, which became effective on November 18, 2022 (333-268264). In November 2022, we also entered into a sales agreement, or the Sales Agreement, with Cowen and Company LLC, under which we may issue and sell shares of our common stock, from time to time, having an aggregate offering price of up to $75.0 million, subject to the terms and conditions of the Sales Agreement. Through the filing date of this Annual Report on Form 10-K, we have not issued or sold any shares of our common stock pursuant to the Sales Agreement. Issuances or sales of common stock pursuant to the Sales Agreement, if any, would be made under the Form S-3 and the corresponding prospectus related to the issuance and sale of shares of common stock pursuant to the Sales Agreement.

Cash Flows

The following table provides information regarding our cash flows for each period presented (in thousands):

	Year Ended December 31,	
	2023	2022
Net cash used in:		
Operating activities	$ (68,620)	$ (75,723)
Investing activities	(486)	(1,867)
Financing activities	(6,550)	(69)
Net decrease in cash, cash equivalents and restricted cash	$ (75,656)	$ (77,659)

Operating Activities

Our cash flows from operating activities are greatly influenced by our use of cash for operating expenses and working capital requirements to support our business. We have historically experienced negative cash flows from operating activities as we invested in research and development of our product candidates, including preclinical studies, clinical trials, manufacturing and manufacturing process development. The cash used in operating activities resulted primarily from our net losses adjusted for non-cash charges, which are generally due to stock-based compensation, depreciation and amortization, as well as changes in components of operating assets and liabilities, which are generally due to increased expenses and timing of vendor payments.

During the year ended December 31, 2023, net cash used in operating activities of $68.6 million was primarily due to our net loss of $76.4 million and changes in operating assets and liabilities of $1.7 million, partially offset by net non-cash expenses of $9.4 million.

During the year ended December 31, 2022, net cash used in operating activities of $75.7 million was primarily due to our net loss of $88.2 million, partially offset by net non-cash expenses of $10.5 million and changes in operating assets and liabilities of $2.0 million.

Investing Activities

During the years ended December 31, 2023 and 2022, net cash used in investing activities of $0.5 million and $1.9 million, respectively, was due to purchases of property and equipment.

Financing Activities

During the year ended December 31, 2023, net cash used in financing activities of $6.5 million consisted of repayments of debt principal and payments on our finance lease for certain lab equipment, partially offset by proceeds from the issuance of common stock under our employee stock purchase plan and the exercise of stock options.

During the year ended December 31, 2022, net cash used in financing activities of $0.1 million consisted primarily of payments on our finance lease for certain lab equipment, partially offset by proceeds received from the exercise of stock options.

Capital Requirements and Going Concern

We expect our future capital requirements to increase substantially over time in connection with our ongoing research and development activities, particularly as we advance our current and planned clinical development of our product candidates and maintain the research efforts and preclinical activities associated with our other existing programs and discovery platform. In addition, we expect to continue to incur additional costs associated with operating as a public company. As a result, we expect to incur substantial operating losses and negative operating cash flows for the foreseeable future.

Inflation generally affects us by increasing our cost of labor and certain services. We do not believe that inflation had a material effect on our financial statements included elsewhere in this Annual Report on Form 10-K. However, the United States has recently experienced historically high levels of inflation. If the inflation rate continues to increase it may affect our expenses, such as employee compensation and research and development charges due to, for example, increases in the costs of labor and supplies. Additionally, the United States is experiencing a workforce shortage, which in turn has created a competitive wage environment that may also increase our operating costs in the future.

As of December 31, 2023, we had cash and cash equivalents of $44.7 million. Based on our current operating plans, we anticipate that our cash and cash equivalents as of December 31, 2023, together with (i) the $30.0 million upfront payment under the license agreement with Gilead, (ii) the approximately $13.5 million in proceeds from the initial private placement with Gilead, which closed on March 28, 2024, and (iii) the approximately $11.3 million in gross proceeds from our private placement, which is expected to close on April 2, 2024 (subject to customary closing conditions), and after giving effect to (a) one-time costs and anticipated future cost savings associated with our strategic portfolio reprioritization and workforce reduction announced in March 2024 and (b) the repayment in the first quarter of 2024 of the outstanding loan balance under our loan and security agreement with PacWest, will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2025. However, we have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we anticipate. In addition, since these amounts may not be sufficient to fund our operations for at least twelve months from the date of issuance of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K, there is substantial doubt about our ability to continue as a going concern. Our management has developed plans to fund our operations, which primarily consist of raising additional capital through one or more of the following: additional equity or debt financings; additional collaborations, partnerships or licensing transactions; or other sources. However, there can be no assurance that we will be able to complete any such transaction on acceptable terms or otherwise, and we may be unable to obtain sufficient additional capital. If we are not able to secure sufficient additional capital in the near term, we may in the future need to implement additional cost reduction strategies, which could include delaying, limiting, further reducing or eliminating both internal and external costs related to our operations and research and development programs. The accompanying consolidated financial statements included elsewhere in this Annual Report on Form 10-K have been prepared on a going

concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business for the foreseeable future. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

Because of the numerous risks and uncertainties associated with product development, and because the extent to which we may enter into additional collaborations with third parties for the development of our product candidates is unknown, we may incorrectly estimate the timing and amounts of increased capital outlays and operating expenses associated with advancing the research and development of our product candidates. Our funding requirements and timing and amount of our operating expenditures will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of research and development for our current and future product candidates, including our current and planned clinical trials for our clinical-stage product candidates, XTX101, XTX301 and XTX202, and ongoing preclinical development for our current and future product candidates;
- our ability to implement and maintain cost reduction strategies, as well as the timing of such cost reductions;
- the scope, prioritization and number of our research and development programs;
- the scope, costs, timing and outcome of regulatory review of our product candidates;
- the costs of securing manufacturing materials for use in preclinical studies, clinical trials and, for any product candidates for which we receive regulatory approval, if any, commercial supply;
- the costs and timing of future commercialization activities for any of our product candidates for which we receive regulatory approval;
- the amount and timing of revenue, if any, received from commercial sales of any product candidates for which we receive regulatory approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property and proprietary rights and defending any intellectual property-related claims;
- the extent to which we may acquire or in-license other products, product candidates, technologies or intellectual property, as well as the terms of any such arrangements;
- our ability to maintain our clinical collaboration to further develop XTX101, our Fc-enhanced, tumor-activated anti-CTLA-4, in combination with atezolizumab, including the cost-sharing arrangements of such collaboration;
- the timing and amount of milestones, equity investments and other contingent payments under our partnership with Gilead for XTX301;
- the costs of maintaining our operations and continuing to operate as a public company; and
- whether we are able to overcome the substantial doubt about our ability to continue as a going concern.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product 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 several years, if ever. Accordingly, we will need to obtain substantial additional capital to achieve our business objectives.

Our expectation with respect to our ability to fund our currently planned operations is based on estimates that are subject to various risks and uncertainties. Our operating plan may change as a result of many factors currently unknown to management and there can be no assurance that our current operating plan will be achieved in the time frame anticipated by us, and we may exhaust our available capital resources sooner than we expect.

Adequate additional capital may not be available to us on acceptable terms, or at all. Market volatility resulting from adverse changes in domestic and international fiscal, monetary and other policies and political relations, regional or global conflicts, uncertainty around global economic conditions, instability in financial markets, current or future pandemics or other factors could also adversely impact our ability to access capital as and when needed. To the extent that we raise additional capital through the sale of equity or securities convertible into or exchangeable for equity, the ownership interest of our existing stockholders may be diluted, and the terms of such securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. Additional debt and preferred equity, if available, may also involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require that we issue warrants, which could potentially dilute the ownership interest of our existing stockholders.

Contractual Obligations

In the normal course of business, we enter into agreements that contain contractual obligations, of which the most significant to date include our loan and security agreement with PacWest, an operating lease for our corporate headquarters and certain license agreements.

Loan and Security Agreement

In November 2019, we entered into a loan and security agreement with PacWest, as amended, which we refer to as the loan agreement, under which we borrowed $10.0 million under a term loan. Borrowings under the loan agreement were collateralized by substantially all of our assets, excluding intellectual property. Interest on amounts outstanding accrued at a variable annual rate equal to the greater of (i) the prime rate plus 0.25% or (ii) 4.75%. As of December 31, 2023, the interest rate on the term loan was 8.75%. We made interest-only payments on the outstanding balance through December 31, 2022. We commenced making equal monthly payments of principal plus interest in January 2023, and we were required to make such payments until the term loan matured on June 30, 2024. As of December 31, 2023, the outstanding principal balance under the loan agreement was $3.3 million. In the first quarter of 2024, we repaid all amounts outstanding under the loan agreement, and PacWest released all security interests in our and our subsidiaries' assets.

