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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

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 001-40881

Pyxis Oncology, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**83-1160910**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
150 Cambridgepark Drive Cambridge, Massachusetts	**02140**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 221-9059

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	PYXS	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 15(d) of the Act. YES ☐ NO ☒

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

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

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

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

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

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

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

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

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

The aggregate market value of the Registrant's common stock held by non-affiliates as of June 30, 2022 the last business day of the Registrant's most recently completed second fiscal quarter, was approximately $76.9 million, as computed by reference to the closing price of the common stock on the Nasdaq Global Select Market on that date.

As of March 21, 2023, the Registrant had 36,980,621 shares of common stock, $0.0001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2023 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2022.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business, operations and financial performance and condition. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. These statements involve known and unknown risks and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

Unless the context requires otherwise, references in this Annual Report on Form 10-K to "Pyxis Oncology," the "Company," "we," "us," and "our" refer to Pyxis Oncology, Inc. and its subsidiary. In some cases, you can identify forward-looking statements by terms such as "may," "would," "should," "expects," "plans," "anticipates," "could," "intends," "target," "projects," "contemplates," "believes," "estimates," "predicts," "outlook," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report on Form 10-K are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Some of the key factors that could cause actual results to differ from our expectations include:

- our ability to develop and advance our current or future product candidates and programs, and to successfully initiate and complete clinical trials;
- the ability of our clinical trials to demonstrate the safety, purity and potency of our product candidates and other positive results;
- the size of the market opportunity for our product candidates, including our estimates of the number of patients who suffer from the cancers we are targeting;
- our manufacturing, commercialization and marketing capabilities and strategy;
- our plans to expand our pipeline of product candidates and further develop the FACT Platform;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- regulatory developments in the United States and Europe and other foreign countries:
- our expectations and plans to obtain funding for our operations, including from our existing and potential future collaboration and licensing agreements;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates:
- our continued reliance on third parties to manufacture our product candidates for preclinical studies, and, in the future, to conduct clinical trials and manufacture product candidates for such clinical trials;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

In addition, statements such as "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K and, although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events or otherwise.

SUMMARY RISK FACTORS

You should consider carefully the risks described under "Risk Factors" in Part II, Item 1A of this Annual Report on Form 10-K. References to "Pyxis Oncology," the "Company," "we," "us," and "our" in this section titled "Summary Risk Factors" refer to Pyxis Oncology, Inc. and its wholly owned subsidiary. A summary of the risks that could materially and adversely affect our business, financial condition, operating results and prospects include the following:

- We are a clinical stage biopharmaceutical company with a limited operating history and have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.
- We will require substantial additional capital to finance our operations, obtain regulatory approval for our product candidates, and commercialize our product candidates. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce or eliminate one or more of our research and product development programs or future commercialization efforts.
- We are heavily dependent on the success of PYX-201 and PYX-106, which are in the early stages of development, and if PYX-201 and/or PYX-106 are not successful in clinical trials or do not receive regulatory approval or licensure or are not successfully commercialized, our business will be materially and adversely affected.
- Our product candidates may fail in development or suffer delays that materially and adversely affect their commercial viability. If we or our existing or future collaborators are unable to initiate and complete clinical development of, obtain regulatory approval or licensure for or commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- Our preclinical studies and clinical trials may fail to demonstrate adequately the safety, purity and potency of any of our product candidates, which would prevent or delay development, regulatory approval or licensure and commercialization.
- Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approval or licensure or commercialize these programs on a timely basis or at all.
- We face competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If these companies develop technologies or product candidates more rapidly than we do or if their technologies are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.
- Clinical testing and product development is a lengthy and expensive process with an uncertain outcome. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the clinical testing and the development and commercialization of our product candidates.
- The regulatory licensure and approval processes of the FDA and other comparable regulatory authorities are lengthy, time-consuming and inherently unpredictable and, if we are ultimately unable to obtain marketing licensure or approval for our product candidates, our business will be substantially harmed.
- If we fail to attract and retain qualified senior management and key scientific personnel, our business may be materially and adversely affected.
- We face risks related to health epidemics and outbreaks, including the COVID-19 pandemic, which could significantly disrupt our preclinical studies and clinical trials, and therefore our receipt of necessary regulatory licensure or approvals could be delayed or prevented.
- We rely on third parties to manufacture our product candidates. Any failure by a third party manufacturer to produce acceptable raw materials or product candidates for us or to obtain authorization from the FDA or comparable foreign regulatory authorities relating thereto may delay or impair our ability to initiate or complete our clinical trials, obtain regulatory licensure or approvals or commercialize approved products.
- If we are unable to obtain and maintain patent protection for our product candidates, or if the scope of the patent protection obtained is not sufficiently broad, or if our patents are insufficient to protect our product candidates for an adequate amount of time, or if we are unable to obtain adequate protection for our proprietary know-how, we may not be able to compete effectively in our markets.

- If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates or we could lose certain rights to grant sublicenses.
- Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. If we breach our University of Chicago, Pfizer, or Biosion license agreements or any of the other agreements under which we acquired, or will acquire, intellectual property rights covering our product candidates, we could lose the ability to continue the development and commercialization of the related product candidate(s).
- We are subject to stringent and changing obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation, fines and penalties, a disruption of our business operations, including our clinical trials, harm to our reputation, and other adverse effects on our business or prospects.
- Our internal computer systems, or those of any of our existing or future CROs, manufacturers, other contractors, consultants, or collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of or destruction of our proprietary and confidential data, employee data or personal data, which could result in additional costs, significant liabilities, harm to our reputation and material disruption of our operations.
- If the market opportunities for any product that we develop are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.

PART I

Item 1. Business.

Overview

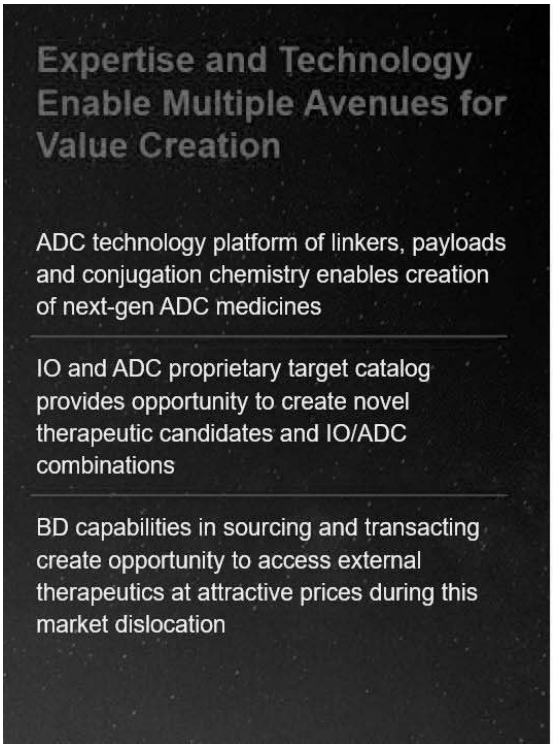
We are a clinical-stage oncology company focused on developing a multi-modality portfolio of next-generation therapeutics to target difficult-to-treat cancers and improve quality of life for patients. We develop our product candidates with the objective to directly kill tumor cells, and to address the underlying pathologies created by cancer that enable its uncontrollable proliferation and immune evasion. We consider multi-modality as a variety of technologies, either stand-alone or in combination with others, to build effective cancer therapeutics for patients. Since our launch in 2019, we have developed a broad portfolio that includes novel antibody drug conjugate, or ADC, product candidates, immuno-oncology, or IO, product candidates, and monoclonal antibody, or mAb, preclinical discovery programs that we are developing as monotherapies and in combination with other therapies.

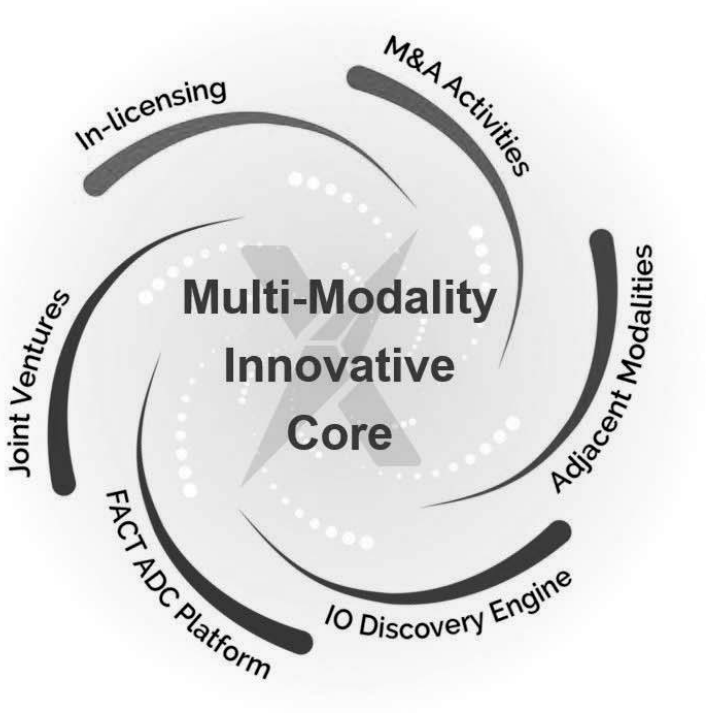
We have assembled a team with deep experience and proficiency in oncology research and development and plan to leverage our team's decades of experience in drug development to bring a variety of innovative therapies through the clinic. The collective experience across our team spans the spectrum of both pharmaceuticals and biotechnology.

We believe that the diversification of a multi-modality approach optimizes our ability to effectively progress multiple assets for the benefit of patients. By leveraging our expert knowledge of the tumor microenvironment, or TME, and our established business development record, we are developing cancer therapies and technologies through multiple avenues (see Figure 1) including:

- **Platform Development:** We are capitalizing on years of industry innovation and advancement in ADC platforms to develop and design our product candidates. For example, our PYX-201 product candidate is built utilizing the Flexible Antibody Conjugation Technology, or FACT, platform technology in-licensed from Pfizer Inc., or Pfizer. The FACT Platform leverages over a decade of investment refining the technical components of ADCs to improve the clinical properties of ADCs. Using our expertise in site-specific antibody conjugation, we are developing next-generation ADCs with customized linker-payload combinations aimed at increasing stability and, consequently, a reduced off target side-effect profile potentially enhancing the therapeutic index, or TI. We are leveraging our FACT ADC Platform to further build our pipeline while we consider expansion opportunities into adjacent modalities.
- **Target Catalog**: We have a large proprietary target catalog that is based on our own discovery activities and the in-licensed intellectual property, or IP, which formed the founding of the company from the University of Chicago out of the work of Dr. Thomas Gajewski's laboratory. We believe that our target catalog will enable us to identify new ways to exploit multiple components of the TME for tumor targeting, either as new IO, or ADC targets.
- **Forging Creative Business Models and Alliances:** We are continuously evaluating business development and alliance opportunities with a variety of third parties. We aim to be unconstrained by conventional ideas and practices to overcome the many and complex challenges of cancer treatment. We are creating development optionality by engaging in creative business models to further expand the pipeline such as our joint venture with Alloy Therapeutics, known as Voxall Therapeutics, LLC, or Voxall. See "Licensing and Collaboration Agreements" in Item 1. Business in this Annual Report on Form 10-K.
- **Product In-Licensing and Acquisitions:** We selectively seek to in-license product candidates to expand our product pipeline. For example, our PYX-106 (Anti-Siglec-15) product candidate was in-licensed from Biosion USA, Inc. Additionally, we also in-licensed PYX-201 (EDB ADC) from Pfizer. We are actively evaluating opportunities to acquire product candidates which we believe could enable us to add to our portfolio as we build a durable, multi-asset, multi-modality diversified oncology company.

Figure 1





Our Portfolio

Our portfolio consists of both ADC and IO product candidates. Our pipeline is balanced across programs with an emphasis on solid tumors. We in-licensed two ADC programs in March 2021 from Pfizer and one IO program from Biosion USA, Inc. in March 2022. We have additional preclinical mAb discovery programs derived from work at the laboratory of Dr. Thomas Gajewski. We retain full worldwide development and commercialization rights to all our product candidates, with the exception of PYX-106 in Greater China (mainland China, Hong Kong, Macau and Taiwan). In December 2022, we announced clearance of our investigation new drug applications, or IND, by the U.S. Food and Drug Administration, or FDA, for PYX-201 and PYX-106. We are enthusiastic to have transitioned to a clinical stage oncology company and look forward to leveraging our team's experience to execute our clinical trials with the aim of providing patients with safer and more efficacious treatment options.

The following is our current clinical development pipeline:

Program	Potential Indications	Discovery	Preclinical	Phase 1	Most Recent Milestone Achieved	Next Milestone
Antibody-drug Conjugates (ADC)						
Anti-EDB (PYX-201)	e.g., breast, head and neck, lung, and thyroid cancer				Dosing Initiated in 1Q23	Preliminary Data in Early 2024
Immuno-oncology (IO)						
Anti-Siglec-15 (PYX-106)	e.g., bladder, cholangio-carcinoma, colorectal, and kidney cancer				IND Clearance November 2022	First Subject Dosing Early 2Q23

PYX-201

Our lead ADC product candidate is PYX-201, an investigational, novel ADC consisting of an Immunoglobulin G1, or IgG1, anti-fibronectin Extradomain-B, or EDB, mAb site-specifically conjugated to an auristatin derivative via a cathepsin B-cleavable linker. Fibronectin is a glycoprotein found in the extracellular matrix. Fibronectin EDB regulates blood vessel morphogenesis, which provides the tumor access to nutrition and oxygen, a means to remove waste, and a pathway for metastasizing cells. EDB is overexpressed in many malignancies and is minimally expressed in most normal adult tissues, making it a potentially attractive means to target tumors while sparing healthy cells. In preclinical models of patient-derived xenograft, or PDX models, we observed tumor regression with single agent PYX-201. In addition, we observed that the treatment of preclinical syngeneic tumor models with PYX-201 resulted in enhanced T-cell infiltration into the TME, which is a hallmark of immunogenic cell death, or ICD, enabling synergistic activity in combination with a checkpoint inhibitor.

In December 2022, we announced clearance of our IND by the FDA for PYX-201 to initiate a Phase 1 clinical trial. During the first quarter of 2023, we announced dosing of the first subject in a Phase 1 trial of PYX-201, referred to as PYX-201-101. PYX-201-101 is an open-label, multicenter, dose-escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of PYX-201 and identify recommended doses for further study. Patients with relapsed or refractory solid tumors, including non-small cell lung cancer, or NSCLC, hormone receptor positive breast cancer, ovarian cancer, thyroid cancer, pancreatic ductal adenocarcinoma, or PDAC, soft tissue sarcoma, or STS, hepatocellular carcinoma, or HCC, and kidney cancer are eligible to enroll. We anticipate reporting preliminary data from this Phase 1 clinical trial, including biomarker results and early signs of potential clinical activity, in early 2024.

PYX-106

Our lead IO product candidate is PYX-106, an investigational, fully human IgG1 isotype Siglec-15-targeting antibody designed to block Siglec-15 mediated suppression of T-cell proliferation and function. We plan to initially develop this asset for the treatment of solid tumors. We licensed worldwide rights, other than in Greater China (mainland China, Hong Kong, Macau and Taiwan), to PYX-106 from Biosion USA, Inc.

In December 2022, we announced clearance of our IND by the FDA for PYX-106 to initiate a Phase 1 clinical trial. During the first quarter of 2023, we began activating clinical trial sites and are currently screening patients for enrollment in the Phase 1 trial, referred to as PYX-106-101. PYX-106-101 is a first-in-human, Phase 1, multicenter, open-label dose escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PYX-106 in patients with relapsed or refractory solid tumors. This Phase 1 dose escalation trial includes patients who have developed solid tumors and disease progression through standard therapy and patients for whom standard of care therapy that prolongs survival is unavailable or unsuitable. This trial will enroll patients with solid tumors including non-small cell lung cancer without driver mutations/translocations, breast cancer, endometrial cancer, thyroid cancer, kidney cancer, cholangiocarcinoma, bladder cancer, colorectal cancer, and head and neck squamous cell carcinoma, or HNSCC. We anticipate dosing patients in early second quarter of 2023. We anticipate reporting preliminary data from this Phase 1 clinical trial, including biomarker results and early signs of potential clinical activity, in late 2023.