Lease Agreement

We lease building space for our corporate headquarters at 828 Winter Street in Waltham, Massachusetts under a non-cancellable operating lease that expires in March 2030. Our operating lease includes the option to extend the term for a period of five years at the then-market rental rate. As of December 31, 2023, the remaining required payments for our operating lease, not including the optional extension period, are approximately $11.7 million. For further information regarding our operating lease agreement, please see Note 7, *Leases,* to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Other Contractual Obligations

We are party to certain agreements that require us to pay third parties upon achievement of certain development, regulatory or commercial milestones or upon the consummation of specified transactions. Amounts related to contingent payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory and commercial milestones that may not be achieved or upon the consummation of specified transactions that may not occur. We have not included payments contingent upon the achievement of certain development, regulatory or commercial milestones on our consolidated balance sheets. For further information regarding certain of our license agreements and amounts that could become payable in the future under those agreements, please see Note 6, *Collaboration Agreements and Intellectual Property Licenses,* to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

In addition, we are party to certain agreements with contract research organizations for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes. Such contracts are generally cancellable by us for convenience with up to 90 days of notice. We may be subject to certain termination fees or wind-down costs upon termination of these agreements. The exact amount of such costs are generally not fixed or estimable.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

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

Research and Development Expenses and Related Accruals

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs and laboratory supplies, depreciation, manufacturing expenses and external costs of outside vendors engaged to conduct planned clinical development, preclinical development, manufacturing and manufacturing process development and other research support activities. All costs associated with research and development activities are expensed as incurred.

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with certain service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced. In certain instances, we prepay for services to be provided in the future. These amounts are initially capitalized and subsequently expensed as the services are performed.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid balance accordingly. Nonrefundable advance payments for goods and services that will be used in future research and development activities are initially capitalized and subsequently expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting accrued amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts incurred.

Stock-Based Compensation

We issue stock-based awards to employees, directors and non-employees, generally in the form of stock options. We measure employee stock-based compensation based on the grant date fair value of the stock-based awards and recognize stock-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award, in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation—Stock Compensation*, or ASC 718. We recognize forfeitures as they occur. We classify stock-based compensation expense in the consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's salary and related costs are classified or in which the award recipient's service payments are classified, as applicable.

Determination of the Fair Value of Stock-Based Awards

We estimate the fair value of our stock options granted with service-based conditions using the Black-Scholes option pricing model, which requires inputs of subjective assumptions, including: (i) the expected volatility of our common stock, (ii) the expected term of the award, (iii) the risk-free interest rate, (iv) expected dividends and (v) the fair value of our common stock. We completed our IPO in October 2021, and as a result there has not been a significant amount of time for which there has been a public market for the trading of our common stock, including a lack of company-specific historical and implied volatility data, therefore we base the estimate of expected volatility on the historical volatilities of a representative group of publicly traded guideline companies. For these analyses, we select companies with comparable characteristics and with historical share price information that approximates the expected term of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period that approximates the calculated expected term of our stock options. We will continue to apply this method until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We estimate the expected term of our stock options granted to employees and directors using the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, whereby the expected term equals the average of the vesting term and the original contractual term of the option. We utilize this method as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term and the plain nature of our stock-based awards. The expected dividend yield is assumed to be zero as we have no current plans to pay any dividends on common stock. We have elected to use the expected term for stock options granted to non-employees, using the simplified method, as the basis for the expected term assumption. However, we may elect to use either the contractual term or the expected term for stock options granted to non-employees on an award-by-award basis. Subsequent to the completion of our IPO in October 2021, the fair value of our common stock has been determined based on the share price of our common stock on the Nasdaq Global Select Market.

Emerging Growth Company and Smaller Reporting Company Status

As an emerging growth company, or EGC, under the Jumpstart Our Business Startups Act of 2012, or JOBS Act, we may delay the adoption of certain accounting standards until such time as those standards apply to private companies. Other exemptions and reduced reporting requirements under the JOBS Act for EGCs include presentation of only two years of audited financial statements in a registration statement for an IPO, an exemption from the requirement to provide an auditor's report on internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, an exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation, and less extensive disclosure about our executive compensation arrangements.

In addition, the JOBS Act provides that an EGC can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an EGC to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or

private companies, we can adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an emerging growth company. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We may remain classified as an EGC until December 31, 2026, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have annual gross revenues of $1.235 billion or more in any fiscal year, we would cease to be an emerging growth company as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1 billion of non-convertible debt over a three-year period.

We are also a "smaller reporting company," meaning that the market value of our shares held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our shares held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies.

Recent Accounting Pronouncements

For a description of recent accounting pronouncements, see Note 2, *Summary of Significant Accounting Policies,* to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company, as defined by Rule 12b-2 of the Securities Exchange Act of 1934, as amended, and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, Exhibits and Financial Statement Schedules, of this Annual Report on Form 10-K.

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

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our Chief Executive Officer (our principal executive officer) and our Senior Vice President, Finance and Accounting (our principal financial and accounting officer) evaluated the effectiveness of our disclosure controls and procedures as of

December 31, 2023. Based upon such evaluation, our Chief Executive Officer and Senior Vice President, Finance and Accounting have concluded that, as of December 31, 2023, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Internal control over financial reporting refers to the process designed by, or under the supervision of, our principal executive officer and our principal financial officer, and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

(1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;

(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and

(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the consolidated financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its 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. Also, projections of any evaluation of effectiveness of internal control over financial reporting to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate. Because of such limitations, there is a risk that material misstatements may 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 into the process safeguards to reduce, though not eliminate, this risk.

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting. Management has used the framework set forth in the report entitled "Internal Control—Integrated Framework (2013)" published by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) to evaluate the effectiveness of our internal control over financial reporting. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2023.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this Annual Report on Form 10-K that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On March 30, 2024, Tomas Heyman notified us of his resignation as a Class I director, effective as of our 2024 annual meeting of stockholders, which is currently expected to be held in June 2024. Mr. Heyman's resignation did not result from any disagreement with us on any matter relating to our operations, policies or practices.

Director and Officer Trading Arrangements

A portion of the compensation of our directors and officers (as defined in Rule 16a-1(f) under the Exchange Act) is in the form of equity awards and, from time to time, directors and officers may engage in open-market transactions with respect to the securities acquired pursuant to such equity awards or other of our securities, including to satisfy tax withholding obligations when equity awards vest or are exercised, and for diversification or other personal reasons.

Transactions in our securities by directors and officers are required to be made in accordance with our insider trading policy, which requires that the transactions be in accordance with applicable U.S. federal securities laws that prohibit trading while in possession of material nonpublic information. Rule 10b5-1 under the Exchange Act provides an affirmative defense that enables directors and officers to prearrange transactions in our securities in a manner that could negate a claim of insider trading for transactions undertaken while in possession of material nonpublic information.

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as such terms are defined in Items 408(a) and 408(c) of Regulation S-K, respectively) during the fourth quarter of 2024.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

Except to the extent provided below, the information required by this Item 10 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission, or the SEC, with respect to our 2024 Annual Meeting of Stockholders within 120 days of the end of the fiscal year to which this report relates, which information is incorporated herein by reference.

We post our Code of Business Conduct and Ethics, which applies to our directors, officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, in the "Corporate Governance" sub-section of the "Investor Relations" section (ir.xiliotx.com) of our corporate website https://xiliotx.com/. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K. Our website is not incorporated by reference into this Annual Report on Form 10-K and you should not consider any information contained in or accessible from our website to be a part of this Annual Report on Form 10-K.

Item 11. Executive Compensation

The information required by this Item 11 will be included in the section captioned "Executive Compensation" in our definitive proxy statement for our 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the

end of the fiscal year to which this Annual Report on Form 10-K relates, which information is incorporated herein by reference.

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

The information required by this Item 12 will be included in the section captioned "Security Ownership of Certain Beneficial Owners and Management" in our definitive proxy statement for our 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates, which information is incorporated herein by reference.

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

The information required by this Item 13 will be included in the sections captioned "Related Person Transactions," "Policies for Related Person Transactions" and "Director Independence" in our definitive proxy statement for our 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates, which information is incorporated herein by reference.

Item 14. Principal Accountant's Fees and Services

The information required by this Item 14 will be included in the section captioned "Audit Fees and Services" our definitive proxy statement for our 2024 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year to which this Annual Report on Form 10-K relates, which information is incorporated herein by reference.

Part IV

Item 15. Exhibits and Financial Statement Schedules

(1) Financial Statements

The following documents are included on pages set forth in Part II, Item 8 of this Annual Report on Form 10-K and are filed as part of this Annual Report on Form 10-K.

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(2) Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit Number	Filing Date
3.1	Restated Certificate of Incorporation of the Registrant	8-K	001-40925	3.1	October 26, 2021
3.2	Second Amended and Restated Bylaws of the Registrant	8-K	001-40925	3.1	April 3, 2023
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1	333-259973	4.1	October 1, 2021
4.2	Form of Prefunded Warrant	8-K	001-40925	4.1	March 28, 2024
4.3	Description of the Registrant's securities registered pursuant to Section 12 of the Securities and Exchange Act of 1934, as amended	10-K	001-40925	4.3	March 1, 2022
10.1	2020 Stock Incentive Plan, as amended	S-1	333-259973	10.2	October 1, 2021
10.2	Form of Stock Option Agreement under 2020 Stock Incentive Plan	S-1	333-259973	10.3	October 1, 2021
10.3	Form of Restricted Stock Agreement under 2020 Stock Incentive Plan	S-1	333-259973	10.4	October 1, 2021
10.4	2021 Stock Incentive Plan	S-1	333-259973	10.5	October 18, 2021
10.5	Form of Stock Option Agreement under the 2021 Stock Incentive Plan	S-1	333-259973	10.6	October 18, 2021
10.6	Form of Non-Employee Director Stock Option Agreement under the 2021 Stock Incentive Plan	S-1	333-259973	10.7	October 18, 2021

10.7	Form of Restricted Unit Agreement under the 2021 Stock Incentive Plan	8-K	001-40925	10.1	January 3, 2024
10.8	2021 Employee Stock Purchase Plan	S-1	333-259973	10.8	October 18, 2021
10.9	2022 Inducement Stock Incentive Plan	10-K	001-40925	10.8	March 2, 2023
10.10	Form of Stock Option Agreement under the 2022 Inducement Stock Incentive Plan	10-K	001-40925	10.9	March 2, 2023
10.11	Form of Restricted Stock Unit Agreement under the 2022 Inducement Stock Incentive Plan	10-K	001-40925	10.10	March 2, 2023
10.12	Sales Agreement, dated September 9, 2022, by and between the Registrant and Cowen and Company, LLC	S-3	333-268264	1.2	November 9, 2022
10.13#	Employment Agreement, dated September 30, 2021, by and between the Registrant and René Russo	S-1	333-259973	10.15	October 1, 2021
10.14#	Amended and Restated Employment Agreement, dated June 15, 2022, by and between the Registrant and Martin Huber, M.D.	8-K	001-40925	10.1	June 16, 2022
10.15#	Consulting Agreement, dated September 8, 2023, by and between the Registrant and Martin Huber, M.D.	10-Q	001-40925	10.3	November 9, 2023
10.16#	Second Amended and Restated Employment Agreement, dated August 3, 2023, by and between the Registrant and Christopher Frankenfield	8-K	001-40925	10.1	August 3, 2023
10.17#	Employment Agreement, dated September 5, 2023, by and between the Registrant and Kevin Brennan	8-K	001-40925	10.1	September 5, 2023
10.18#	Employment Agreement, dated September 5, 2023, by and between the Registrant and Katarina Luptakova, M.D.				*
10.19	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors	S-1	333-259973	10.20	October 1, 2021
10.20	Amended and Restated Non-Employee Director Compensation Policy	10-Q	001-40925	10.1	August 14, 2023
10.21†	Cross-License Agreement, dated as of December 16, 2020, by and between the Registrant and AskGene Pharma, Inc.	S-1	333-259973	10.11	October 1, 2021
10.22†	Amended and Restated Exclusive License Agreement, dated as of August 16, 2016, by and between the Registrant and City of Hope	S-1	333-259973	10.12	October 1, 2021
10.23†	License Agreement, dated as of September 26, 2016, as amended, by and between the Registrant and WuXi Biologics (Hong Kong) Limited	S-1	333-259973	10.13	October 1, 2021
10.24	Lease, dated as of August 26, 2019, by and between the Registrant and PPF OFF 828-830 Winter Street, LLC	S-1	333-259973	10.14	October 1, 2021
10.25	Securities Purchase Agreement, dated March 28, 2024, among the Registrant and the persons party thereto	8-K	001-40925	10.1	March 28, 2024
10.26	Registration Rights Agreement, dated March 28, 2024, among the Registrant and the persons party thereto	8-K	001-40925	10.2	March 28, 2024
21.1	Subsidiaries of the Registrant				*
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm				*
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				*

31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	*
32.1+	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	*
97#	Executive Compensation Clawback Policy	*
101.INS	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	*
101.SCH	Inline XBRL Taxonomy Extension Calculation Linkbase Document	*
101.CAL	Inline XBRL Taxonomy Extension Definition Linkbase Document	*
101.DEF	Inline XBRL Taxonomy Extension Label Linkbase Document	*
101.LAB	Inline XBRL Taxonomy Extension Presentation Linkbase Document	*
104	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)	

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* Filed herewith.

\# Indicates management contract or compensatory plan or arrangement.

† Portions of this exhibit have been omitted pursuant to Item 601 of Regulation S-K promulgated under the Securities Act because the information is not material and is a type of information that the registrant treats as private or confidential.

\+ The certifications attached as Exhibit 32.1 are being furnished solely to accompany this Annual Report on Form 10-K and will not be deemed to be "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that section. Such certifications will not be deemed to be incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent that the Registrant specifically incorporates it by reference into such filing.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

XILIO THERAPEUTICS, INC.

Date: April 1, 2024

By: /s/ René Russo
René Russo
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ René Russo René Russo	President, Chief Executive Officer and Director *(Principal Executive Officer)*	April 1, 2024
/s/ Kevin Brennan Kevin Brennan	Senior Vice President, Finance and Accounting *(Principal Financial and Accounting Officer)*	April 1, 2024
/s/ Paul J. Clancy Paul J. Clancy	Chair of the Board	April 1, 2024
/s/ Sara M. Bonstein Sara M. Bonstein	Director	April 1, 2024
/s/ Daniel Curran Daniel Curran	Director	April 1, 2024
/s/ Tomas J. Heyman Tomas J. Heyman	Director	April 1, 2024
/s/ Robert Ross Robert Ross	Director	April 1, 2024
/s/ Christina Rossi Christina Rossi	Director	April 1, 2024
/s/ Yuan Xu Yuan Xu	Director	April 1, 2024

Xilio Therapeutics, Inc.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

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

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2020.

Boston, Massachusetts
April 1, 2024

XILIO THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	December 31, 2023	December 31, 2022
ASSETS		
Current assets		
Cash and cash equivalents	$ 44,704	$ 120,385
Prepaid expenses and other current assets	3,423	4,111
Total current assets	48,127	124,496
Restricted cash	1,587	1,562
Property and equipment, net	5,942	7,255
Operating lease right-of-use asset	5,125	5,585
Other non-current assets	145	267
Total assets	$ 60,926	$ 139,165
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 1,050	$ 3,125
Accrued expenses	10,497	10,327
Operating lease liability, current portion	1,047	918
Note payable, current portion	3,315	6,667
Other current liabilities	48	82
Total current liabilities	15,957	21,119
Note payable, net of current portion	—	3,165
Operating lease liability, net of current portion	8,142	9,189
Other non-current liabilities	—	45
Total liabilities	24,099	33,518
Commitments and contingencies (Note 8)		
Stockholders' equity		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized, no shares issued or outstanding	—	—
Common stock, $0.0001 par value; 200,000,000 shares authorized at December 31, 2023 and December 31, 2022; 27,613,263 shares issued and 27,607,646 shares outstanding at December 31, 2023; 27,471,607 shares issued and 27,425,447 shares outstanding at December 31, 2022	3	3
Additional paid-in capital	362,336	354,752
Accumulated deficit	(325,512)	(249,108)
Total stockholders' equity	36,827	105,647
Total liabilities and stockholders' equity	$ 60,926	$ 139,165

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

XILIO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share data)

	Year Ended December 31,	
	2023	2022
Operating expenses		
Research and development	$ 52,136	$ 59,201
General and administrative	26,997	29,948
Total operating expenses	79,133	89,149
Loss from operations	(79,133)	(89,149)
Other income, net		
Other income, net	2,729	927
Total other income, net	2,729	927
Net loss and comprehensive loss	$ (76,404)	$ (88,222)
Net loss per share, basic and diluted	$ (2.78)	$ (3.22)
Weighted average common shares outstanding, basic and diluted	27,496,107	27,392,087

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

XILIO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands, except share data)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance at December 31, 2021	27,358,375	$ 3	$ 346,312	$ (160,886)	$ 185,429
Vesting of restricted common stock	64,415	—	—	—	—
Exercise of stock options	2,657	—	16	—	16
Stock-based compensation expense	—	—	8,424	—	8,424
Net loss	—	—	—	(88,222)	(88,222)
Balance at December 31, 2022	27,425,447	$ 3	$ 354,752	$ (249,108)	$ 105,647
Issuance of common stock under employee stock purchase plan	140,192	—	194	—	194
Vesting of restricted common stock	39,250	—	—	—	—
Exercise of stock options	2,757	—	8	—	8
Stock-based compensation expense	—	—	7,382	—	7,382
Net loss	—	—	—	(76,404)	(76,404)
Balance at December 31, 2023	27,607,646	$ 3	$ 362,336	$ (325,512)	$ 36,827