Paused / terminated programs

In August 2022, we paused preclinical development of our anti-CD123 ADC, PYX-203, and anti-KLRG1 IO program, PYX-102. Although these programs remain important to our diversified portfolio of therapeutic candidates, pausing preclinical development efforts currently will allow us to increase the resources available to advance clinical development of PYX-201 and PYX-106. Further, we elected to pause the continued development of our anti-DLK1 ADC, PYX-202, based upon review and analysis of data from preclinical toxicity studies, and the anticipated clinical use and commercial prospects of PYX-202 if approved.

Discovery

In addition to the programs identified above, we are conducting research and development activities on various targets, leveraging our expertise in monoclonal antibodies, ADC conjugation, linker and payload selection, and understanding of immuno-oncology.

Our Strategy

Our goal is to improve the lives of patients with difficult-to-treat cancers by building a superior portfolio of biological products, including ADCs and monoclonal antibody immunotherapies.

Elements of our strategy to achieve our short and long-term goals include:

- **Develop multi-asset, multi-modality, durable portfolio aimed at defeating difficult-to-treat cancers.** We believe that the diversification of a multi-modality approach optimizes our ability to effectively progress multiple assets for the benefit of patients.
- **Progress our product candidates, PYX-201 and PYX-106, through clinical development.** We began activating clinical trial sites and patient enrollment is ongoing for the PYX-106-101 Phase 1 clinical trial. During the first quarter of 2023, we announced dosing of the first subject in a Phase 1 trial of PYX-201, referred to as PYX-201-101. We expect preliminary data from Phase 1 clinical trials of PYX-106-101 and PYX-201-101, including biomarker results and early signs of potential clinical activity, in late 2023 and early 2024, respectively.
- **Pursue a multi-modality approach to cancer therapy addressing various key components of the TME.** Our approach is to leverage our capabilities to develop investigational products that directly target tumor cells and stromal components of the TME with ADCs as well as enhance effector cell function and overcome key mechanisms of immune-suppression with immunotherapeutic mAbs to improve response rates and/or deliver durable responses for more patients.
- **Efficiently progress our preclinical IO programs.** We plan to continue the preclinical development of our pipeline of immunotherapies. If approved, we believe these monoclonal antibody programs have the potential to overcome several of the mechanisms responsible for suppressing immune function and effector cell activity, thus enhancing the anti-tumor immune response in the TME. We also plan to leverage the potential ability of certain ADCs to induce immunogenic cell death to support synergistic combinations with IO agents, including those derived through our own programs.
- **Continue to leverage the FACT Platform and our Target Catalog to expand our pipeline of product candidates.** We plan to continue to mine our target catalog to identify new ways to exploit multiple components of the TME for tumor targeting. Our target catalog may help identify critical immunomodulatory pathways within the TME that can be addressed with monoclonal antibodies. We plan to use our target catalog and the FACT Platform to develop differentiated ADCs with potentially superior clinical activity relative to the current standards of care including monoclonal antibodies. Additionally, we intend to use the FACT Platform to develop ADCs for attractive targets beyond our target catalog.
- **Selectively forge alliances to enhance and expand our product pipeline to further leverage our intellectual property**. We believe that the potential for single agent anti-tumor activity of our current and future products could be enhanced by incorporating potential collaborator technologies. We intend to selectively form alliances with partners to gain access to complementary technologies and expertise to develop and commercialize product candidates with increased potential for anti-tumor activity and the potential for a strong safety profile. We seek to further leverage our intellectual property portfolio through the formation of these alliances.
- **Leverage our team's deep experience and proficiency in oncology research and development to discover and advance novel ADC and immuno-oncology treatments for patients suffering from difficult-to-treat cancers.** We believe our team, which brings deep scientific TME knowledge, functional biology expertise, ADC and IO modality experience, and biologics development capabilities, position us to build a leading oncology company focused on developing product candidates for cancers with high unmet need.

Unmet Need in Oncology

Despite the meaningful advances made in oncology with the approval of several new classes of drugs, there remains significant unmet medical need for novel treatments. According to the World Health Organization, cancer is the second leading cause of death globally, accounting for nearly 10 million deaths in 2020. The key limitations of existing oncology treatments include high toxicity, low or limited response rates, and relapse or recurrence.

Chemotherapy remains one of the most common treatments for cancer, often combined with surgery and radiotherapy depending on the stage and type of tumor. A major challenge in the development of cancer treatments has been the overall complexity and heterogeneity not only of tumors, but of their dynamic surrounding microenvironments. While recent advances in treatment approaches, such as targeting specific tumor mutations that contribute to carcinogenesis or redirecting a patient's immune system to eliminate tumors, have begun to address these challenges, their focus has largely been on tumor cells. We believe that targeting the TME, which has been shown to play a key role in driving tumor progression, growth and multidrug resistance, represents a novel approach for addressing unmet needs in oncology. For example, while the development of immune checkpoint inhibitors has transformed the treatment paradigm for numerous cancers, many patients who respond to these therapies ultimately develop resistance and experience disease progression. Many features of the TME have been shown to influence response and resistance to immune checkpoint inhibitors and targeting the TME has potential to overcome these limitations. Our development efforts aim to leverage our deep understanding of the TME biology with the goal of designing and developing next-generation ADCs, with site-specific conjugation and customized linker-payload combinations, and immunotherapies that target key modulators of the adaptive and innate immune system found within the TME.

Our ADC Product Candidate

PYX-201: Site-Specific Investigational ADC Targeting Onco-Fetal Fibronectin EDB

Overview

Our ADC PYX-201 is an investigational human IgG1 isotype site-specifically conjugated with an auristatin toxin targeting EDB that we plan to initially develop for solid tumors, including NSCLC, hormone receptor-positive breast cancer, ovarian cancer, thyroid cancer, PDAC, STS, HCC, and kidney cancer. We licensed worldwide rights to PYX-201, built on the FACT Platform, from Pfizer. In December 2022, we announced clearance of our IND by the FDA for PYX-201 to initiate a Phase 1 clinical trial. During the first quarter of 2023, we announced dosing of the first subject in a Phase 1 trial of PYX-201, referred to as PYX-201-101. PYX-201-101 is an open-label, multicenter, dose-escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of PYX-201 and identify recommended doses for further study. Patients with relapsed or refractory solid tumors, including NSCLC, hormone receptor positive breast cancer, ovarian cancer, thyroid cancer, PDAC, STS, HCC, and kidney cancer are eligible to enroll.

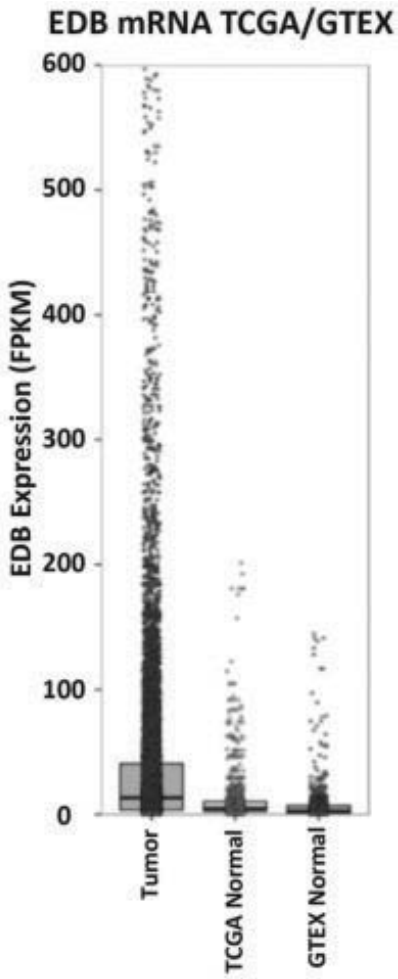
Rationale for Targeting EDB and Mechanism of Action for PYX-201

Fibronectin is a component of the extracellular matrix and its downstream signaling pathways regulate cell adhesion, migration, differentiation, and wound healing. EDB is an alternatively spliced form of fibronectin, which occurs when RNA is re-arranged to produce multiple variants of the same protein. EDB is typically only spliced during embryogenesis and is rarely found in healthy adult tissues. However, cancer cells take advantage of EDB's ability to promote neo-vasculature structures, which are critical to feeding and supporting the uncontrolled growth of a tumor.

EDB is overexpressed in a variety of cancers, including, but not limited to, cancers of the lung, breast, ovary, pancreas, head and neck, thyroid, and brain (refer to Figures 2 and 3). *In vitro* studies have shown that down regulation of EDB resulted in a significant reduction in cancer motility. Furthermore, EDB expression is maintained in distal metastasis in human cancer. EDB meets our criteria of a highly desirable ADC target due to its strict preferential expression in tumor tissue and its role as a driver of the poor prognosis in many cancers.

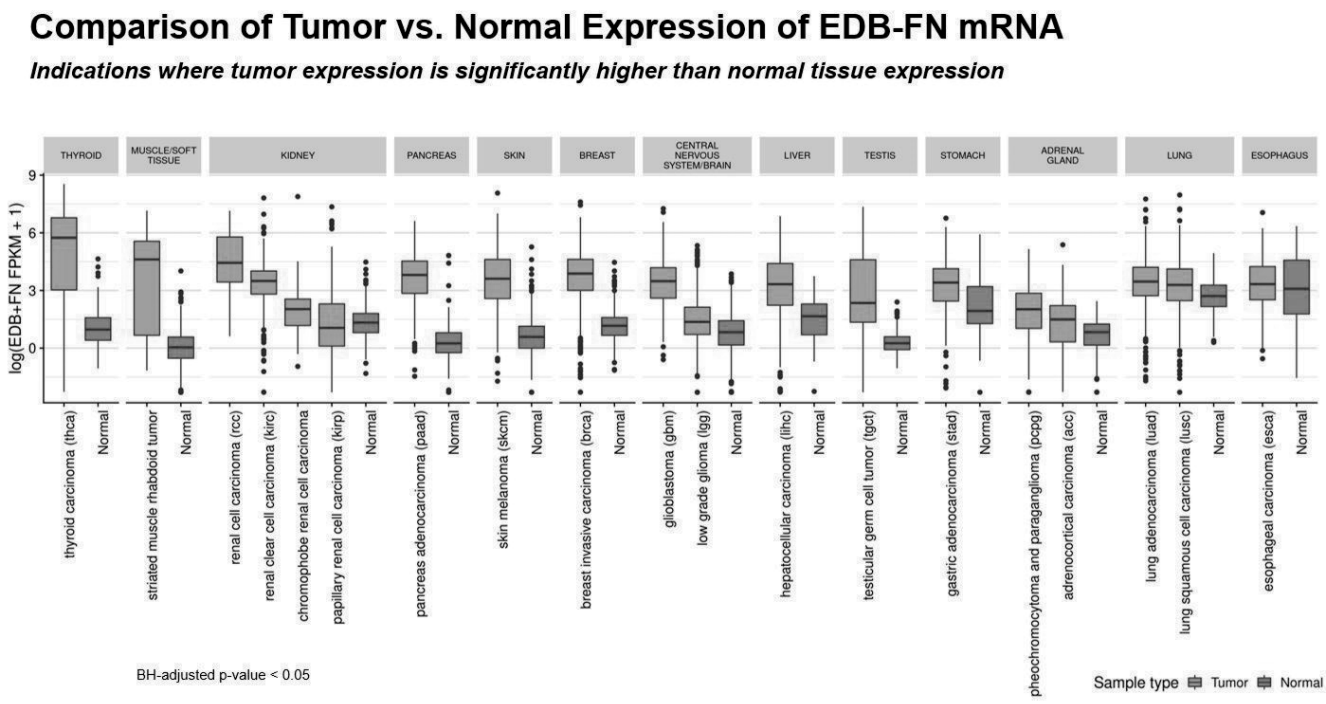
Figure 2

Tumor Type	% Moderate or High (IHC)
Lung Tumors	100
Breast Tumors	92
Ovarian Tumors	83
Head & Neck Tumors	80
Pancreatic Tumors	79



EDB is highly expressed in a variety of solid tumors with restricted normal tissue expression (IHC: Immunohistochemistry; mRNA: Messenger RNA; TCGA: The Cancer Genome Atlas portal; GTEX: Genotype-Tissue Expression portal).

Figure 3



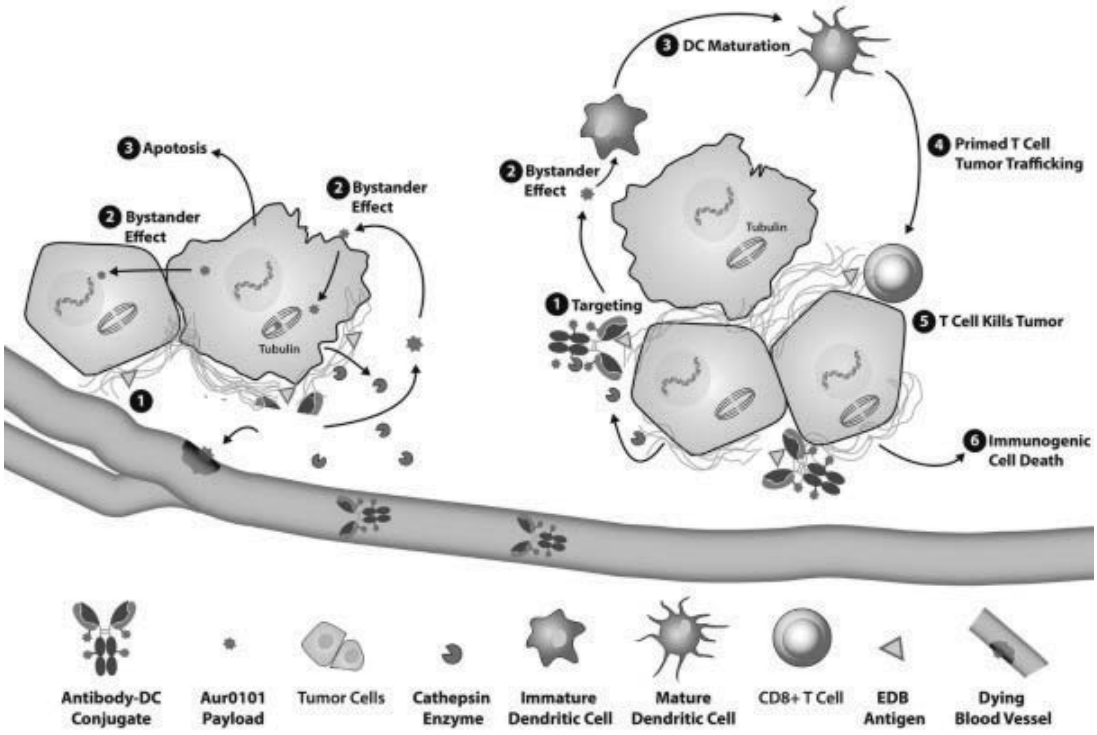
Comparison of tumor versus matched normal samples for indications where statistical significance of the differential expression exceeds a threshold.

PYX-201 was developed using the FACT Platform to produce an ADC designed to be highly stable and target a predictable drug-to-antibody ratio, or DAR, of four. The complementarity-determining regions, or CDRs, of the EDB antibody used in PYX-201, which is the part of the antibody responsible for binding to EDB, is well characterized and has been tested clinically in the form of a radio-conjugated antibody for tumor imaging—demonstrating a high degree of tumor-directed specificity. Furthermore, PYX-201 is designed to optimize linker stability to enable delivery of the auristatin payload without internalization of the ADC into the cancer cell. Unlike currently approved ADCs which bind to the tumor cell surface, PYX-201 is designed to deliver the auristatin payload to the TME consisting of tumor cells, stromal cells and the surrounding blood vessels. PYX-201 is designed to exhibit anti-tumor activity through three distinct modes of action, as illustrated in Figure 4 below. PYX-201 may be internalized prior to extracellular cleavage of the linker due to fibronectin turnover, resulting in the release of the payload in the tumor cell.

1. **Direct killing activity**: After binding to EDB locally expressed in the TME, cathepsin B, a protease which is aberrantly overexpressed in and secreted by invasive and metastatic cancers, cleaves the linker enabling the cell-permeable auristatin toxin to kill both the tumor and stromal cells, and thus may remodel the TME and may enhance T cell activity.
2. **Bystander effect**: Releasing the payload extracellularly within the TME may also confer added cytotoxicity via bystander activity, which may enable killing of cancer cells that do not express EDB.
3. **Immunogenic cell death**: Lastly, auristatin has been shown in preclinical models to drive immunogenic cell death by causing the release of tumor antigens and damage-associated molecular patterns, or DAMPs, and promoting dendritic cell maturation and activation, which together initiate an adaptive immune response.