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

XILIO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2023	2022
Cash flows from operating activities:		
Net loss	$ (76,404)	$ (88,222)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,900	1,847
Non-cash interest expense	157	223
Stock-based compensation expense	7,382	8,424
Loss on disposal of property and equipment	3	1
Changes in operating assets and liabilities:		
Prepaid and other assets	688	344
Operating lease right-of-use asset	460	391
Accounts payable	(2,063)	485
Accrued expenses and other liabilities	175	1,585
Operating lease liability	(918)	(801)
Net cash used in operating activities	(68,620)	(75,723)
Cash flows from investing activities:		
Purchases of property and equipment	(486)	(1,867)
Net cash used in investing activities	(486)	(1,867)
Cash flows from financing activities:		
Repayments of debt principal	(6,667)	—
Payments of finance lease	(85)	(85)
Proceeds from issuance of common stock under employee stock purchase plan	194	—
Proceeds from exercise of stock options	8	16
Net cash used in financing activities	(6,550)	(69)
Decrease in cash, cash equivalents and restricted cash	(75,656)	(77,659)
Cash, cash equivalents and restricted cash, beginning of period	121,947	199,606
Cash, cash equivalents and restricted cash, end of period	$ 46,291	$ 121,947
Supplemental cash flow disclosure:		
Cash paid for interest	$ 573	$ 555
Supplemental disclosure of non-cash activities:		
Capital expenditures included in accounts payable or accrued expenses	$ —	$ 19
Reconciliation to amounts within the consolidated balance sheets:		
Cash and cash equivalents	$ 44,704	$ 120,385
Restricted cash	1,587	1,562
Cash, cash equivalents and restricted cash, end of period	$ 46,291	$ 121,947

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

1. Description of Business, Liquidity and Going Concern

Description of Business

Xilio Therapeutics, Inc. ("Xilio" or the "Company") is a clinical-stage biotechnology company dedicated to discovering and developing tumor-activated immuno-oncology ("I-O") therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. The Company was incorporated in Delaware in June 2020, and its headquarters are located in Waltham, Massachusetts.

Liquidity and Going Concern

Since its inception, the Company has devoted substantially all of its financial resources and efforts to research and development activities. As of December 31, 2023, the Company had an accumulated deficit of $325.5 million and has incurred significant operating losses, including net losses of $76.4 million and $88.2 million for the years ended December 31, 2023 and 2022, respectively. The Company expects its operating losses and negative operating cash flows to continue for the foreseeable future as it continues to advance its product candidates through clinical trials, maintains the infrastructure necessary to support these activities and continues to incur costs associated with operating as a public company. As of December 31, 2023, the Company had cash and cash equivalents of $44.7 million. The Company anticipates that its cash and cash equivalents as of December 31, 2023, together with (i) the $30.0 million upfront payment under the exclusive license agreement with Gilead Sciences, Inc. ("Gilead"), (ii) the approximately $13.5 million in proceeds from the initial private placement with Gilead, which closed on March 28, 2024, and (iii) the approximately $11.3 million in gross proceeds from the Company's private placement, which is expected to close on April 2, 2024 (subject to customary closing conditions), and after giving effect to (a) one-time costs and anticipated future cost savings associated with the Company's strategic portfolio reprioritization and workforce reduction announced in March 2024 and (b) the repayment in the first quarter of 2024 of the outstanding loan balance under the Company's loan and security agreement with Pacific Western Bank ("PacWest"), will be sufficient to fund the Company's operating expenses and capital expenditure requirements into the second quarter of 2025. For further information regarding these transactions and other subsequent events, please see Note 14, *Subsequent Events*. However, the Company has based this estimate on assumptions that may prove to be wrong, and the Company could exhaust its available capital resources sooner than it anticipates. In addition, since these amounts may not be sufficient to fund its operations for at least twelve months from the date of issuance of the consolidated financial statements, there is substantial doubt about the Company's ability to continue as a going concern.

To continue to fund the operations of the Company, management has developed plans, which in the near term primarily consist of raising additional capital through one or more of the following: additional equity or debt financings; additional collaborations, partnerships or licensing transactions; or other sources. However, there can be no assurance that the Company will be able to complete any such transaction on acceptable terms or otherwise, and the Company may be unable to obtain sufficient additional capital. If the Company is not able to secure sufficient additional capital in the near term, the Company may in the future need to implement additional cost reduction strategies, which could include delaying, limiting, further reducing or eliminating both internal and external costs related to its operations and research and development programs.

The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Basis of Presentation

These consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States ("GAAP") and pursuant to the rules and regulations of the U.S. Securities and Exchange Commission (the "SEC"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASUs") of the Financial Accounting Standards Board ("FASB").

In April 2012, the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act") was enacted. Section 107(b) of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. The Company has elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, the Company can adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that the Company either (1) irrevocably elects to "opt out" of such extended transition period or (2) no longer qualifies as an emerging growth company. The Company may take advantage of these exemptions up until December 31, 2026, or such earlier time that it is no longer an emerging growth company.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries: Xilio Development, Inc. ("Xilio Development"), a Delaware corporation, and Xilio Securities Corporation, a Massachusetts corporation. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in accordance with GAAP requires management to make estimates and judgments that may affect the reported amounts of assets and liabilities and related disclosures of contingent assets and liabilities at the date of the financial statements and the related reporting of expenses during the reporting period. Management considers many factors in selecting appropriate financial accounting policies and controls and in developing the estimates and assumptions that are used in the preparation of these consolidated financial statements. Factors that may affect estimates include expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. Significant estimates of accounting reflected in these consolidated financial statements include, but are not limited to, estimates related to accrued expenses, the valuation of stock-based compensation, including stock options and restricted common stock, useful life of long-lived assets and income taxes. Actual results could differ from those estimates.

Segment Information

The Company has one operating segment. Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker in deciding how to allocate resources and assess performance. The Company's chief operating decision-maker is its chief executive officer. The Company and its chief operating decision-maker view the Company's operations and manage its business as a single operating segment. All of the Company's long-lived assets are held in the United States.

Cash Equivalents and Restricted Cash

The Company considers all short-term, highly liquid investments with original maturities of 90 days or less at acquisition date to be cash equivalents. Restricted cash represents a letter of credit issued to the landlord of the Company's facility lease and is reflected in non-current assets on the accompanying consolidated balance sheets.

Concentrations of Credit Risk and Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company holds all cash and cash equivalents at accredited financial institutions. Bank accounts in the United States are insured by the Federal Deposit Insurance Corporation ("FDIC") up to $250,000. Substantially all of the Company's cash and cash equivalents are FDIC insured, including funds held through an insured cash sweep program. The Company has not experienced any losses in its cash and cash equivalents and does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on a third-party manufacturer to supply material and manufacturing process development services for its product candidates and related research and development activities. These research and development programs and activities could be adversely affected by a significant interruption in the supply of such products and services which could have a material adverse effect on the Company's business, financial position and results of operations.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- *Level 1*—Quoted prices in active markets for identical assets or liabilities.

- *Level 2*—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

- *Level 3*—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying values of the Company's cash, prepaid expenses, accounts payable and accrued expenses approximate their fair value due to their short-term nature. The carrying value of the Company's outstanding debt as of December 31, 2023 and 2022 approximates fair value based on the variable interest rate for the borrowings as well as the short duration of the term of the note.

Property and Equipment

Property and equipment is stated at cost, net of accumulated depreciation and amortization. Depreciation and amortization are calculated using the straight-line method over the estimated useful lives of the assets, which are as follows:

	Estimated Useful Life
Computers and software	3 years
Laboratory equipment	5 years
Furniture and fixtures	5 years
Leasehold improvements	Shorter of the useful life or the remaining term of the lease

Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance that do not improve or extend the lives of the respective assets are charged to expense as incurred, while costs of major additions and betterments are capitalized.

Impairment of Long-Lived Assets

The Company periodically evaluates its long-lived assets, which consist of property and equipment, and any leased assets, for impairment whenever events or changes in circumstances indicate that a potential impairment may have occurred. If such events or changes in circumstances arise, the Company compares the carrying amount of the long-lived assets to the estimated future undiscounted cash flows expected to be generated by the long-lived assets. If the estimated aggregate undiscounted cash flows are less than the carrying amount of the long-lived assets, an impairment charge, calculated as the amount by which the carrying amount of the assets exceeds the estimated fair value of the assets, is recorded. The estimated fair value of the long-lived assets is determined based on the estimated discounted cash flows expected to be generated from the long-lived assets. The Company did not recognize impairment charges during the years ended December 31, 2023 and 2022, respectively.

Leases

The Company determines if an arrangement is or contains a lease at inception. Operating leases are included in right-of-use lease assets ("ROU assets") and in both the current portion of lease liabilities and long-term lease liabilities on the Company's consolidated balance sheets. Lease expense for operating leases is recognized on a straight-line basis over the lease term as an operating expense in the consolidated statements of operations and comprehensive loss. Assets subject to finance leases are included in other non-current assets and the related lease obligation is included in other current liabilities and other long-term liabilities on the Company's consolidated balance sheets. Lease expense for finance leases is recognized as depreciation expense and interest expense in the consolidated statements of operations and comprehensive loss using the effective interest method. The Company has elected the short-term lease recognition exemption for short-term leases, which allows the Company not to recognize lease liabilities and ROU assets on the consolidated balance sheets for leases with an original term of twelve months or less.

ROU assets represent the Company's right to use an underlying asset for the lease term, and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease liabilities and their corresponding ROU assets are initially recorded based on the present value of lease payments over the expected remaining lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the option will be exercised. Certain adjustments to the ROU asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments. The incremental borrowing rate reflects the fixed rate at which the Company could borrow, on a collateralized basis, the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. Prospectively, the Company will adjust the ROU assets for straight-line rent

expense or any incentives received and remeasure the lease liability at the net present value using the same incremental borrowing rate that was in effect as of the lease commencement or transition date.