Taken together, we believe that PYX-201 may generate a multi- pronged attack on difficult-to-treat cancers by directly killing cancer cells, modulating the TME, and mobilizing an anti-tumor immune response.

Figure 4



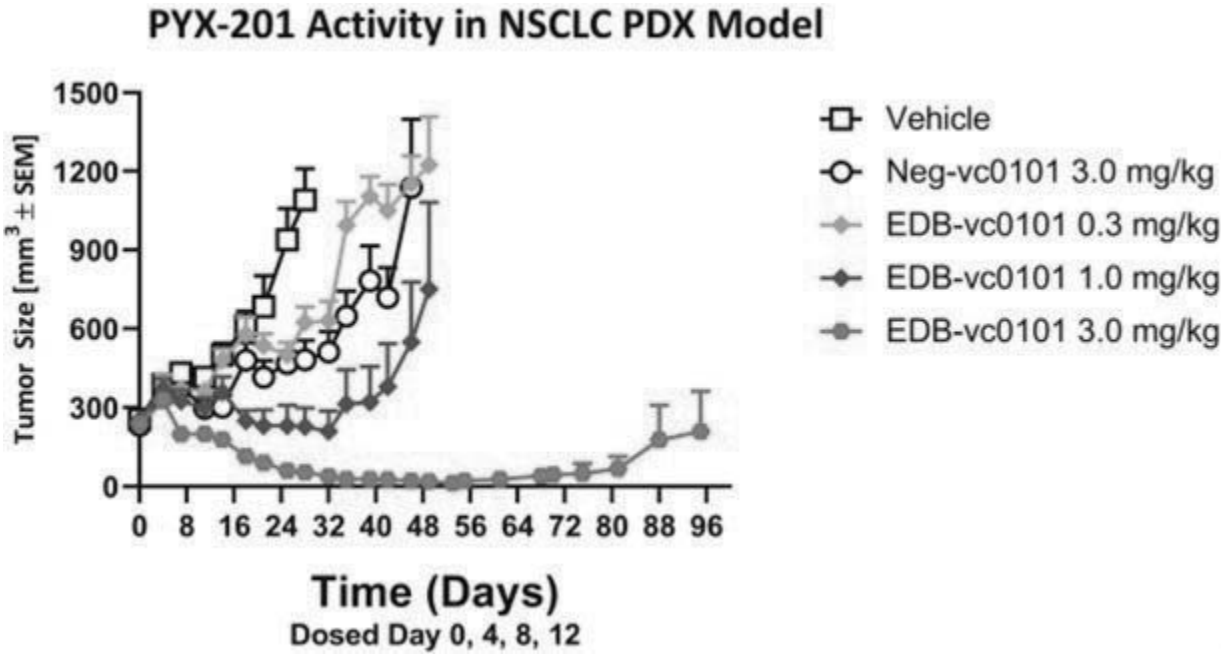
PYX-201 is designed to bind Fibronectin EDB in the surrounding stroma to kill tumor cells and the supporting infrastructure through direct payload-induced cell death, bystander effect and triggering immunogenic cell death based on data from preclinical models.

Preclinical Development

PYX-201 has shown promising preclinical results. In preclinical studies, we have observed strong *in-vivo* activity in NSCLC PDX and in the EMT-6 syngeneic mouse breast cancer models. While PDX mouse models are generated by grafting patient derived cells to immune deficient mice, syngeneic mouse models are grafted with tumors derived from mice which allow the immune system to remain intact. As a result, while PDX models provide the most clinically translatable signals of efficacy in a preclinical setting, syngeneic models allow us to assess the ability of PYX- 201 to generate an immune response. In these syngeneic models, we have been able to show that PYX-201 effectively localizes to cancers and can generate not only significant reductions in tumor burden but can also mobilize an anti-tumor immune response.

For example, in a PDX model of NSCLC, PYX-201 was intravenously administered four days apart for twelve days and a dose-dependent regression in tumor burden and a durable response at 3 mg/kg was observed (Figure 5).

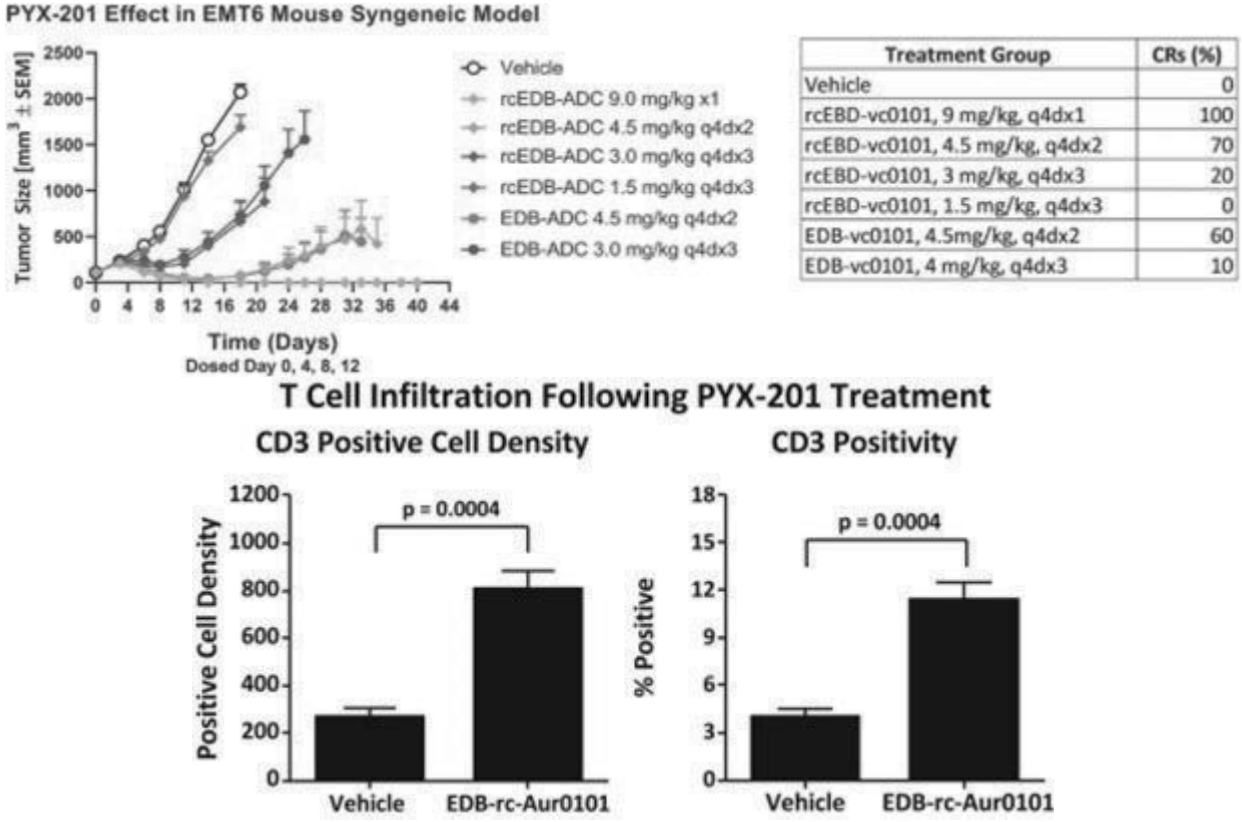
Figure 5



PYX-201 has been shown to be highly active in a PDX model of NSCLC.

The anti-EDB human mAb used in PYX-201 is cross-reactive with mouse EDB-fibronectin. As a result, in syngeneic tumor models conducted in immune competent mice, PYX-201 achieved a durable response with a single dose of 9 mg/kg (Figure 6). In preclinical studies, we observed increased infiltration in CD3 T cells and upregulation of PD-L1, which suggests that PYX-201 may be capable of inducing immunogenic cell death. Combining sub-optimal doses of PYX-201 with checkpoint therapy resulted in synergistic inhibition of tumor growth in the EMT-6 model. Consequently, we believe PYX-201 may synergize with checkpoint inhibitors, as shown in Figure 7. PYX-201 was also well-tolerated in our mouse models and toxicology studies conducted in rat and cynomolgus monkeys. In an exploratory toxicology study in cynomolgus monkeys the highest non-severely toxic dose, or HNSTD, was found to be greater than 12 mg/kg with three doses of PYX-201 administered every three weeks. There was no differential in body weight or food consumption detected and based on the types of toxicities observed (i.e., no fibrosis, neuropathology etc.), all toxicities are reversible, or are expected to be reversible. PYX-201 was observed to have a preclinical relevant therapeutic index of 16 (the HNSTD in monkeys was 144 mg/m^2 and was 16 times greater than the dose required for a complete response in mice of 9 mg/m^2), which we believe is promising based on our experience investigating the relative therapeutic index among different ADC constructs.

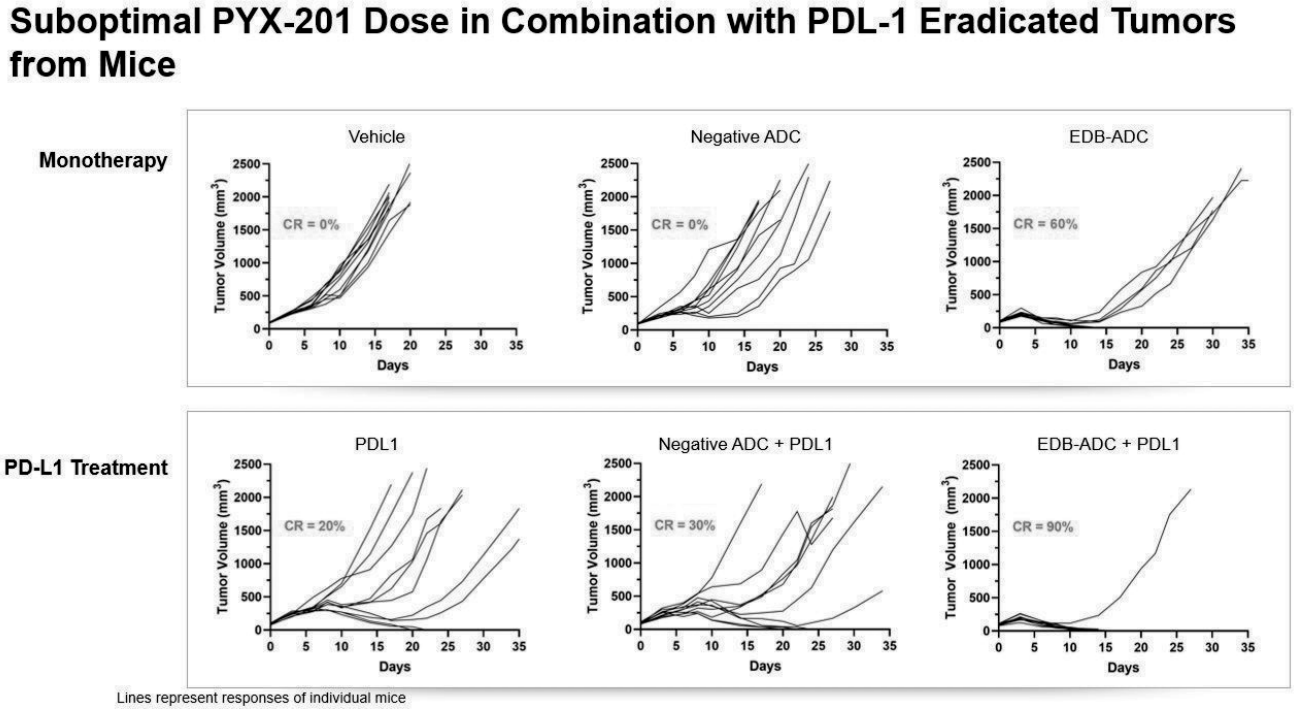
Figure 6



Treatment Group	CRs (%)
Vehicle	0
rcEBD-vc0101, 9 mg/kg, q4dx1	100
rcEBD-vc0101, 4.5 mg/kg, q4dx2	70
rcEBD-vc0101, 3 mg/kg, q4dx3	20
rcEBD-vc0101, 1.5 mg/kg, q4dx3	0
EDB-vc0101, 4.5mg/kg, q4dx2	60
EDB-vc0101, 4 mg/kg, q4dx3	10

PYX-201 treatment in vivo of syngeneic cell-derived tumor models has been associated with enhanced T cell infiltration based on increased CD3 positivity. (CR: complete response; rcEDB: Reverse Chimeric EDB)

Figure 7



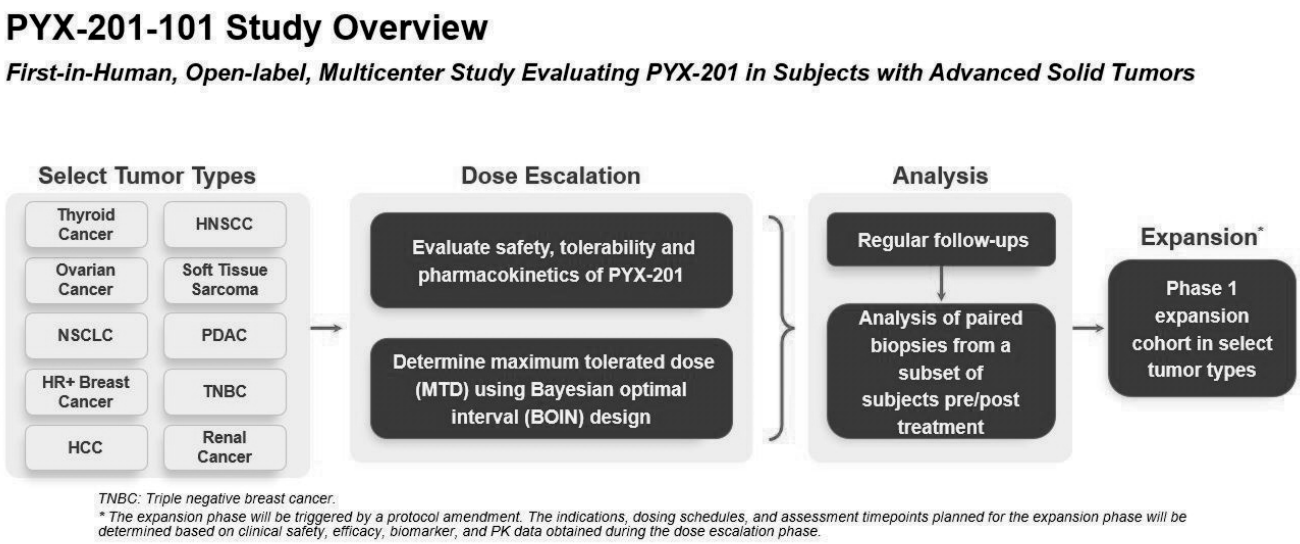
EDB vc0101 ADC combines with anti-PD-L1 to synergistically reduce tumor growth in EMT6 mouse syngeneic model.

Clinical Development Plan

During the first quarter of 2023, we initiated a Phase 1, multicenter, open-label dose escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PYX-201 in patients with relapsed or refractory solid tumors and identify the recommended doses for further study. This Phase 1 dose escalation trial includes patients who have developed solid tumors and have disease progression through standard therapy and patients for whom standard of care therapy that prolongs survival is unavailable or unsuitable. The trial will enroll patients with solid tumors including NSCLC, hormone receptor positive breast cancer, ovarian cancer, thyroid cancer, PDAC, STS, HCC, and kidney cancer.

As illustrated below in Figure 8, the trial is designed as a Phase 1 monotherapy dose escalation trial to investigate the safety and tolerability of PYX-201, to identify a biologically active doses for cohort expansion, and to identify a maximum tolerated dose. We plan to initially enroll patients with NSCLC, breast cancer and other tumor types with a high frequency of EDB expression to identify a recommended dose to evaluate in separate expansion cohorts in select tumor types. We may pursue the development of PYX-201 as a combination therapy with the standard of care as appropriate in future studies. For example, in NSCLC and breast cancer, where immunotherapy is widely used in both first- and second-line settings, PYX-201 may provide a synergistic treatment benefit since the auristatin payload has been observed in preclinical studies to trigger hallmarks of immunogenic cell death. Information on this clinical trial is available on ClinicalTrials.gov (NCT05720117).

Figure 8



We anticipate reporting preliminary data from this Phase 1 clinical trial, including biomarker results and early signs of potential clinical activity, in early 2024.