The Company has lease agreements with lease and non-lease components, which are accounted for as a combined element.

Research and Development Costs and Accruals

Research and development expenses are expensed as incurred and consist of costs incurred in performing research and development activities, including compensation related expenses for research and development personnel, preclinical and clinical activities including cost of supply and manufacturing process development activities, overhead expenses including facilities expenses, materials and supplies, amounts paid to consultants and outside service providers, and depreciation of equipment. Upfront payments made for the licensing of technology are expensed as research and development expenses in the period in which they are incurred. In general, contingent payments are recognized when it becomes probable the payment will be required. Any contingent payments that qualify as a derivative liability are recognized at fair value on the Company's consolidated balance sheets. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The prepaid amounts are expensed as the related goods are delivered or the services are performed.

The Company records accruals for estimated ongoing research and development costs, including costs associated with contracts with third-party contract research organizations and contract manufacturing organizations. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the preclinical studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Collaboration Agreements

The Company analyzes its collaboration agreements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC 808, *Collaborative Arrangements* ("ASC 808"). For arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of ASC 606, *Revenue from Contracts with Customers* ("ASC 606"). For elements of collaboration arrangements that are accounted for pursuant to ASC 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For collaboration agreements where the Company is reimbursed for a portion of its research and development expenses or participates in the cost-sharing of such research and development expenses, such reimbursements and cost-sharing arrangements are reflected as a reduction of research and development expenses in the Company's consolidated statements of operations and comprehensive loss, as the Company does not consider performing research and development services for reimbursement to be a part of its ongoing major or central operations.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the accompanying consolidated statements of operations and comprehensive loss.

Stock-Based Compensation

The Company issues stock-based awards to employees, directors and non-employees, generally in the form of stock options. The Company measures employee stock-based compensation based on the grant date fair value of the stock-based awards and recognizes stock-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award, in accordance with ASC 718, *Compensation—Stock*

Compensation ("ASC 718"). ASC 718 requires all stock-based payments to employees, which includes grants of employee stock awards, to be recognized in the consolidated statements of operations and comprehensive loss based on their grant date fair values.

There are significant judgments and estimates inherent in the determination of the fair value of the common securities. The Company considers the fair value of common stock to be equal to its current share price. The Company estimates the fair value of stock options using the Black-Scholes option pricing model, which uses as inputs the estimated fair value of common stock, and certain management estimates, including the expected stock price volatility, the expected term of the award, the risk-free rate, and expected dividends. Expected volatility is calculated based on reported volatility data for a representative group of publicly traded companies for which historical information is available. The Company selects companies with comparable characteristics with historical share price information that approximates the expected term of the stock-based awards. The Company computes the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period that approximates the calculated expected term of the stock options. The Company will continue to apply this method until a sufficient amount of historical information regarding the volatility of its stock price becomes available. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected term assumption. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, under which the expected term is presumed to be the midpoint between the vesting date and the end of the contractual term. The Company utilizes this method due to lack of historical exercise data and the plain nature of its stock-based awards. The expected dividend yield is assumed to be zero as the Company has no current plans to pay any dividends on common stock. The Company recognizes forfeitures as they occur.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss consistent with the classification of the award recipient's salary and related costs or the award recipient's service payments, as applicable.

Comprehensive Loss

Comprehensive loss is the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss includes net loss and the change in accumulated other comprehensive loss for the period. The Company did not have any items of comprehensive income or loss other than net loss for the years ended December 31, 2023 and 2022.

Net Loss Per Share

The Company calculates basic net loss per share attributable to common stockholders by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, which excludes shares of restricted common stock that are not vested. Diluted net loss per share is calculated by dividing net loss by the weighted average number of shares of common stock outstanding, as applicable, after giving consideration to the dilutive effect of stock options, restricted common stock and warrants that are outstanding during the period. The Company has generated a net loss in all periods presented, so the basic and diluted net loss per share are the same, as the inclusion of the potentially dilutive securities would be anti-dilutive.

Income Taxes

Income taxes for Xilio Therapeutics, Inc. are recorded in accordance with ASC Topic 740, *Income Taxes*, which provides for deferred taxes using an asset and liability approach. Under this method, deferred income tax assets and liabilities are recognized based on future income tax consequences attributable to differences between the financial statement carrying amount of existing assets and liabilities, and their respective income tax basis. Deferred income tax assets and liabilities are measured using enacted income tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of changes in income tax rates on deferred income tax assets and liabilities is recognized as income or expense in the period that includes the enactment date and subject to a valuation allowance which is established for any income tax benefits of which future realization is not more likely than not.

The Company provides reserves for potential payments of tax to various tax authorities related to uncertain tax positions. The tax benefits recorded are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is "more likely than not" to be realized following resolution of any uncertainty related to the tax benefit, assuming that the matter in question will be raised by the tax authorities. At December 31, 2023 and 2022, the Company had not identified any significant uncertain tax positions.

Recent Accounting Pronouncements Not Yet Adopted

In November 2023, the FASB issued Accounting Standards Update 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 that are regularly provided to the chief operating decision maker. The guidance is effective for fiscal years beginning after December 15, 2023 and interim periods within fiscal years beginning after December 15, 2024. Early adoption is permitted. The guidance is to be applied retrospectively to all prior periods presented in the financial statements. Upon transition, the segment expense categories and amounts disclosed in the prior periods should be based on the significant segment expense categories identified and disclosed in the period of adoption. The Company is currently evaluating the potential impact of adopting this new guidance on its consolidated financial statements and related disclosures.

In December 2023, the FASB issued Accounting Standards Update No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which modifies the rules on income tax disclosures to require entities to disclose (1) specific categories in the rate reconciliation, (2) the income or loss from continuing operations before income tax expense or benefit (separated between domestic and foreign) and (3) income tax expense or benefit from continuing operations (separated by federal, state and foreign). ASU 2023-09 also requires entities to disclose their income tax payments to international, federal, state and local jurisdictions, among other changes. The guidance is effective for annual periods beginning after December 15, 2024. Early adoption is permitted for annual financial statements that have not yet been issued or made available for issuance. ASU 2023-09 should be applied on a prospective basis, but retrospective application is permitted. This Company is currently evaluating the potential impact of adopting this new guidance on its consolidated financial statements and related disclosures.

3. Property and Equipment, Net

Property and equipment, net consists of the following as of December 31, 2023 and 2022:

	December 31, 2023	December 31, 2022
Laboratory equipment	$ 5,815	$ 5,587
Computers and software	183	228
Furniture and fixtures	681	636
Leasehold improvements	5,124	5,124
Construction in process	—	98
Total property and equipment	11,803	11,673
Less: accumulated depreciation	(5,861)	(4,418)
Property and equipment, net	$ 5,942	$ 7,255

The Company incurred depreciation and amortization expense related to property and equipment of $1.8 million and $1.7 million for the years ended December 31, 2023 and 2022, respectively.

4. Accrued Expenses

Accrued expenses consist of the following as of December 31, 2023 and 2022:

	December 31, 2023	December 31, 2022
External research and development	$ 4,867	$ 3,178
Personnel-related	4,690	5,413
Professional and consulting fees	845	1,536
Other	95	200
Total accrued expenses	$ 10,497	$ 10,327

5. Loan and Security Agreement

In November 2019, the Company's wholly owned subsidiary, Xilio Development, entered into a loan and security agreement (as amended and restated in May 2023, the "Loan Agreement") with PacWest, with the Company as a guarantor. Under the Loan Agreement, in November 2019, Xilio Development borrowed $10.0 million under a term loan. Interest on amounts outstanding under the Loan Agreement accrued at a variable annual rate equal to the greater of (i) the prime rate plus 0.25% or (ii) 4.75%. As of December 31, 2023, the interest rate on the term loan was 8.75%. Xilio Development was required to make interest-only payments on any outstanding balances through December 31, 2022. Xilio Development commenced making equal monthly payments of principal plus interest in January 2023.

As of December 31, 2023, the Company and Xilio Development were in compliance with all covenants under the Loan Agreement. Xilio Development had the following future loan principal payments under the Loan Agreement at December 31, 2023:

	Minimum Loan Payments
2024	$ 3,333
Total future principal payments	3,333
Less: unamortized discount	(18)
Total note payable	$ 3,315

The Company recognized $0.7 million and $0.8 million of interest expense related to the Loan Agreement for the years ended December 31, 2023 and 2022, respectively, which is reflected in other income, net on the consolidated statements of operations and comprehensive loss.

In the first quarter of 2024, Xilio Development repaid all amounts outstanding under the Loan Agreement, and PacWest released all security interests in Xilio Development's and its affiliates' assets.

6. Collaboration Agreements and Intellectual Property Licenses

Clinical Trial Collaboration with F. Hoffmann-La Roche

In July 2023, the Company and F. Hoffmann-La Roche Ltd. ("Roche") entered into a clinical trial collaboration (the "Roche Clinical Collaboration") pursuant to a clinical supply agreement to evaluate XTX101 in combination with atezolizumab (Tecentriq®) in a Phase 1/2 clinical trial consisting of a Phase 1 dose escalation cohort assessing the combination in patients with advanced solid tumors and a planned Phase 2 clinical trial assessing the combination in patients with microsatellite stable colorectal cancer.

Under the clinical supply agreement, the Company is eligible to receive specified cost-sharing payments from Roche, and each company will supply its respective anti-cancer agent to support the Phase 1/2 clinical trial. The Company is responsible for conducting the Phase 1/2 clinical trial and retains global development and commercialization rights to XTX101.

The Company concluded that the cost-sharing payments from the Roche Clinical Collaboration are not in the scope of ASC 606 because the Company does not consider performing research and development services for reimbursement to be part of its ongoing major or central operations. Therefore, the Company applied a reasonable, rational, and consistently applied accounting policy election to record the cost-sharing payments from the Roche Clinical Collaboration as a reduction of research and development expenses in the consolidated statements of operations and comprehensive loss for the period in which a study development event is achieved. During the year ended December 31, 2023, the Company recognized a reduction of research and development expenses of $2.0 million.

Cross-License Agreement with AskGene

In December 2020, Xilio Development entered into a cross-license agreement with AskGene Pharma, Inc. ("AskGene") pursuant to which AskGene granted Xilio Development certain exclusive licenses for AskGene patent rights related to non-antigen binding IL-2 products in the field of oncology and certain co-exclusive licenses for AskGene patent rights related to antigen binding IL-2 products in all fields. Under the agreement, AskGene retains rights to the AskGene patent rights in Singapore, Thailand, Malaysia, Vietnam, the People's Republic of China, Taiwan, Macau, Hong Kong, Korea and India (the "AskGene territory") and granted licenses to Xilio Development for the AskGene patent rights worldwide, excluding the AskGene territory (the "Xilio Development territory").

Under the agreement, Xilio Development paid AskGene an upfront payment of $6.0 million, and for any licensed IL-2 product, Xilio Development is obligated to pay AskGene up to $13.0 million in the aggregate upon the achievement of specified regulatory milestones. In addition, subject to specified conditions, for any IL-2 licensed product, Xilio Development is obligated to pay AskGene percentage royalties in the mid-single digits on aggregate annual net sales of IL-2 licensed products in the Xilio Development territory during the applicable royalty term.

During the term of the agreement, AskGene has agreed not to exploit any non-antigen binding IL-2 product comprised of specified masking technology in the field of oncology in the Xilio Development territory.

In addition, Xilio Development granted a non-exclusive, royalty-free, non-transferable, worldwide license to AskGene for specified Xilio patent rights related to non-antigen binding IL-2 products in the field of immunology and for specified Xilio patent rights related to antigen binding IL-2 products in all fields. Subject to the terms of the agreement and during the time period specified, Xilio Development also granted AskGene an option to obtain a license in the AskGene territory to develop and commercialize IL-2 licensed products. If AskGene exercises its option to develop and commercialize IL-2 licensed products in the AskGene territory, then the parties will negotiate and enter into a license agreement for AskGene's exclusive development and commercialization of such products in the AskGene territory, and AskGene would be obligated to pay Xilio Development percentage royalties in the mid-single digits on aggregate annual net sales of such licensed products in the AskGene territory.

The Company accounted for the agreement as an asset acquisition, as the Company only acquired licenses to specified patents from AskGene (an input) and no additional processes or outputs as a part of the agreement. The $6.0 million upfront payment was recorded as research and development expense in the consolidated statement of operations and comprehensive loss during the year ended December 31, 2020, as the acquired licenses were determined to have no alternative future use and the technological feasibility of the intellectual property has not yet been reached. Any additional payments that are contingent upon achievement of development and regulatory milestones or upon sales of licensed products will not be recognized until it becomes probable that the Company will be required to make such payments.

Amended and Restated Exclusive License Agreement with City of Hope

In August 2016, Xilio Development entered into an amended and restated exclusive license agreement with City of Hope pursuant to which City of Hope granted Xilio Development an exclusive worldwide license to specified patent rights related to the Company's anti-CTLA-4 monoclonal antibody program.

Under the agreement, the Company issued 24,019 shares of common stock to City of Hope. For the first three licensed products or licensed services to achieve specified development and regulatory milestones, Xilio Development is obligated to pay City of Hope up to $10.3 million in the aggregate per licensed product or licensed service. In addition, subject to

specified conditions, Xilio Development is obligated to pay City of Hope tiered royalties in the low single digits on aggregate annual net sales of licensed products or licensed services on a country-by-country basis until the expiration of the last-to-expire patent or patent application licensed from City of Hope covering the applicable licensed product or licensed service in such country. Xilio Development is also obligated to pay City of Hope a portion of any consideration Xilio Development receives for the grant of sublicenses under the agreement ranging from a low double digit to mid-twenties percentage of such consideration, subject to specified conditions under that agreement at the time that Xilio Development grants any such sublicense.

The Company incurred no costs related to the payment of specified development milestones under the agreement during the years ended December 31, 2023 and 2022. Any additional payments that are contingent upon achievement of development and regulatory milestones or upon sales of licensed products will not be recognized until it becomes probable that the Company will be required to make such payments.

CTLA-4 Monoclonal Antibody License Agreement with WuXi Biologics

In September 2016, the Company entered into a license agreement with WuXi Biologics (Hong Kong) Limited ("WuXi Biologics"), as amended in December 2017, pursuant to which WuXi Biologics granted the Company an exclusive worldwide license to specified monoclonal antibodies and patent rights and know-how controlled by WuXi Biologics, including certain patent rights related to the Company's anti-CTLA-4 monoclonal antibody program.

For each product that exploits the rights licensed under the agreement, the Company is obligated to pay WuXi Biologics up to approximately $25.8 million in the aggregate for specified development and regulatory milestones. In addition, subject to specified conditions, the Company is obligated to pay WuXi Biologics tiered royalties in the low to mid-single digits on aggregate annual worldwide net sales of licensed products during the applicable royalty term.

The Company incurred no costs related to the payment of specified development milestones under the agreement during the years ended December 31, 2023 and 2022. Any additional payments that are contingent upon the achievement of development and regulatory milestones or sales of licensed products will not be recognized until it becomes probable that the Company will be required to make such payments.

7. Leases

The Company has an operating lease for its headquarters and a finance lease for certain lab equipment. In August 2019, the Company entered into a facility lease agreement with a landlord providing funding for tenant improvements and occupancy of approximately 27,830 square feet of office and laboratory space (the "premises") at 828 Winter Street, Waltham, Massachusetts. The initial term of the lease expires in March 2030, unless terminated earlier in accordance with the terms of the lease. The Company has a right to a five-year option to extend at then-market rates. The Company is obligated to pay its portion of real estate taxes and costs related to the premises, including costs of operations, maintenance, repair, replacement, and management of the leased premises, which it began paying simultaneous with the rent commencement date in March 2020. As of December 31, 2023 and 2022, the Company has a letter of credit for the benefit of its landlord in the amount of $1.6 million, collateralized by a money market account, which is recorded as restricted cash on the consolidated balance sheets.

The components of lease expense were as follows:

	Year Ended December 31,	
	2023	2022
Operating lease cost	$ 1,225	$ 1,225
Variable lease cost	982	959
Total lease costs	$ 2,207	$ 2,184
Finance lease cost:		
Amortization of right-of-use asset	$ 85	$ 85
Interest on lease liability	6	12

Supplemental balance sheet information related to the leases was as follows (in thousands, except for remaining lease term and discount rates):

	Year Ended December 31,	
	2023	2022
Operating Lease:		
Operating lease right-of-use asset	$ 5,125	$ 5,585
Operating lease liability, current portion	$ 1,047	$ 918
Operating lease liability, net of current portion	$ 8,142	$ 9,189
Finance Lease:		
Other non-current assets	$ 134	$ 219
Other current liabilities	48	82
Other liabilities, long-term	—	45
Weighted-average remaining lease term (in years):		
Operating lease	6.2	7.2
Finance lease	0.7	1.7
Weighted-average discount rate:		
Operating lease	8.0 %	8.0 %
Finance lease	6.9 %	6.9 %

Supplemental cash flow information related to leases was as follows:

	Year Ended December 31,	
	2023	2022
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	$ 1,683	$ 1,634
Financing cash flows from finance leases	85	85

Future minimum lease payments under non-cancellable leases as of December 31, 2023 are as follows:

	Operating Lease	Finance Lease
2024	$ 1,733	$ 49
2025	1,785	—
2026	1,839	—
2027	1,894	—
2028	1,951	—
Thereafter	2,516	—
Total future minimum lease payments	11,718	49
Present value adjustment	(2,529)	(1)
Present value of lease liabilities	$ 9,189	$ 48

8. Commitments and Contingencies

Indemnification Agreements

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third-party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has never incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. The Company has also entered into indemnification agreements with its directors that may require the Company to indemnify its directors against liabilities that may arise by reason of their status or service as directors to the fullest extent permitted by Delaware corporate law. The Company currently has directors' and officers' liability insurance.