Immuno-Oncology Programs and Target Catalog Overview

Background on Current Immuno-Oncology Therapeutics

The advent of immuno-oncology therapeutics, particularly immune checkpoint inhibitors, has shifted the treatment paradigm for oncology. The immune system has the capability to recognize and eliminate cancer, but tumor cells take advantage of immune checkpoint pathways, which normally prevent autoimmunity, to suppress and evade immune effector cell activity. The first generation of drugs that interrupt these pathways, including PD-L1 and cytotoxic T-lymphocyte associated protein 4, or CTLA-4, inhibitors, has generated significant enthusiasm due to their ability to achieve durable responses in some patients. While these drugs provide significant therapeutic benefit for durable responders, response rates remain low for most patients, particularly for tumors with low levels of T-cells infiltrating the tumor. These non-inflamed (i.e., "cold") tumors can suppress the adaptive immune response through a variety of mechanisms within the TME.

Target Catalog Overview

We have a large proprietary target catalog that we have assembled through both our own discovery activities and through an exclusive license from the University of Chicago for the work on immunotherapy targets out of Dr. Thomas Gajewski's laboratory. We are also building a large "cold" tumor target discovery database leveraging several human tumor databases.

The target catalog is based upon findings from an *in vivo* mouse model system which examined tumor tissue for functional and dysfunctional T cells based on the ability of the T cells to produce the cytokine IL-2. Furthermore, since 4-1BB and LAG3 positive T cells do not secrete IL-2, the CD8+ T cells were sorted based on cell surface marker expression i.e., 4-1BB and LAG3, which further defined functional or dysfunctional T cells. Gene expression analysis identified upregulated cell surface molecules in dysfunctional cells which included well established markers such as PD1, CTLA4, and TIM3, while many other novel targets were identified of which we have prioritized a select subset for discovery research based on bioinformatics and deep biological rationale.

Our cold tumor target discovery database used RNA-seq transcriptome analysis of human tumor databases to identify potential novel targets involved in regulation of T cell function and/or infiltration leading to cold tumors. We have supplemented this database with additional resources which we continue to mine to identify additional novel targets for immunomodulation. These cold tumor targets are potentially dominant immune suppressors that are expressed across a variety of tumor associated cells, including immune cells, tumors cells, and stroma, offering the potential to uncover not only novel IO mechanisms, but additional novel targets for our ADC platform.

Immuno-Oncology Programs Overview

We have initiated multiple monoclonal antibody programs that address critical immunomodulatory pathways within the TME and are exploring additional potential targets. Our programs address critically important tumor infiltrating immune cell populations, such as macrophages, T cells, and natural killer, or NK, cells, which may play crucial roles in limiting tumor growth and metastasis. In addition to singling out specific cell types, we believe our IO programs also address mechanisms responsible for T cell exhaustion and the immunosuppressive effects of the TME on T and NK cells. These effects can occur due to chronic exposure to tumor antigens within the TME and direct exposure to immunosuppressive cytokines and other signaling molecules. Though PD-L1 therapies can help reinvigorate T cells, they are often not sufficient to overcome T cell exhaustion and many patients do not respond to standard checkpoint therapy. Several immunosuppressive pathways can also directly limit T cell activity and other critical components of the anti-tumor immune response, such as direct tumor killing by NK cells. Therapies that target both T cell and NK cells to counteract these pathways have the promise to restore immune effector function, either alone or in combination with checkpoint inhibitors. Furthermore, MDSCs/TAMs are another major component of the TME with significant immunosuppressive activity. These cells represent a mixed population of immature myeloid cells and are actively recruited to the TME where they broadly suppress immune activity. MDSCs and tumor-associated macrophages, or TAMs, support tumor growth by depriving other immune cells of key amino acids essential for immune function, producing signaling molecules that block immune effector function, and enhancing activation of regulatory T cells. Furthermore, MDSCs and TAMS promote tumor angiogenesis and growth and are a marker associated with poor outcomes and linked to poor response to PD-L1 therapy. We believe our IO programs represent potential novel therapies that have the potential to overcome multiple protumor mechanisms by enhancing T and NK cell activity, or by inhibiting immune suppressive functions of MDSCs and TAMs within the TME.

PYX-106: Investigational IgG1 isotype anti-Siglec-15 Targeting Antibody

Overview

PYX-106 is an investigational fully human IgG1 isotype antibody that is designed to block Siglec-15 mediated suppression of T-cell proliferation and function. PYX-106 aims to address critically important tumor infiltrating immune cell populations, such as macrophages, T cells, and NK cells, which may play crucial roles in limiting tumor growth and metastasis. In addition to singling out specific cell types, we believe PYX-106 may also address mechanisms responsible for T cell exhaustion and the immunosuppressive effects of the TME on T and NK cells. We believe that our in-licensed anti-Siglec-15 mAb PYX-106 has the potential to provide additional benefit to cancer patients either alone or in combination with other therapies, including other immuno-therapies. We licensed worldwide rights other than in Greater China (mainland China, Hong Kong, Macau and Taiwan) to PYX-106 from Biosion USA, Inc.

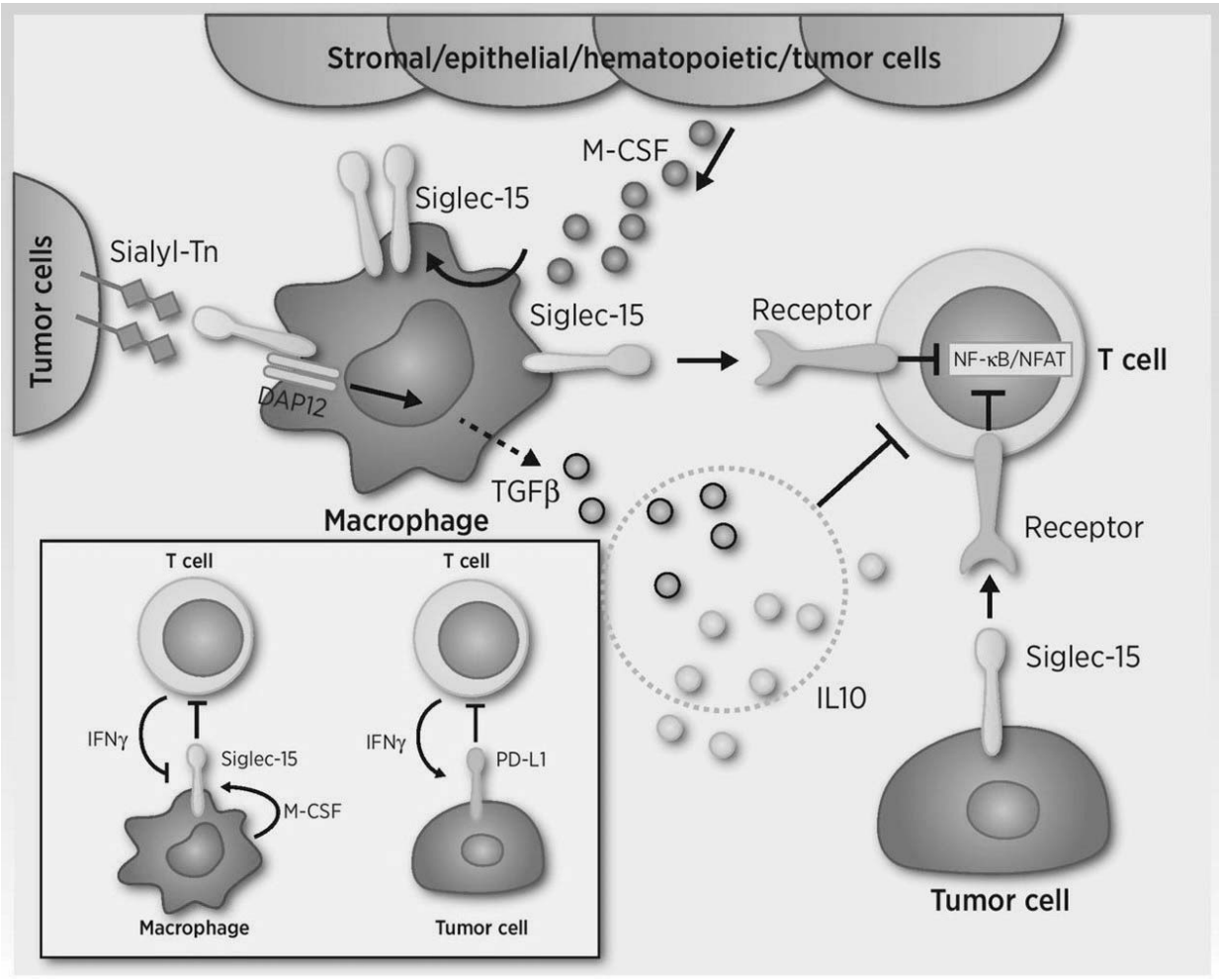
In December 2022, we announced clearance of our IND by the FDA for PYX-106 to initiate a Phase 1 clinical trial. During the first quarter of 2023, we began activating clinical trial sites and are currently screening patients for enrollment in the Phase 1 trial, referred to as PYX-106-101. PYX-106-101 is a first-in-human, Phase 1, multicenter, open-label dose escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PYX-106 in patients with relapsed or refractory solid tumors. This Phase 1 dose escalation trial includes patients who have developed solid tumors and disease progression through standard therapy and patients for whom standard of care therapy that prolongs survival is unavailable or unsuitable. This trial will enroll patients with solid tumors including non-small cell lung cancer without driver mutations/translocations, breast cancer, endometrial cancer, thyroid cancer, kidney cancer, cholangiocarcinoma, bladder cancer, colorectal cancer, and head and neck squamous cell carcinoma.

Rationale for Targeting Siglec-15 and Mechanism of Action for our Siglec-15 targeting antibody

Siglec-15 is a member of the Siglec family (Sialic acid-binding ImmunoGlobulin Lectins), a distinct subgroup of immunoglobulin, or Ig, superfamily proteins involved in immune regulation. Siglec recognize and bind to sialic acid on the surface of cells and this binding can affect cell signaling on immune cells. Siglec-15 is a single-pass type I membrane protein that has been shown to associate with the activating adaptor proteins DNAX activation protein (DAP)12 and DAP10 via its lysine residue in the transmembrane domain, implying that it functions as an activating signaling molecule. While Siglec-15 is minimally expressed on normal tissues, it is highly expressed on both tumor cells and M2 macrophages in the TME across multiple tumor types, including thyroid cancer, HNSCC, lung cancer, breast cancer and cholangiocarcinoma. The increased presence of highly immunosuppressive M2 macrophages within tumors leads to impaired T cell proliferation and function, causing a decreased anti-tumor immune response. Additionally, Siglec-15 may exacerbate this immunosuppressive effect by interacting with tumor associated myeloid cells to promote their survival and differentiation to drive a tumor-promoting environment. Interestingly, Siglec-15 appears to function independently from the PD-L1 pathway with largely non-overlapping expression in select tumor samples. Therefore, targeting Siglec-15 in the TME may be a promising therapeutic option for patients less likely to respond to a PD-1/PD-L1 targeted therapy.

An overview of the role of Siglec-15 in regulating the immune system and driving anti-tumor immune dysfunction is depicted in Figure 9 below.

Figure 9

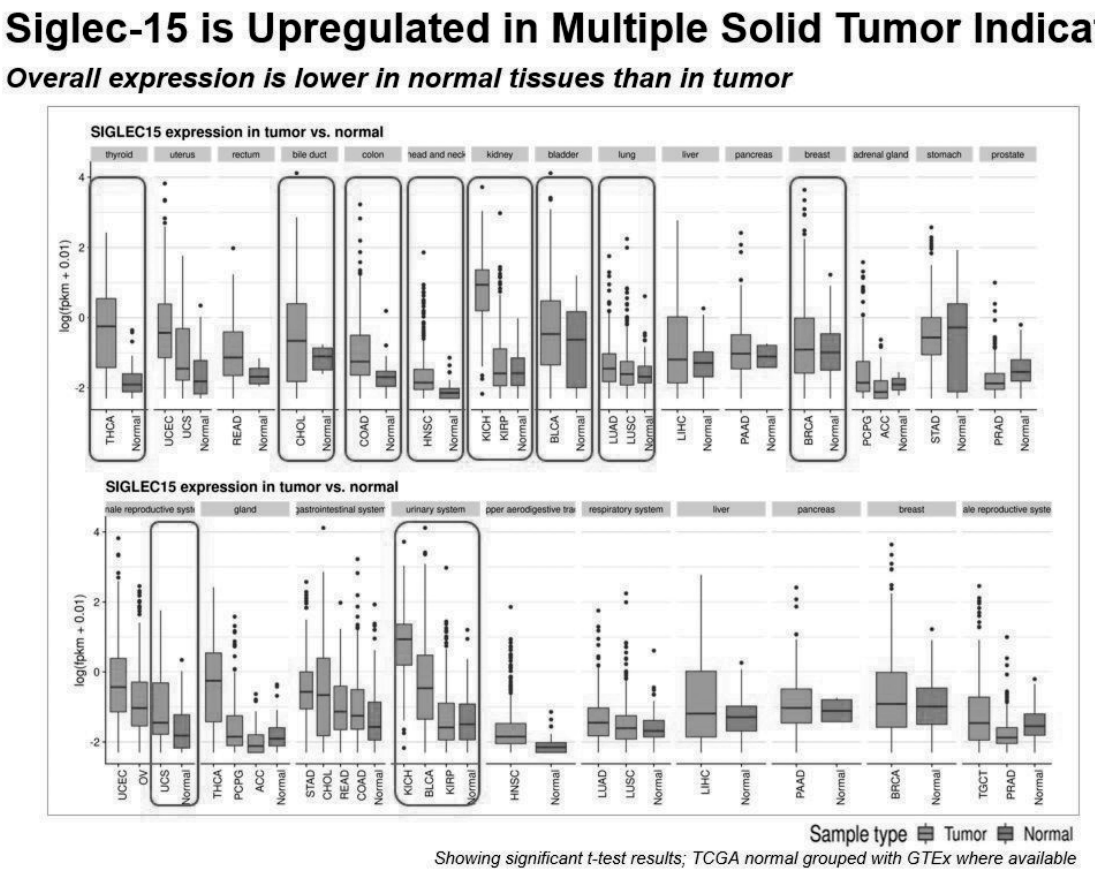


Source: American Association for Cancer Research Journal - Cancer Clinical Research Review - Siglec-15 as an Emerging Target for Next-generation Cancer Immunotherapy by Jingwei Sun, Qiao Lu, Miguel F. Sanmamed and Jun Wang

Our Siglec-15 targeting antibody is a fully human monoclonal antibody and is engineered with high affinity to block Siglec-15 induced immune suppression and therefore restore T cell proliferation, function and anti-tumor immunity in the TME. Overall, by binding and blocking Siglec-15 activity on myeloid cells and tumors, our Siglec-15 targeting antibody is designed to enhance immune cell mediated tumor cell kill. Given the broad tumor expression profile of Siglec-15, our Siglec-15 targeting antibody has the potential to treat multiple oncology indications including those where PD-1/PD-L1 directed cancer therapies are ineffective.

Expression data for Siglec-15 in tissues where tumor expression was significantly higher than normal tissue expression are depicted in Figure 10. Of the indications tested, NSCLC, breast cancer, uterine cancer, thyroid cancer, kidney cancer, cholangiocarcinoma, bladder cancer, colorectal cancer, and sarcoma all show higher expression of Siglec-15 in tumor compared to normal samples. The low expression of Siglec-15 across the range of normal tissues tested suggests limited potential for effects in nontumor tissues of therapies targeting Siglec-15. Significantly higher expression in most tumor types indicates that patients with such tumors may respond to anti-Siglec-15 antibody treatment.

Figure 10



Siglec-15 is broadly expressed across a range of solid tumors with higher expressing tumors, with kidney and thyroid cancer where the difference is substantial.