To date, the Company has not incurred any material costs as a result of such indemnifications. The Company is not aware of any claims under indemnification arrangements, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2023 or 2022.

Legal Proceedings

The Company is not currently a party to any material legal proceedings.

9. Preferred Stock and Common Stock

Undesignated Preferred Stock

As of December 31, 2023 and 2022, the Company's certificate of incorporation, as amended, authorized the Company to issue up to 5,000,000 shares of undesignated preferred stock at $0.0001 par value per share. As of December 31, 2023 and 2022, there were no shares of preferred stock issued or outstanding.

Common Stock

As of December 31, 2023 and 2022, the Company is authorized to issue up to 200,000,000 shares of common stock, $0.0001 par value per share under its certificate of incorporation, as amended.

The voting, dividend and liquidation rights of the holders of shares of common stock are subject to and qualified by the rights, powers and preferences of the holders of shares of the Company's undesignated preferred stock, if and when such shares are issued. The rights, preferences and privileges of the Company's common stock are as follows:

Voting

The holders of shares of common stock are entitled to one vote for each share of common stock held at any meeting of stockholders and at the time of any written action in lieu of a meeting of stockholders.

Dividends

The holders of shares of common stock are entitled to receive dividends, if and when declared by the Company's board of directors. No dividends have been declared by the Company's board of directors or paid by the Company to the holders of common stock since the issuance of the common stock.

Liquidation

Upon the dissolution, liquidation or winding up of the Company, whether voluntary or involuntary, holders of the common stock will be entitled to receive, pro rata based on the number of shares held by each such holder, all assets of the Company

available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding preferred stock.

Shares Reserved for Future Issuance

The Company has reserved for future issuances the following shares of common stock as of December 31, 2023 and 2022:

	December 31, 2023	December 31, 2022
Stock options	9,456,237	8,084,121
Employee Stock Purchase Plan	701,244	566,720
Warrants	2,631	2,631
Total shares reserved for future issuance	10,160,112	8,653,472

10. Stock-Based Compensation

Equity Incentive Plans

2020 Stock Incentive Plan

Under the 2020 Stock Incentive Plan (as amended, the "2020 Plan"), the Company was authorized to issue shares of common stock to the Company's employees, officers, directors, consultants and advisors in the form of options, restricted stock awards or other stock-based awards.

2021 Stock Incentive Plan

In September 2021, the Company's board of directors and stockholders adopted the 2021 Stock Incentive Plan (the "2021 Plan"), which became effective immediately prior to the IPO in October 2021. Upon effectiveness of the 2021 Plan, the Company ceased granting awards under the 2020 Plan. The 2021 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units, and other stock-based awards. The Company initially reserved 6,579,016 shares of common stock under the 2021 Plan. The 2021 Plan provides that the number of shares reserved and available for issuance under the 2021 Plan will be cumulatively increased on January 1 of each calendar year by 5% of the number of shares of common stock outstanding on such date or such lesser amount determined by the Company's board of directors. On January 1, 2024, the number of shares reserved for issuance under the 2021 Plan automatically increased by 1,380,663 shares. As of December 31, 2023, there were 1,780,442 shares available for future grant under the 2021 Plan.

2022 Inducement Plan

In 2022, the Company's board of directors adopted the 2022 Inducement Stock Incentive Plan pursuant to Nasdaq Rule 5635(c)(4) (the "2022 Inducement Plan"). In accordance with Rule 5635(c)(4), stock-based incentive awards under the 2022 Inducement Plan may only be made to a newly hired employee who has not previously been a member of the Company's board of directors, or an employee who is being rehired following a bona fide period of non-employment by the Company as a material inducement to the employee's entering into employment with the Company. An aggregate of 275,000 shares of the Company's common stock has been reserved for issuance under the 2022 Inducement Plan. As of December 31, 2023, there were 220,000 shares available for future grant under the 2022 Inducement Plan.

2021 Employee Stock Purchase Plan

In 2021, the Company's board of directors and stockholders adopted the 2021 Employee Stock Purchase Plan (the "2021 ESPP"), which became effective immediately prior to the IPO in October 2021. The Company initially reserved 292,031 shares of common stock for issuance under the 2021 ESPP. The 2021 ESPP provides that the number of shares of common

stock reserved for issuance under the 2021 ESPP will be cumulatively increased on January 1 of each calendar year by 1% of the number of shares of the Company's common stock outstanding on such date or such lesser amount determined by the Company's board of directors (up to a maximum increase of 584,062 shares of common stock per year). On January 1, 2024, the number of shares reserved for issuance under the 2021 ESPP was increased by 276,132 shares. The Company issued 140,192 shares under the 2021 ESPP during the year ended December 31, 2023 and no shares under the 2021 ESPP during the year ended December 31, 2022. As of December 31, 2023, there were 701,244 shares available for future issuance under the 2021 ESPP.

Total Stock-Based Compensation Expense

During the years ended December 31, 2023 and 2022, the Company recorded compensation expense related to stock options and restricted common stock for employees and non-employees, which was allocated as follows in the consolidated statements of operations and comprehensive loss:

	Year Ended December 31,	
	2023	2022
Research and development expense	$ 2,189	$ 2,427
General and administrative expense	5,193	5,997
Total stock-based compensation expense	$ 7,382	$ 8,424

Stock Options

A summary of stock option activity under the Company's Stock Incentive Plans is as follows:

	Number of Stock Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value [1] (In thousands)
Outstanding as of December 31, 2022	4,960,553	$ 8.04	8.6	$ 89
Granted	3,738,555	$ 2.75		
Exercised	(2,757)	$ 2.82		
Cancelled/forfeited	(1,240,556)	$ 7.26		
Outstanding as of December 31, 2023	7,455,795	$ 5.52	8.0	$ —
Exercisable as of December 31, 2023	3,103,732	$ 7.04	6.6	$ —

(1) The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock as of the end of the period.

Using the Black-Scholes option pricing model, the weighted average fair value of options granted to employees and directors during the years ended December 31, 2023 and 2022 was $2.02 per share and $5.58 per share, respectively. The Company satisfies stock option exercises with newly issued shares of common stock. The aggregate intrinsic value of stock options exercised during each of the years ended December 31, 2023 and 2022 was less than $0.1 million.

The following assumptions were used in determining the fair value of options granted to employees during the years ended December 31, 2023 and 2022:

	Year Ended December 31,	
	2023	2022
Risk-free interest rate	3.57 - 4.40 %	1.47 – 4.22 %
Expected dividend yield	0 %	0 %
Expected term (in years)	5.5 - 6.1	5.3 – 6.1
Expected volatility	81.7 - 87.3 %	80.8 – 87.6 %

As of December 31, 2023, the Company had unrecognized stock-based compensation expense of $12.5 million related to stock options issued to employees and directors, which is expected to be recognized over a weighted average period of 2.0 years.

Restricted Stock

A summary of the Company's restricted stock activity and related information is as follows:

	Number of Shares of Restricted Stock	Weighted Average Grant Date Fair Value
Unvested as of December 31, 2022	46,160	$ 5.51
Vested	(39,250)	$ 5.51
Canceled/Forfeited	(1,293)	$ 5.51
Unvested as of December 31, 2023	5,617	$ 5.51

In June 2020, the Company granted 552,546 shares of common stock underlying restricted stock awards, and the Company has not subsequently granted any additional restricted stock awards. The Company recorded stock-based compensation expense for restricted stock granted to employees, directors and non-employees of $0.3 million and $0.4 million for the years ended December 31, 2023 and 2022. During the years ended December 31, 2023 and 2022, the aggregate fair value of the restricted stock awards that vested was $0.1 million and $0.3 million, respectively. As of December 31, 2023, total unrecognized compensation cost related to unvested restricted stock awards was less than $0.1 million, which is expected to be recognized during the first quarter of 2024.

11. Net Loss Per Share

The following table sets forth the outstanding common stock equivalents, presented based on amounts outstanding at each period end, that were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have been anti-dilutive.

	Year Ended December 31,	
	2023	2022
Unvested restricted common stock	5,617	46,160
Outstanding stock options	7,455,795	4,960,553
Warrants	2,631	2,631
Unvested employee stock purchase plan shares	68,642	77,222
Total common stock equivalents	7,532,685	5,086,566

12. Income Taxes

The Company has not recorded a current or deferred tax provision for the years ended December 31, 2023 and 2022. The effective income tax rate differed from the amount computed by applying the federal statutory rate to the Company's loss before income taxes as follows:

	Year Ended December 31,	
	2023	2022
Tax effected at statutory rate	21.0 %	21.0 %
State taxes	6.5	5.2
Stock-based compensation	(1.4)	(0.6)
Non-deductible expenses	(0.8)	(0.9)
Federal research and development credits	3.5	2.8
Change in valuation allowance	(28.8)	(27.5)
Effective income tax rate	0.0 %	0.0 %

Deferred tax assets consist of the following as of December 31, 2023 and 2022:

	Year Ended December 31,	
	2023	2022
Deferred tax assets:		
Federal net operating loss carryforwards	$ 43,953	$ 37,277
State net operating loss carryforwards	11,433	9,267
Capitalized research and development expenditures	24,485	14,469
Research and development credit carryforwards	10,359	7,104
Lease liability	2,510	2,761
Accruals and reserves	210	241
Intangible assets	1,793	1,917
Stock-based compensation	1,213	1,374
Total deferred tax assets:	95,956	74,410
Valuation allowance	(92,978)	(71,003)
Subtotal	2,978	3,407
Deferred tax liabilities:		
Property and equipment	(1,578)	(1,881)
Right of use asset	(1,400)	(1,526)
Total deferred tax liabilities	(2,978)	(3,407)
Net deferred tax assets	$ —	$ —

The Company has had no income tax expense due to operating losses incurred since inception. Deferred tax assets are reduced by a valuation allowance if, based on the weight of available positive and negative evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on this, the Company has provided a valuation allowance for the full amount of the net deferred tax assets as the realization of the deferred tax assets is not determined to be more likely than not. During the year ended December 31, 2023, the valuation allowance increased by $22.0 million primarily due to the Company's book loss and capitalized research and development expenditures reported in the period and the generation of additional research and development credits.