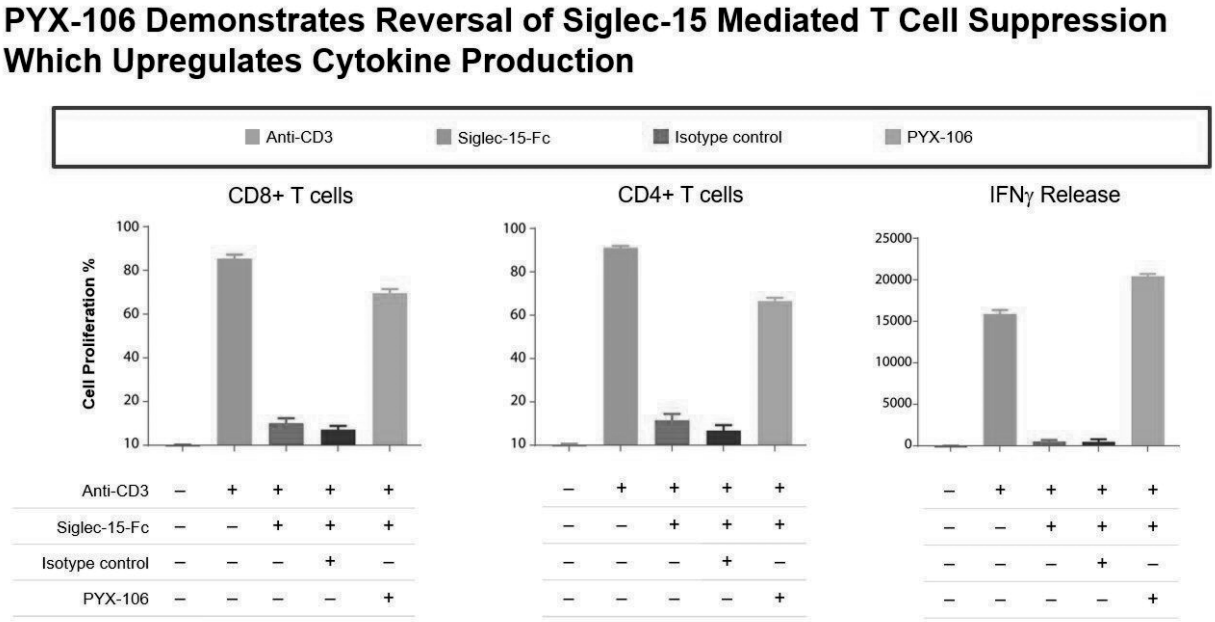
Preclinical Development

Blocking Siglec-15 with an antibody such as PYX-106 may overcome the immunosuppressive TME and enhance the antitumor activity of other immune checkpoint inhibitors. We have conducted a preclinical study in various animal models to evaluate the effect of blocking Siglec-15 and our observed results provide sufficient scientific rationale in both *ex vivo* and *in vivo* studies.

In an *in vivo* mouse syngeneic tumor model, PYX-106 demonstrated significant inhibition of tumor growth when administered at 15 mg/kg twice weekly for 6 weeks compared to the control group. PYX-106 resulted in an approximately 60% decrease in tumor volume at doses of 5 mg/kg and 15 mg/kg, with the decrease reaching statistical significance in the latter dose group. Moreover, the inhibition of tumor growth was not accompanied by any changes in behavior, body weight, or spleen weight within the mice.

In an *ex vivo* study using normal human peripheral blood mononuclear cells, or PBMCs, which are blood cells that are considered critical components in the immune system, PYX-106 was able to reverse Siglec-15-mediated suppression of T cell proliferation and interferon-gamma, or IFN-γ, secretion. The numbers of CD4+ and CD8+ T cells and secretion of IFF-γ were increased substantially while the negative control antibody had no effect on the suppression of proliferation. The effects of a single concentration of anti-Siglec-15 antibodies on T-cell proliferation using PBMCs are shown in Figure 11. The addition of the anti-CD3 antibody led to proliferation of both CD4+ and CD8+ T cells, which was reduced by addition of Siglec-15. The addition of the negative control antibody had no effect on this suppression of proliferation. PYX-106 reversed this suppression.

Figure 11



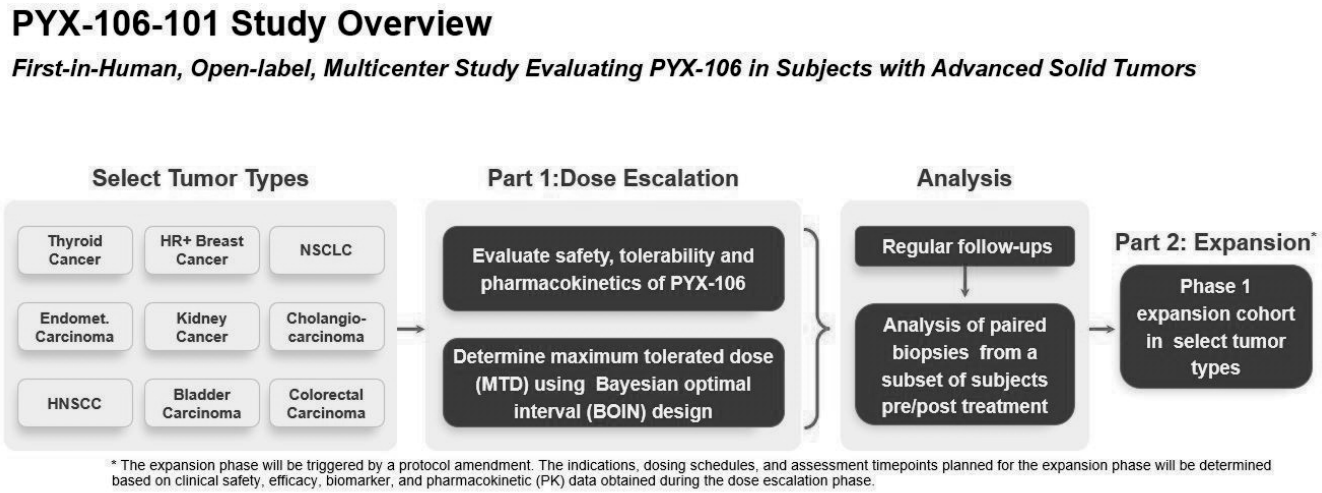
Illustrates an ex vivo assay using PBMCs, from normal healthy donors. In preclinical studies, PYX-106 reverses Siglec-15 mediated T cell suppression, upregulating the immune system to fight the cancer cells and prevent tumor growth.

Clinical Development Plan

In December 2022, we announced clearance of our IND by the FDA for PYX-106 to initiate a Phase 1 clinical trial. During the first quarter of 2023, we began activating clinical trial sites and are currently screening patients for enrollment in the Phase 1 trial, referred to as PYX-106-101. PYX-106-101 is a first-in-human, Phase 1, multicenter, open-label dose escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PYX-106 in patients with relapsed or refractory solid tumors. This Phase 1 dose escalation trial includes patients who have developed solid tumors and disease progression through standard therapy and patients for whom standard of care therapy that prolongs survival is unavailable or unsuitable. This trial will enroll patients with solid tumors including non-small cell lung cancer without driver mutations/translocations, breast cancer, endometrial cancer, thyroid cancer, kidney cancer, cholangiocarcinoma, bladder cancer, colorectal cancer, and head and neck squamous cell carcinoma.

As illustrated below in Figure 12, this trial is designed as a Phase 1 monotherapy dose escalation trial to investigate the safety and tolerability of PYX-106, to identify a biologically active dose for cohort expansion and to identify a maximum tolerated dose. As part of the trial, tumor samples will be collected from participants to enable biomarker analysis. Patients with relapsed or refractory solid tumors known to have significant infiltration of M2 macrophages and expression of Siglec-15, including non-small cell lung cancer, breast cancer, endometrial cancer, thyroid cancer, kidney cancer, cholangiocarcinoma, bladder cancer, colorectal cancer, and head and neck squamous cell carcinoma, are eligible to enroll. Information on this clinical trial is available on ClinicalTrials.gov (NCT05718557).

Figure 12

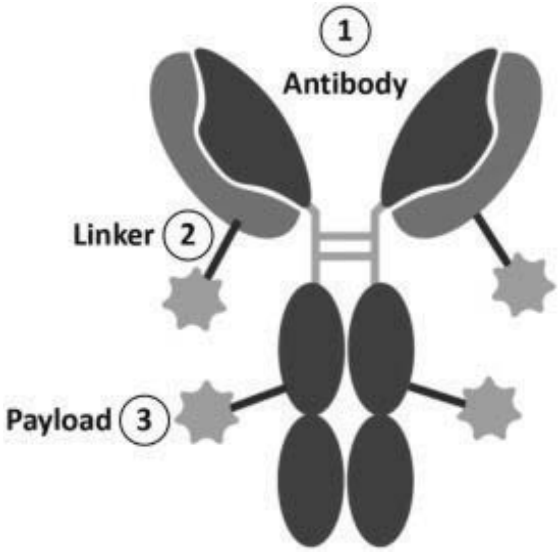


We anticipate dosing patients in early second quarter 2023. We anticipate reporting preliminary data from this Phase 1 clinical trial, including biomarker results and early signs of potential clinical activity, in late 2023.

Overview of Antibody Drug Conjugates

ADCs are a therapeutic class in which cytotoxic chemotherapy molecules are linked to a targeting mAb to effectively deliver the tumor killing effect into tumor lesions while limiting systemic toxicity. Systemic toxicity limits the efficacy of chemotherapy, a highly cytotoxic class of anti-tumor medicines. ADCs can significantly improve the therapeutic window of toxic payloads even more cytotoxic than traditional chemotherapies by targeting their delivery to tumorous cells and their local environment and sparing healthy tissue. ADCs achieve this level of precision by pairing payloads with monoclonal antibodies, proteins that can recognize their target antigens with great specificity. ADCs are an established and fast-growing class of biological products. To date, thirteen ADCs have been FDA approved, of which nine have entered the market since 2019.

Figure 13



Schematic representation of an ADC, highlighting the three key components; targeted antibody, linker, and payload or cytotoxic agent (dark blue: mAb heavy chain; pink: mAb light chain).

The clinical properties of ADCs are a function of three components (as show in Figure 13 above):

(1) A monoclonal antibody that selectively targets a distinct antigen preferentially expressed on tumor cells or other cells in the tumor microenvironment;

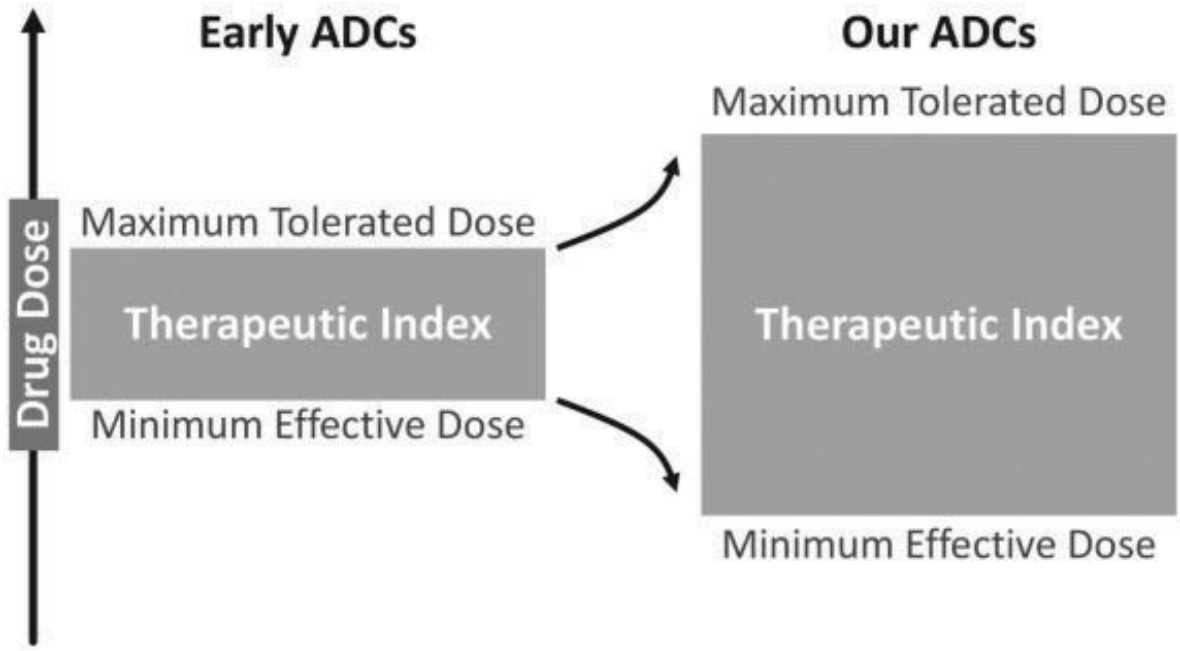
(2) A linker that joins together the antibody and the payload; and

(3) A payload that can effectively kill the targeted cell.

Ideal ADC targets typically have highly tumor restricted expression to spare healthy tissues, are accessible to circulating antibodies, and have well-defined internalization kinetics or can be effectively bound within the TME. Once administered, an ADC will travel in the bloodstream until it encounters its target antigen followed by release of the toxic payload.

A measure of drug tolerability for ADCs is the preclinical therapeutic index, which is calculated from data to estimate the safety profile (refer to Figure 14). This measure is the preclinical ratio of the HNSTD in monkeys versus the minimally effective dose, or MED, in mouse tumor models. The therapeutic index is defined formulaically as HNSTD (mg/m^2) in monkeys / mouse minimal tumor regression dose (mg/m^2). As further illustrated in Figure 14 below, a wider therapeutic index is a key attribute of an ADC's potential clinical success.

Figure 14



The therapeutic index is a measure to estimate the clinical tolerability profile of ADCs based upon the ratio of maximum tolerated dose, or MTD, in monkeys versus the MED in rodents from preclinical studies.

Key Areas of Innovation for Engineering the Next-Generation ADCs

Optimizing the Linker

The linker that joins the payload to the antibody should prevent the payload's premature release while in circulation and ensure efficient release of the payload into the target cell(s) and/or the TME. There are two general classes of linkers:

(1) Cleavable linkers are designed to conditionally unload cytotoxic agents within the tumor cell or TME in response to the presence of tumor-associated factors such as proteases or highly acidic conditions. Typically, cleavable linkers carry uncharged payloads, allowing the drug to diffuse out of the target cell to kill surrounding "bystander cells." Bystander killing can also occur when the uncharged payload is unleashed within the TME.

(2) In contrast, non-cleavable linkers remain intact upon internalization and rely on lysosomal degradation of the entire construct to achieve sufficient payload release. Non-cleavable ADCs typically release their payloads as charged catabolites, which traps the toxin within the cell where it was internalized. As a result, non-cleavable ADCs are naturally well suited to address cancers with a high and uniform expression of the target antigen since cells lacking the target antigen will not be directly affected.

We believe our toolbox of cleavable and non-cleavable linkers allows us to select the optimal linker tailored to each program. We select our linkers based on several factors, including but not limited to the level and distribution of the target antigen and rates of antigen turnover, internalization, lysosomal processing, and degradation.

Site-Specific Conjugation

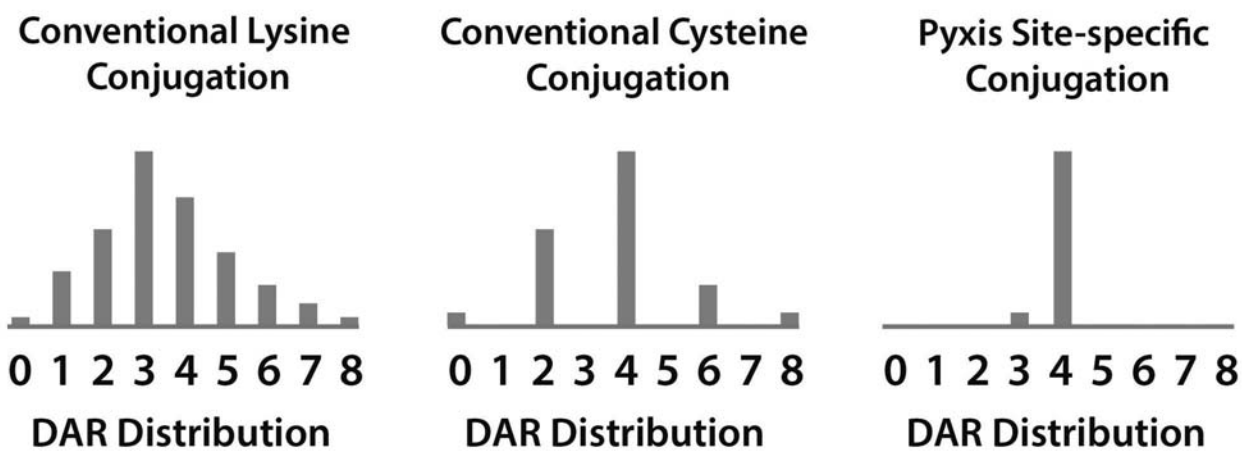
Site-specific conjugation chemistry enables the engineering of next-generation ADCs with predictable DAR with improved ADC pharmacokinetics, or PK, observed preclinically. This improved PK results in minimizing premature payload release and less off-target toxicity and as a result improves the overall TI of the ADC.

DAR is defined as the number of payload moieties attached to each antibody, which typically range from zero to eight. Ideally, there is limited variability in DAR to allow for ADCs with predictable PK and more predictable efficacy. Variability in DAR and stability are primarily a consequence of the technology used to conjugate the linker to the antibody. The two conventional conjugation approaches employed in conventional ADC conjugation technology utilize either lysine residues or the interchain disulfides located on an antibody. These approaches result in a stochastic mixture of conjugates consisting of a heterogeneous pool of synthesized ADCs, as shown in Figure 15 below. Each bar in the graph consists of an ADC with the number of payloads indicated on the X-axis. Each one of these parts of the mixture of conjugates contributes to the efficacy and toxicity making it difficult to optimize for either property.

In addition to DAR, research has shown conjugate stability and the resulting rate of payload release can vary significantly between specific conjugation sites. Hence, conventional conjugation suffers from unpredictable and premature payload release outside of the tumor resulting in off target toxicities.

Together with our extensive toolbox of linkers, we believe our site-specific conjugation chemistry offers us the advantage of fine-tuning and optimizing the cleavage of the drug in the TME while limiting off-tumor release and allowing for predictable DAR distribution. Site-specific conjugation technologies have led to improved ADC predictability with narrow distribution of DAR to facilitate CMC manufacture and consistent potency (refer to Figure 15).

Figure 15



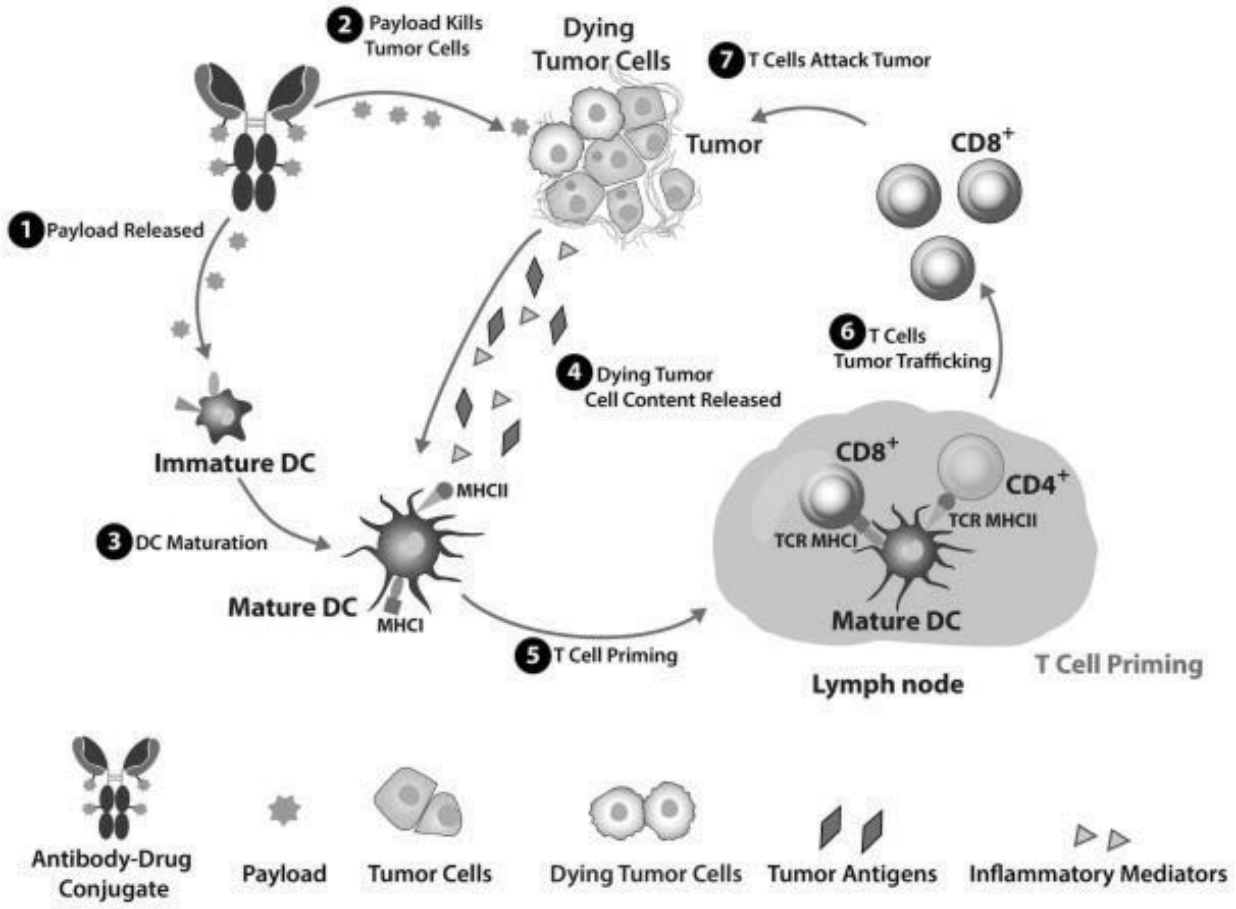
Depicted above is an illustrative example of DAR distribution for a DAR 4 ADC using different conjugation chemistries which highlights how our site-specific conjugation technology allows for linker/payload to be precisely conjugated, leading to more predictable DAR ADCs. This also improves CMC characteristics and enhances stability of ADCs to maximize tumor delivery of the payload.

The Selection of Cytotoxic Payload

The chemotherapeutic payload is a highly potent toxin that would otherwise carry devastating side effects as a systemically delivered monotherapy. There are several potential payloads, including antineoplastic auristatins, which act on microtubules to inhibit cell division, and alkylating or intercalating agents, which damage DNA.

While an ADC's primary mode of action is to induce direct cell death through the payload, ADCs can exploit multiple avenues of anti-tumor action beyond direct cytotoxicity. For example, a growing area of interest is applying ADCs to induce ICD allowing for synergy with immunotherapy modalities including checkpoint inhibitors. Rapid cancer cell death caused by ADCs results in the release of damage-associated molecular patterns and tumor antigens, stimulating a tumor-specific immune response and recruitment of T cells into the TME (Figure 16). An emerging area of interest is utilizing ADCs to disrupt various aspects of the TME, such as angiogenesis or tumor-associated fibroblasts. Furthermore, certain payloads, such as auristatins, have been shown to engender the maturation and activation of dendritic cells, a critical compartment of the immune system responsible for initiating and regulating the innate and adaptive immune response.

Figure 16



Overview of the process by which ADCs, particularly those with certain payloads, can potentially trigger hallmarks of immunogenic cell death to enhance tumor cell killing.

ADCs have and may continue to revolutionize the treatment paradigm for several cancers. Despite the improvements that have been seen with currently marketed ADCs, these ADCs still have limitations that impact dosing, and are associated with significant adverse events. We have designed our product candidates to overcome the limitations of ADCs that use conventional conjugation with the aim of providing patients with safer and more efficacious treatment options. We believe that our combined expertise in ADC design and insights into TME biology have the potential to yield a holistic treatment spanning multiple mechanisms for patients with difficult-to-treat cancers that will overcome the current limitation of ADCs and result in better outcomes for patients.

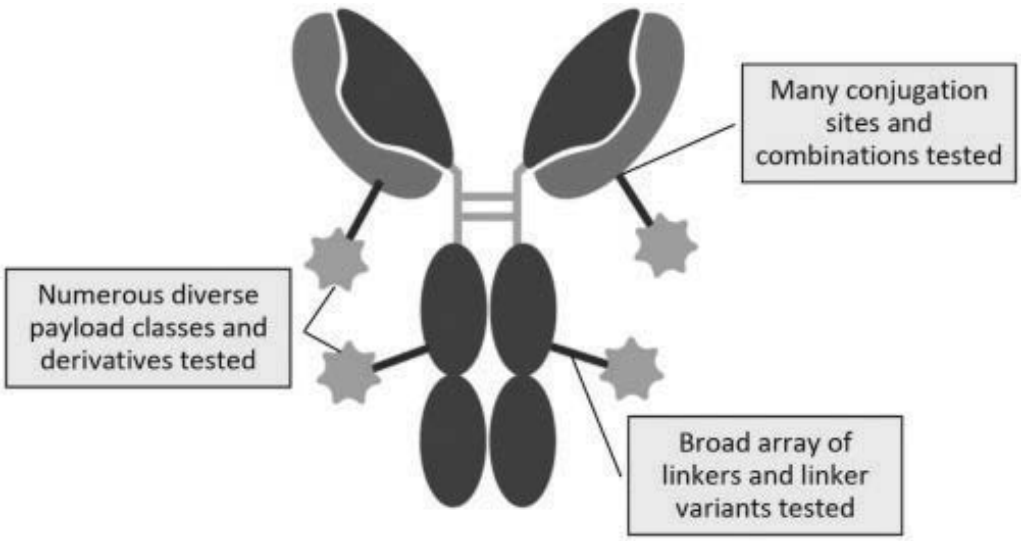
FACT Platform

We are developing next-generation ADCs using customized linker-payload combinations that are novel and supported by the preclinical data and site-specific conjugation techniques derived from the FACT Platform. We believe that these payloads and linkers could be readily applied to any IgG1 antibodies using our site-specific conjugation techniques to efficiently develop novel product candidates. We initially licensed the FACT Platform from Pfizer in December 2020, before securing an exclusive license to the FACT Platform in October 2022, and benefit from over a decade of research and investment by Pfizer. See "Licensing and Collaboration Agreements" in Item 1. Business in this Annual Report on Form 10-K. We believe that the site-specific conjugation techniques and ADC technology which underpin the FACT Platform enable us to develop next-generation ADCs with more favorable drug properties than traditional technologies based on preclinical studies.

Despite the clinical successes of ADCs as a therapeutic class, many ADCs still utilize conventional non-site-specific conjugation techniques that result in a heterogeneous mixture of ADCs with varying DAR. Recently, preclinical research carried out by Pfizer to empirically assess the impact of conjugation sites on ADC stability and activity in rodent models has indicated that site-specific conjugation techniques may enable enhanced pharmacologic properties and predictable DAR to potentially improve the therapeutic index.

Though multiple reports have shown that site-specific conjugation techniques often result in ADCs with a wider therapeutic index, greater stability, and better efficacy in preclinical *in vivo* models than traditional non-specific, conventional ADC conjugates, less is understood about how to optimize these sites, as optimization relies upon empirical data generation for each specific linker-payload combination. We believe that the FACT Platform has demonstrated that there are multiple biochemical parameters of ADCs impacting performance *in vivo* and established a framework for optimized conjugation sites for a variety of linker-payload combinations (Figure 17).

Figure 17



The FACT Platform technology is designed to empirically define optimal conjugation sites for linker-payloads to generate highly stable and predictable ADCs with potential for improved therapeutic indices.

Pfizer optimized sites for linker-payload conjugation through empirical research

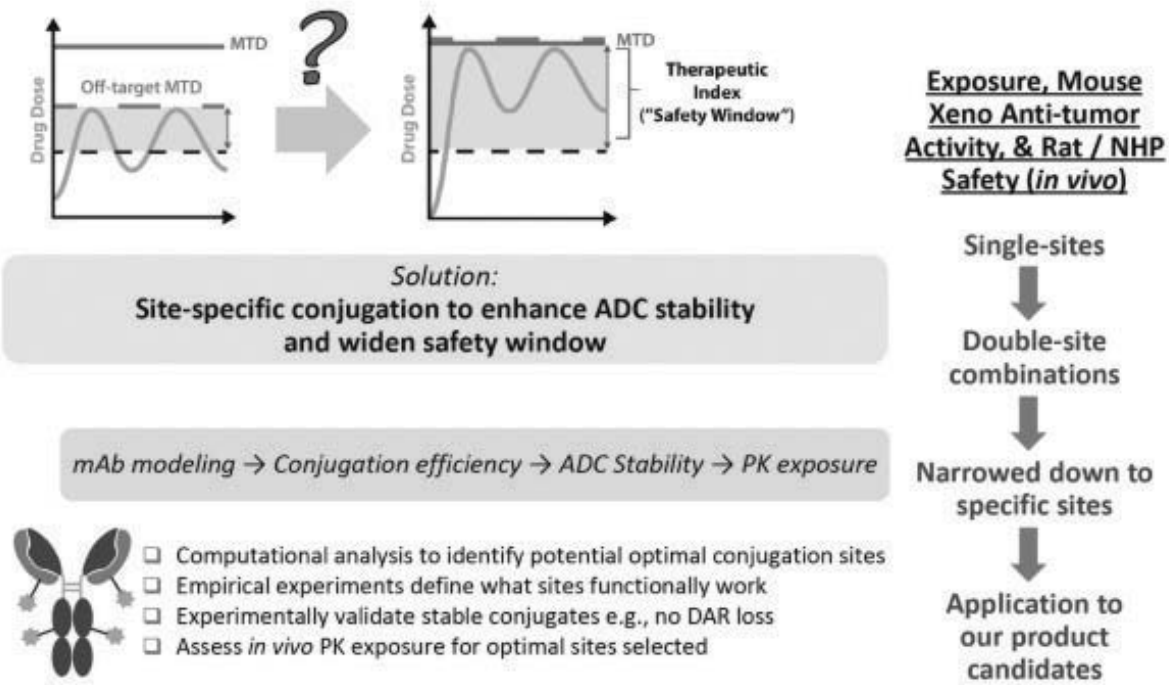
We believe that the FACT Platform provides a toolkit of novel and validated payloads, cleavable and non-cleavable linkers, and a strong understanding of optimized conjugation sites. The FACT Platform provides the basis for our ADC product candidate, PYX-201, and preclinical program, PYX-203, and will underpin our development of future ADCs that we believe are optimized for, and guided by the following design elements:

- **ADC cytotoxicity**. Target tumor cells require delivery of a certain threshold of payload molecules based on the payload's biochemical properties to induce cell killing at specific dose levels. Our ADC programs are designed to provide anti-tumor cytotoxicity and, as applicable, immunogenic cell death based on data from preclinical models.
- **Plasma stability and maintenance of the linker-payload**. ADCs must be optimized for systemic circulation to prevent premature linker cleavage or release of the linker-payload construct in the blood plasma that can result in off-target toxicity. We are designing our ADC candidates to optimize for stability when in circulation *in vivo* to avoid premature cleavage and support maximal payload delivery to the target site.
- **Efficient proteolytic cleavage of the linker for payload release**. The timing and rate of linker cleavage is important for achieving optimal delivery and release of a specific payload at the target site. We believe that we have the capability to utilize both cleavable and non-cleavable linkers to achieve potential therapeutic effects that are optimized for individual payloads and targets.
- **High target specificity**. Our ADC programs are founded on the identification of promising tumor targets and developing highly specific antibodies against these tumor targets. We draw upon our empirical understanding of site-specific conjugation sites and linker-payload toolkit to select combinations that we believe are well-suited for individual targets.
- **Defined and target specific DAR.** Intrinsic to the FACT Platform and conjugation techniques is the development of products with a consistent DAR, which we believe may enable us to develop a product with optimized stability, tolerability, and cytotoxicity.