As of December 31, 2023, the Company had $209.3 million and $180.9 million of federal and state operating loss carryforwards, respectively. Of the federal net operating loss carryovers, $204.5 million are not subject to expiration and the remaining federal and state net operating loss carryovers begin to expire in 2035. These loss carryforwards are available to reduce future federal taxable income, if any. As of December 31, 2023, the Company had federal and state research and development credit carryovers of $7.8 million and $3.1 million, which may be available to offset any future income tax and which will begin to expire in 2033. These loss and credit carryforwards are subject to review and possible adjustment by the appropriate taxing authorities.

Utilization of the Company's net operating loss ("NOL") carryforwards and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future in accordance with Section 382 of the Internal Revenue Code of 1986, as amended ("Section 382") as well as similar state provisions. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and taxes, respectively. In general, an ownership change as defined by Section 382 results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. Since its formation, the Company has raised capital through the issuance of capital stock on several occasions. These financings could result in an "ownership change" as defined by Section 382. The Company has not yet completed a detailed study of its inception to date ownership change activity.

The Company follows the provisions of ASC 740-10, *Accounting for Uncertainty in Income Taxes*, which specifies how tax benefits for uncertain tax positions are to be recognized, measured, and recorded in financial statements; requires certain disclosures of uncertain tax matters; specifies how reserves for uncertain tax positions should be classified on the balance sheet; and provides transition and interim period guidance, among other provisions. As of December 31, 2023, and 2022, the Company has not recorded tax reserves associated with any unrecognized tax benefits. The Company's policy is to recognize interest and penalties accrued on any uncertain tax positions as a component of income tax expense, if any, in its statements of income. As of December 31, 2023, and 2022, the Company had no reserves for uncertain tax positions. For the years ended December 31, 2023 and 2022, no estimated interest or penalties were recognized on uncertain tax positions. The Company has not recorded any interest or penalties on any unrecognized tax benefits since its inception.

The Company has not conducted a study of its research and development credit carryforwards. This study may result in an adjustment to research and development credit carryforwards; however, until a study is completed, and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheets or statements of operations and comprehensive loss if an adjustment were required.

The 2017 Tax Cuts and Jobs Act ("TCJA") included a multitude of tax provisions, including several deferred changes that became effective for tax years ending after December 31, 2021. Included in the provisions was the TCJA's amendment to Section 174 of the Internal Revenue Code of 1986, as amended ("Section 174"), which now requires U.S.-based and non-U.S-based research and experimental expenditures to be capitalized and amortized over a period of five or 15 years, respectively, for amounts paid in tax years starting after December 31, 2021. Prior to the TCJA amendment, Section 174 allowed taxpayers to either immediately deduct research and experimental expenditures in the year paid or incurred. The Company applied this required change in accounting method beginning in 2022.

The Company's tax returns remain open to examination by the Internal Revenue Service and the Commonwealth of Massachusetts for the years ended December 31, 2020 to December 31, 2022. In addition, the Company's tax carryover attributes such as net operating losses or credits from earlier periods are also subject to examination. The Company is currently not subject to any examinations by the Internal Revenue Service or any other tax authorities for any tax years.

13. 401(k) Plan

The Company maintains a defined contribution savings plan for employees that is defined to qualify under Section 401(k) of the Internal Revenue Code, as amended, (the "401(k) Plan") in which substantially all employees are eligible to participate. Under the 401(k) Plan, all employees who meet minimum age and service requirements may elect to defer a portion of their annual compensation on a pre-tax basis or post-tax basis, up to the maximum amount prescribed by statute. For each participating employee, the Company makes matching contributions equal to 100% of the first 3% of compensation contributed, plus 50% of the next 2% of compensation contributed, for a maximum of up to 4% of the employee's eligible compensation. Matching contributions are fully vested at the time of contribution. The Company incurred expenses related to matching contributions on behalf of employees to the 401(k) Plan of $0.7 million and $0.3 million during the years ended December 31, 2023 and 2022, respectively.

14. Subsequent Events

License Agreement and Issuance of Common Stock

On March 27, 2024, Xilio Development entered into an exclusive license agreement with Gilead Sciences, Inc. ("Gilead"), pursuant to which it granted Gilead an exclusive global license to develop and commercialize XTX301, the Company's tumor-activated IL-12 product candidate, and specified other molecules directed to IL-12.

Under the license agreement, the Company is eligible to receive approximately $43.5 million in upfront payments, including a cash payment of $30.0 million and an initial equity investment by Gilead of approximately $13.5 million in the Company's common stock at a purchase price of $1.97 per share.

In connection with the execution of the license agreement, on March 27, 2024, the Company entered into a stock purchase agreement with Gilead pursuant to which the Company agreed to initially issue and sell 6,860,223 of its shares of common stock to Gilead in a private placement at a purchase price of $1.97 per share for an aggregate purchase price of approximately $13.5 million.

The initial Gilead private placement closed on March 28, 2024, and the $30.0 million upfront cash payment is payable by Gilead within a specified time period promptly following signing of the license agreement.

March 2024 Private Placement

On March 28, 2024, the Company entered into a securities purchase agreement with certain existing accredited investors pursuant to which the Company agreed to sell and issue to the investors in a private placement an aggregate of 1,953,125 shares of the Company's common stock at a purchase price of $0.64 per share, and to certain investors in lieu of shares of the Company's common stock, prefunded warrants to purchase up to an aggregate of 15,627,441 shares of the Company's common stock at a purchase price of $0.6399 per prefunded warrant. The private placement is anticipated to close on April 2, 2024, subject to customary closing conditions.

Strategic Portfolio Reprioritization and Workforce Reduction

On March 27, 2024, the board of directors of the Company approved a strategic portfolio reprioritization and restructuring. As part of the strategic portfolio reprioritization and restructuring, the Company plans to undertake efforts to further reduce its expenses and streamline its operations, including a reduction in headcount of 15 employees, representing approximately 21% of the Company's workforce immediately prior to the workforce reduction.

SENIOR LEADERSHIP TEAM

RENÉ RUSSO, PHARM.D.
PRESIDENT AND CHIEF EXECUTIVE OFFICER

ULI BIALUCHA, PH.D.
CHIEF SCIENTIFIC OFFICER

SCOTT COLEMAN, PH.D.
CHIEF DEVELOPMENT OFFICER

STACEY DAVIS
CHIEF BUSINESS OFFICER

CHRIS FRANKENFIELD
CHIEF OPERATING OFFICER

KATARINA LUPTAKOVA, M.D.
CHIEF MEDICAL OFFICER

BOARD OF DIRECTORS

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PAUL J. CLANCY
CHAIR OF THE BOARD
FORMER EXECUTIVE VICE PRESIDENT AND CHIEF FINANCIAL OFFICER AT ALEXION PHARMACEUTICALS, INC.

SARA BONSTEIN
CHIEF FINANCIAL OFFICER OF INSMED, INC.

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CHIEF OPERATING OFFICER OF BLUEPRINT MEDICINES CORPORATION

YUAN XU, PH.D.
FORMER CHIEF EXECUTIVE OFFICER AT LEGEND BIOTECH CORPORATION

The 2024 annual meeting of stockholders will be held on Thursday, June 13, 2024 at 11 a.m. EDT online at www.virtualshareholdermeeting.com/XLO2024.

INDEPENDENT AUDITORS
Ernst & Young LLP

SEC FORM 10-K
A copy of Xilio Therapeutics' Form 10-K filed with the Securities and Exchange Commission is available free of charge from the company's investor relations department by emailing investors@xiliotx.com or sending a written request to: Investor Relations, Xilio Therapeutics, Inc., 828 Winter Street, Suite 300, Waltham, MA 02451.

THE TRANSFER AGENT
The transfer agent is responsible, among other things, for handling stockholder questions regarding address changes, duplicate mailings and changes in ownership or name in which shares are held. These requests may be directed to the transfer agent at the following address: Computershare Trust Company, N.A., 250 Royall Street, Canton, MA 02021, www.computershare.com, +1800 962 4284.

April 25, 2024