We believe that the FACT Platform conveys several distinct advantages and flexibility in the development of our ADC candidates, including the following:

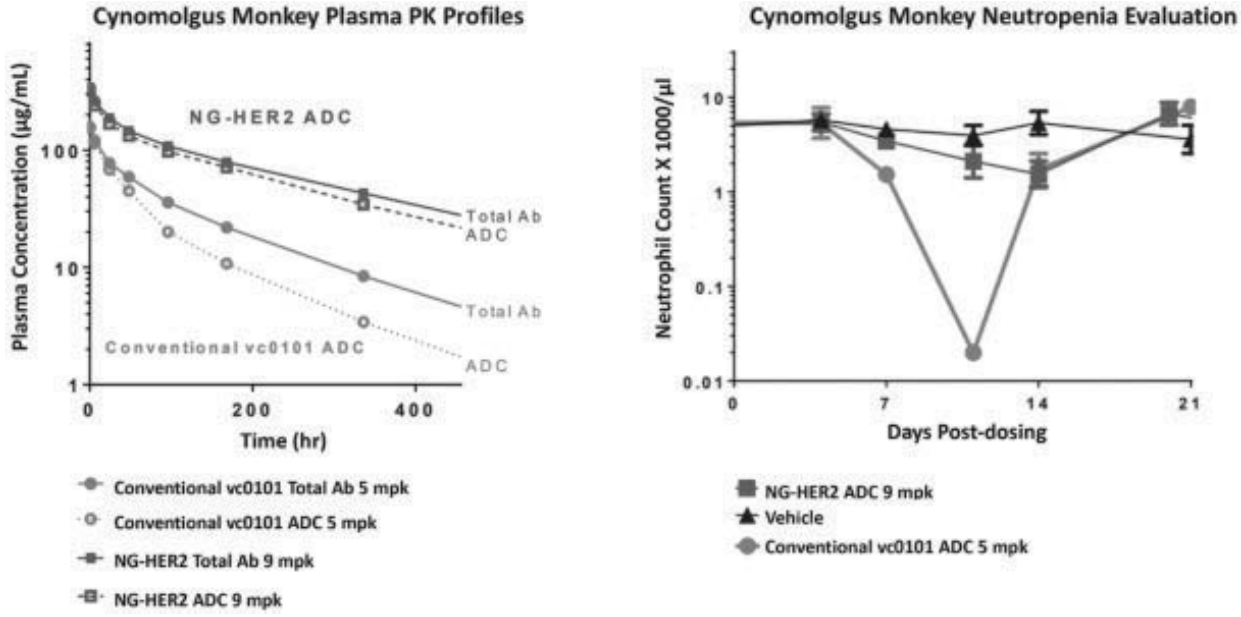
- **Improved anti-tumor activity in preclinical models with optimized conjugation sites for linker-payload combinations**. The FACT Platform is designed to select for optimal conjugation sites that are specific to each linker-payload combination. We employ site-specific conjugation techniques to conserved regions found within the antibody backbones that do not affect antigen binding or other normal antibody functional properties, such as Fc binding when appropriate, which we believe makes our conjugation technology broadly applicable to a wide variety of IgG monoclonal antibodies. Leveraging our diverse toolkit of improved and novel payloads, cleavable and non-cleavable linkers, and deep understanding of optimized site-specific conjugation sites, we have developed payload and linker combinations that can readily be applied to other antibodies in the same class. For example, our auristatin analogues, a potent microtubule inhibitor, and CPI, a highly potent DNA-cross-linking agent, have site-specific conjugation engineering with several linkers alongside IgG1 antibodies. These payloads and linkers could be readily applied to other IgG1 antibodies to efficiently develop novel product candidates.
- **Potential for improved therapeutic index and ADC stability**. We believe that our site-specific conjugation technology has potential to mitigate off-target liabilities of ADCs contributing to an enhanced plasma stability and enhanced therapeutic index. As shown in Figures 18 and 19, applying the FACT Platform to a well-established antibody, NG-HER2-ADC, to generate a model ADC was observed to mitigate toxicity and increase the TI and PK exposure and half-life of the ADC *in vivo*. The rate of linker cleavage and release of the linker/payload construct has been observed to be heavily dependent on the conjugation location and we optimize our linkers for both specific targets and payloads. As a result, we believe the FACT Platform and our empirical understanding of optimal site-specific conjugation may allow us to generate candidates against a broad set of targets that result in superior cell killing.

Figure 18



Schematic illustration of how the therapeutic index of a model ADC generated using the FACT Platform can potentially mitigate toxicity while maximizing PK exposure in vivo. (NHP: non-human primates)

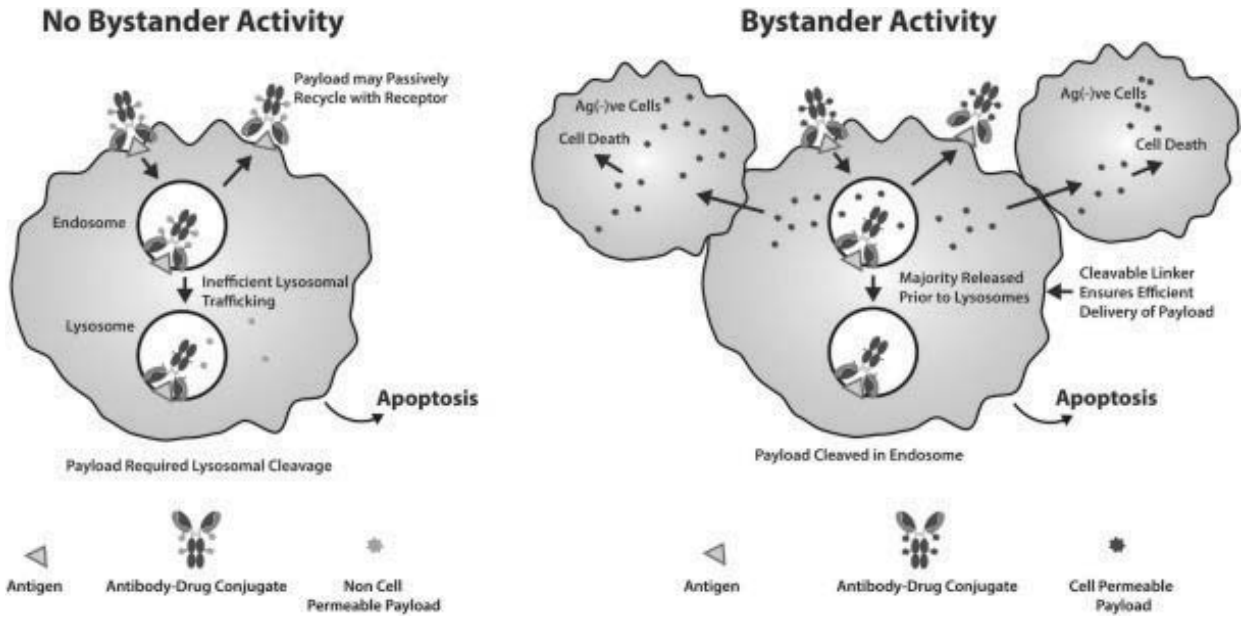
Figure 19



Comparison of stability and exposure in cynomolgus monkeys of Pfizer's NG-HER2-ADC using the same linker-payload and conjugation site chemistry as our PYX-201 ADC was observed to improve the stability and tolerability over conventional ADCs conjugated with the same linker-payload in preclinical studies (NG: next generation).

- **Enhanced anti-tumor activity through bystander activity**. As depicted in Figure 20 below, bystander activity occurs when payloads that are delivered to target cells diffuse into and kill neighboring cells in the tumor microenvironment and is of particular importance if the target is not uniformly expressed on all tumor cells. Bystander activity also has the potential to overcome resistance that may occur over time to treatment with ADCs, carrying non-bystander active payloads, as anti-tumor activity is not directly tied to antigen expression at the target site and destruction of a single target cell. We believe our toolkit of novel and validated payloads, linkers and site-specific conjugation techniques will allow us to further develop ADC candidates with bystander activity that may result in greater clinical activity, especially in cases with heterogeneous target expression.

Figure 20



The following table summarizes the potential advantages of our next-generation ADC platform that utilizes preclinically optimized payloads and site-specific conjugation compared to the currently approved ADCs using conventional conjugation:

	Pyxis Oncology's Next-Generation ADCs	Conventional ADCs
Potential Therapeutic Index	• 8 – 16	• 1 – 5
Linker	• Site-specific conjugated linkers designed to target a specific DAR and high therapeutic index	• Non-site-specific conjugation results in heterogenous DAR
	• Highly stable linkers designed to prevent premature release of payload	• Many linkers are labile, resulting in premature release of payload and systemic toxicity
Payload	• Extensive array of payloads available to match tumor biology for optimal tumor killing	• Due to the labile nature of linkers, some conventional ADCs are built with less potent payloads
	• Payloads include microtubule inhibitors and DNA damaging agents whose potential mechanism of action has been shown to induce immunogenic cell death in preclinical models for combination with immunotherapy	

Forging Creative Business Models and Alliances

We continuously evaluate a robust set of business development opportunities to build alliances with partners. The set of opportunities include, but are not limited to, joint ventures, spin-offs, discovery partnerships and licenses. Furthermore, we intend to retain the optionality to explore the potential for creative business models.

The Voxall Joint Venture

One such endeavor is Voxall Therapeutics, LLC, or Voxall, which is a 50:50 co-owned joint venture formed by us and Alloy Therapeutics, Inc., or Alloy, to accelerate the discovery and development of drugs to address cancer and autoimmune diseases.

We bring to Voxall targets from our target catalog and expertise in stromal and immune biology while Alloy contributes its ATX-Gx transgenic mouse and other discovery services which accelerate antibody drug discovery. Both parties provide full-time employees and project execution and project oversight. Under the collaboration agreement, the parties will conduct research under a mutually agreed research plan for up to six research programs focused on mutually selected targets. With this initial wave of targets, we retain an exclusive option to obtain an exclusive license to further develop and commercialize development candidates at our discretion.

Additional Discovery Efforts

We believe our broad expertise enables us to pioneer our scientific understanding in immune biology of the TME and beyond. We have a flexible pathway to do so via platform development, forging creative business models and alliance building, in-licensing and leveraging target catalogs to expand our portfolio of differentiated therapeutics for difficult-to-treat cancers. The realization of this vision will necessitate rapid innovation and operational excellence from a scientific and business perspective. As such, our mission is to take the next step towards creating an oncology company of the future — an oncology company unconstrained by conventional ideas and conventional practices, an oncology company that will rise to meet the many and complex challenges of difficult-to-treat cancers, and an oncology company that will have a significant impact on the lives of patients with limited effective treatment options.

Competition

The biotechnology and pharmaceutical industries, including the oncology subsector, are characterized by rapidly evolving technologies, intense competition, and a strong defense of intellectual property and proprietary technologies. Any product candidates that we successfully commercialize may be competitive with currently marketed therapies and any new therapies commercialized in the future. While we believe our technology, drug development expertise, leadership team and strong scientific understanding of cancer targets and biology provides us with certain competitive advantages, we face potential competition from many sources, including major pharmaceutical companies, biotechnology companies, academic institutions, and other public and private research institutions.

Many companies are active across various stages of development in the oncology subsector and are marketing and developing products that employ similar ADC and immunotherapy approaches. As of February 2023, we estimate that there are more than 500 industry-sponsored active clinical trials involving more than 140 unique ADCs, which may result in continued interest and subsequent transactions in the space. Additionally, there are several large and small companies working on various immunotherapy approaches for treatment of cancer. Multiple companies are also involved in the development of ADC therapeutics and immunotherapies, including, but not limited to, ADC Therapeutics SA, Astellas Pharma, Inc., AstraZeneca plc, Daiichi Sankyo Company, Ltd., Genentech, Inc., Gilead Sciences, Inc, GlaxoSmithKline, plc, Pfizer Inc., Rakuten Medical, Inc., Seagen, Inc., Nextcure, Inc. and Abcure, Inc.

Our ADC and immunotherapy candidates may face substantial competition from alternative therapeutic modalities, such as CAR-T therapies, bispecific antibodies, and small molecules that are being developed for the same cancer types that we are targeting with our pipeline candidates. These approaches could prove to be more effective, safer, or convey other advantages over any products resulting from our technology. In addition, we also face competition on specific targets, including the target of our PYX-201 candidate, EDB, from Philogen S.p.A., and the target of our PYX-106 product candidate, BSI-060T, from Nextcure, Inc.'s lead program - NC318. In November 2022, Nextcure announced that NC318 would not move forward in the Phase 2 monotherapy clinical trial, although NC318 has been observed to be safe and well-tolerated in patients. Additionally, there is a wide array of activity in the development of immunotherapies for oncology which may be competitive with our preclinical discovery programs. Furthermore, if any of our product candidates are approved in oncology indications such as lung, hematological and other cancers, they may compete with existing approaches to treating cancer including surgery, radiation, and drug therapy, including conventional chemotherapy, biological products, and targeted drug small molecule therapies.

Our competitors may possess greater scientific, research and development capabilities, as well as greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. These competitors compete with us on the basis of establishing clinical trial sites and patient registration, recruiting and retaining qualified scientific and management personnel, and acquiring new technologies that may be complementary to, or necessary for, our programs. Our commercial opportunity for our product candidates may be dependent on the ability of our competitors to develop new products that may be more effective, safer, or less expensive than any products that we may develop. Our competitors may succeed in developing competing products before we do, obtaining marketing approval for products and gaining acceptance for such products in the same markets that we are targeting. Smaller or earlier-stage companies that seek collaborative arrangements with large and established companies, may prove to be significant competitors. In addition, our ability to compete may be affected by the availability of reimbursement from government and other third-party payors. Competitive factors affecting the success of our programs, if approved, will likely be based on their safety and effectiveness, the timing and scope of marketing approvals, the availability and cost of supply, the depth of marketing and sales capabilities, and reimbursement coverage.

Chemistry, Manufacturing and Controls

We believe the manufacturing of our ADCs and monoclonal antibodies requires considerable expertise, know-how, and resources. We do not own or operate and currently have no plans to establish any cGMP compliant manufacturing facilities. We currently rely, and expect to continue to rely, on external contract manufacturing organizations, or CMOs, for the manufacture of product to support non-clinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. Furthermore, the raw materials and intermediates for our product candidates may be sourced, in some cases, from a single-source supplier. As part of the manufacture and design process for our product candidates, we rely on internal scientific and manufacturing know-how and trade secrets and the know-how and trade secrets of third party manufacturers. We believe that this strategy allows us to maintain a more efficient infrastructure by eliminating the need for us to invest in our own manufacturing facilities, equipment and personnel while also enabling us to focus our expertise and resources on the development of our current product candidates. We maintain agreements with our CMOs that include confidentiality and intellectual property provisions to protect our proprietary rights related to our product candidates. We have personnel with significant technical, manufacturing, analytical, quality, including Current Good Manufacturing Practices, or cGMP, and project management experience to oversee our CMOs and to manage manufacturing and quality data and information for regulatory compliance purposes.

Commercialization Plans

We retain full commercialization rights for all our product candidates, including those obtained through exclusive collaboration agreements, with the exception of PYX-106 in Greater China (mainland China, Hong Kong, Macau and Taiwan) and the right of first negotiation granted to Pfizer for PYX-201. We have not yet established our own commercial organization or distribution capabilities because our product candidates are still in preclinical or clinical development. Should any of our candidates receive marketing approval or licensure in the United States or elsewhere, we will need to develop a plan to realize the commercial value of the approved product candidate. At the appropriate time, we plan to build our own specialized sales and marketing organization to support the sales commercialization of approved candidates in the United States. We may also pursue collaboration, co-promotion, distribution and/or other marketing arrangements with one or more third parties to commercialize our product candidates in markets outside the United States. We may also pursue these arrangements for situations in which a larger sales and marketing organization is necessary to realize the full commercial value of any approved wholly owned or collaboration product candidates.

Licensing and Collaboration Agreements

License Agreement with Pfizer Inc.

In December 2020, we entered into a license agreement, as amended, or the Pfizer License Agreement, with Pfizer Inc., or Pfizer, for worldwide development and commercialization rights to two of Pfizer's proprietary ADC product candidates (now referred to as PYX-201 and PYX-203), as well as other ADC product candidates directed to the licensed targets. The Pfizer License Agreement became effective for the Company in March 2021. The initial exclusively licensed targets are extra domain B (EDB of fibronectin) and CD123 and we have the option to expand the scope of our license to add other licensed targets. Pfizer also granted us a non-exclusive license to use Pfizer's FACT Platform technology to develop and commercialize the licensed ADCs. In March 2021, we entered into an amendment to the Pfizer License Agreement to include additional know-how within the scope of our license. Pursuant to the Pfizer License Agreement, we incurred a combined $25.0 million for license fee, consisting of an upfront fee of $5.0 million and issued 12,152,145 shares of Series B convertible preferred stock in 2021 to Pfizer.

On October 6, 2022, we entered into an amended and restated license agreement, or the A&R License Agreement, with Pfizer, which amends and restates the Pfizer License Agreement. Pursuant to the A&R License Agreement, Pfizer granted us exclusive worldwide rights under Pfizer's FACT Platform technology to develop and commercialize ADC product candidates directed to certain licensed targets, including PYX-201 and PYX-203, and products containing the ADC product candidates. Additional ADC targets may be licensed for a nominal upfront payment and milestones. Further, we granted the right of first negotiation to Pfizer, on an exclusive basis, to purchase or to develop, manufacture and commercialize licensed ADCs and licensed products in one or more countries directed to EDB and CD123. In accordance with the terms of the A&R License Agreement, we agreed to pay $8.0 million to Pfizer and issued 2,229,654 shares of our common stock. Additionally, we will issue such number of shares of common stock 180 days following the effective date, or the Issuance Date, equivalent to $5.0 million at a per share price equal to the closing price of our common stock on the business day prior to the Issuance Date, such that Pfizer's ownership interest in us shall not exceed nineteen and a half percent (19.5%) with any difference in value between the value of shares and $5.0 million being payable in cash.

We are also obligated to pay future contingent payments and royalties, including up to an aggregate of $665 million in milestones for the first four licensed ADCs. In addition, we are required to pay future contingent payments including development, regulatory and commercial milestones for ADCs for each additional licensed target beyond the first four licensed ADC targets developed and commercialized via the FACT Platform. Additionally, if ADC licensed products are launched, we will pay Pfizer tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to mid-teens. Our royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. We are also obligated to pay Pfizer a percentage of certain sublicensing revenue ranging from twenty percent to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

Under the Pfizer License Agreement, we are obligated to use commercially reasonable efforts to nominate a clinical candidate within four years of a target becoming a licensed target. We are also required to use commercially reasonable efforts to develop and seek regulatory approval for at least one licensed product directed to each licensed target in the United States and at least one other major market country (France, Germany, Italy, Japan, Spain and the United Kingdom), and to commercialize any licensed product in each such country after receiving regulatory approval. We control prosecution and enforcement with respect to any exclusively licensed patents, and Pfizer has prosecution and enforcement rights if we elect not to exercise such rights.

The Pfizer License Agreement will remain in effect until the expiration of the last to expire royalty term, unless terminated in accordance with the following: (1) by either party for the other party's material breach if such party fails to cure such breach within the specified cure period; (2) by either party upon certain insolvency events of the other party; or (3) prior to receipt of the first regulatory approval for a licensed product, by us for any reason upon 90 days' prior written notice, or after receipt of the first regulatory approval for a licensed product, by us for any reason upon one years' prior written notice.

License Agreement with the University of Chicago

In April 2020, we entered into a license agreement, or the University License Agreement, with the University of Chicago, or the University, to obtain an exclusive license under certain patents resulting from research performed, in-part, by our scientific founder, Dr. Thomas Gajewski, as well as a non-exclusive license to certain know-how and materials. Under the terms of the license, we have the exclusive global right to develop and commercialize products that are covered by a valid claim of a licensed patent, incorporate or use the licensed know-how and materials or are known to assess, modulate or utilize the activity of certain specified biological targets.

In partial consideration for the license from the University, we issued to the University 48,919 shares of our common stock in 2020. Pursuant to the University License Agreement, we are obligated to pay to the University an annual maintenance fee of $10,000 commencing on the third anniversary of the effective date, potential development and commercial milestones of up to an aggregate of $7.7 million as well as running royalties on net sales of licensed products at varying rates ranging from less than one percent to the low single digits, subject to a minimum annual royalty ranging from $1.0 million to $3.0 million during certain years following the first commercial sale of a licensed product. Our royalty obligations apply on a licensed product-by-licensed product and country-by-country basis until: (1) for licensed products covered by a valid claim of a licensed patent in a given country, the expiration of such valid claims; and (2) for all other licensed products, 10 years from the first commercial sale of a licensed product in a given country. We are also obligated to pay the University a percentage of certain sublicensing revenue ranging from low- to mid-teens based on the date of entering into the applicable sublicense.

Under the University License Agreement, we are obligated to use commercially reasonable efforts to develop and bring licensed products to market, meet certain preclinical and clinical development milestones by specific dates, and promote and sell licensed products after receipt of regulatory approval, subject to certain free and payment-based extensions. The University controls prosecution of the licensed patents at our cost and we have the first right to enforce the licensed patents subject to the University's backup enforcement rights.

The University License Agreement will remain in effect on a licensed product-by-licensed product basis until the expiration of all royalty obligations with respect to a licensed product, unless terminated in accordance with the following: (1) by the University upon 30 days' prior written notice for any uncured payment breaches or 90 days prior written notice for all other uncured breaches; (2) by the University upon certain insolvency events or dissolution by us or any affiliate; or (3) by us in full or with respect to a particular licensed product at the end of the calendar quarter following the calendar quarter when we provide written notice of termination.

The Voxall Joint Venture with Alloy Therapeutics, Inc.

In March 2021, we entered into definitive transaction agreements with Alloy to finance and operate Voxall, a joint venture company formed in collaboration with Alloy to leverage Pyxis Oncology's site-specific target catalog and Alloy's ATX-Gx™ platform and antibody discovery services.

Voxall granted to both Pyxis Oncology and Alloy 50% of the voting membership units of Voxall in exchange for certain initial contributions. Our initial contribution included $50,000 and a non-exclusive fully paid-up license to certain intellectual property owned or controlled by us to enable the collaboration with Voxall as further described below. Alloy's initial contribution included $50,000 and the execution of a license agreement and a services agreement to enable the collaboration with Voxall as further described below. Voxall is governed by a board of directors consisting of an equal number of our representatives and Alloy's representatives. We have designated our CEO, Lara Sullivan M.D., as our board representative. The protective provisions under Voxall's operating agreement require the approval of both Pyxis Oncology and Alloy before Voxall may take certain actions.

In connection with the formation of Voxall, we entered into a three-year research collaboration with Alloy and Voxall to identify and select certain biological targets and create development candidate antibodies directed to those targets for further preclinical development, clinical development and commercialization. Under the collaboration agreement, the parties will conduct research under a mutually agreed research plan and budget for up to six research programs focused on mutually selected targets. Each of us and Alloy will provide research support for the collaboration through separate services agreements with Voxall, which services will be paid in the form of promissory notes issued by Voxall. Voxall will own all intellectual property arising from the collaboration, subject to certain exceptions for intellectual property relating to Alloy's ATX-Gx™ platform.

If a development candidate antibody under a research program meets certain mutually agreed selection criteria, we will have the exclusive option to obtain an exclusive license from Voxall to further develop and commercialize all the development candidate antibodies discovered under that research program. We may in-license one research program on certain pre-agreed financial terms. For all other in-licensed research programs, we will be obligated to pay fair market value as determined by a third-party valuation. Any research program that we do not in-license may be licensed by Voxall to a third party.

Agreements with LegoChem Biosciences, Inc.

In December 2020, we entered into a license agreement, or the LegoChem License Agreement, and an opt-in, investment and additional consideration agreement, or the Opt-In Agreement, with LegoChem Biosciences, Inc., or LegoChem. Pursuant to the LegoChem License Agreement, we obtained worldwide (other than Korea) development and commercialization rights for LCB67, an ADC product candidate targeting DLK-1, and products containing the licensed compound. We paid $9.0 million in March 2021 to LegoChem, which was recorded as research and development expenses. Additionally, we may purchase certain initial quantities of licensed products from LegoChem for an estimated cost of $7.0 million and are also obligated to make future contingent payments including development, regulatory and commercial milestones as well as running royalties on net sales of licensed products at varying rates. In the third quarter of the calendar year 2022, we stopped the continued development of LCB67, based on review and analysis of data from the toxicity studies, and anticipated clinical use and commercial prospects of anti-DLK1 ADC.

In addition, as part of the Opt-in Agreement, LegoChem exercised an option to pay $8.0 million to us, in exchange for the right to receive a milestone payment, or the Extra Milestone Payment, of $9.6 million upon the earliest to occur of certain events, including the date of pricing or offer of the first public offering of its common stock or if we are the subject of a change in control transaction. Upon our IPO in October 2021, the extra milestone payment event triggered, and we paid $9.6 million in January 2022 to LegoChem.

License Agreement with Biosion USA, Inc.

On March 28, 2022, we entered into a license agreement, or the Biosion License Agreement, with Biosion USA, Inc., or Biosion, pursuant to which we obtained an exclusive, worldwide (other than Greater China (mainland China, Hong Kong, Macau and Taiwan)) license for development, manufacture and commercialization rights for BSI-060T, a Siglec-15 targeting antibody, an IO product candidate (now referred to as PYX-106), and products containing the licensed compound. Under the terms of the Biosion License Agreement, each party granted to the other party a right of first offer to obtain an exclusive license in the other party's territory (Greater China for Biosion, and the rest of the world for Pyxis) to develop, manufacture and commercialize any bi-specific or multi-specific antibody any antibody-drug conjugate controlled by a party or its affiliate that inhibits, modulates or binds to Siglec-15 as an intended mechanism of action.

Pursuant to the Biosion License Agreement, we agreed to pay an upfront fee of $10 million and are obligated to pay future contingent payments including development, regulatory and commercial milestones up to an aggregate of $217.5 million in case of normal approval and $222.5 million in case of accelerated approval. Additionally, if products are launched, we will pay Biosion tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to low teens. Our royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. We are also obligated to pay Biosion a percentage of certain sublicensing revenue ranging from mid-double to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

Under the Biosion License Agreement, we are obligated to use commercially reasonable efforts to clinically develop and seek regulatory approval for at least one licensed product in the licensed territory, and to commercialize such licensed product following receipt of regulatory approval. We control prosecution and enforcement with respect to the licensed patents in the licensed territory.

The Biosion License Agreement will remain in effect on a licensed product-by-licensed product and country-by-country basis until the expiration of the applicable royalty term, unless terminated in accordance with the following: (1) by either party for the other party's material breach if such party fails to cure such breach within the specified cure period; (2) by either party upon certain insolvency events of the other party; (3) by us for scientific or safety reasons; (4) any time following completion of our first clinical trial for a licensed product, by us for convenience; or (5) by Biosion if we cease development and commercialization activities for licensed products for a specified period of time, subject to certain exceptions.

Intellectual Property

Our intellectual property is critical to our business, and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates, new therapeutic approaches and potential indications, and other inventions that are important to our business. We also rely on trade secrets and proprietary know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our patent portfolio includes patents and patent applications that are exclusively licensed from the University of Chicago, Pfizer, and Biosion, and patent applications that are owned by us. Our patent portfolio includes patents and patent applications that cover our product candidates PYX-201, PYX-203, PYX-106 and PYX-102 and the use of these candidates for therapeutic purposes in certain territories. Our proprietary technology has been developed primarily through relationships with academic institutions, Pfizer, Biosion and contract research organizations.

For our product candidates, we will, in general, initially pursue patent protection covering compositions of matter and methods of use. Throughout the development of our product candidates, we seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including through additional methods of use, process of making, formulation and dosing regimen-related claims.

For all patent applications, we determine claiming strategy on a case-by-case basis. Advice of counsel and our business model and needs are always considered. We file patent applications containing claims for protection of useful applications of our proprietary technologies and any products, as well as new applications and/or uses we discover for existing technologies and products, assuming these are strategically valuable. We continuously reassess the number and type of patent applications, as well as the existing patent claims to ensure that maximum coverage and value are obtained for our processes and compositions, given existing patent office rules and regulations. Further, claims may be modified during patent prosecution to meet our intellectual property and business needs.

We recognize that the ability to obtain patent protection and the degree of such protection depends on a number of factors, including the extent of the prior art, the novelty and non-obviousness of the invention and the ability to satisfy the enablement requirement of the patent laws. The patent positions of immuno-oncology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted or further altered even after patent issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our future product candidates or for our platform technology. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Regardless of the coverage we seek under our existing patent applications, there is always a risk that an alteration to the product or process may provide sufficient basis for a competitor to avoid infringement claims. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and courts can reinterpret patent scope after issuance. Moreover, many jurisdictions, including the United States, permit third parties to challenge allowed or issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. Moreover, we cannot provide any assurance that any patents will be issued from our pending or any future applications or that any current or future issued patents will adequately protect our products.

In total, our patent portfolio, including patents licensed from the University of Chicago, Pfizer and Biosion, and patents owned by us, comprises 26 different patent families, filed in various jurisdictions worldwide, including families directed to composition of matter for antibodies and antibody drug conjugates, families directed towards the manufacture, use, and compositions of antibodies and antibody drug conjugates generally, and families directed to methods of treating cancer and identifying potential targets. Our patent portfolio as of December 31, 2022, is outlined below.

Composition of Matter Patents

PYX-201 Anti-EDB Antibody-Drug Conjugate. We have exclusively licensed from Pfizer a patent family for antibodies and antibody-drug conjugates that bind to the extra domain B splice variant of fibronectin, that includes four issued patents, one each in Australia, Japan, Russia, and South Korea, and pending applications in Australia, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Mexico, Singapore, South Africa, and the United States that claim the composition of matter and certain methods of use with respect to PYX-201. The 20-year term of the patents in this family runs through 2037, absent any available patent term adjustments or extensions.

PYX-203 Anti-CD123 Antibody-Drug Conjugate. We have exclusively licensed from Pfizer a patent family for antibodies and antibody-drug conjugates that specifically bind to CD123, that includes two issued patents in South Korea and Taiwan, and pending applications in Australia, Brazil, Canada, China, Colombia, Europe, Hong Kong, India, Indonesia, Israel, Japan, South Korea, Malaysia, Mexico, New Zealand, Peru, Philippines, Russia, Saudi Arabia, Singapore, South Africa, Taiwan, and the United States that claim the composition of matter and certain methods of use with respect to PYX-203. The 20-year term of the patents in this family runs through 2038, absent any available patent term adjustments or extensions.

PYX-106 Anti-Siglec-15 Antibody. We have exclusively licensed from Biosion USA, Inc. a patent family for monoclonal antibodies that specifically bind human Siglec15, that recently entered the PCT national stage and now has pending applications in Australia, Brazil, Canada, Egypt, Europe, India, Indonesia, Israel, Japan, Malaysia, Mexico, New Zealand, Philippines, Russia, Saudi Arabia, Singapore, South Africa, South Korea, United Arab Emirates, and the United States. The 20-year term of the patent in this family runs through 2041, absent any available patent term adjustments or extensions.

GPNMB Antibodies and Methods of Use. We own a pending PCT application directed to compositions with binding specificity for glycoprotein nonmetastatic melanoma protein B. The 20-year term for patents in this family runs through 2042, excluding any extension of patent term that may be available. If we elect to do so, we are able to file national stage entry applications for this patent family through 2023.

ADC Patent Rights

Spliceostatin analogs. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture useful in antibody-drug conjugates generally, directed toward novel cytotoxic spliceostatin analogs and derivatives, to antibody drug conjugates that includes twenty-seven issued patents in Australia, Belgium, Brazil, Canada, China, Germany, Denmark, Spain, Finland, France, United Kingdom, Hong Kong, Ireland, India, Italy, Japan, South Korea, Mexico, Netherlands, Russia, Sweden, Turkey, and the United States, and no pending applications. The 20-year term of the patents in this family runs through 2033, absent any available patent term adjustments or extensions.

Tubulysin analogs and methods for their preparation. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture useful in antibody-drug conjugates generally, directed toward cytotoxic tubulysin analogs and derivatives, to antibody drug conjugates thereof, that includes one issued patent in the United States, and no pending applications. The 20-year term of the patent in this family runs through 2037, absent any available patent term adjustments or extensions.

Heteroaryl Sulfone-based Conjugation Handles, Methods for Their Preparation, and Their Use in Synthesizing Antibody Drug Conjugates. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture useful in antibody-drug conjugates generally, directed toward heteroaryl sulfone-based conjugation handles for use in synthesizing antibody-drug conjugates, that includes one issued patent in Canada, and pending applications in the United States, Europe and Japan. The 20-year term of the patents in this family runs through 2037, absent any available patent term adjustments or extensions.

Purification of Antibody Drug Conjugates Using a Sodium Phosphate Gradient. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture useful in antibody-drug conjugates generally, directed toward methods of removing high molecular weight species, in particular aggregates, from antibody drug conjugate preparations, by contacting preparations of the antibody drug conjugate reaction mixture with a hydroxyapatite resin and selectively eluting the ADC from the resin using a gradient comprising sodium phosphate, that includes six issued patents in France, Germany, Ireland, Italy, Spain, and the United Kingdom, and a pending application in the United States. The 20-year term of the patents in this family runs through 2036, absent any available patent term adjustments or extensions.

Bifunctional Cytotoxic Agents Containing the CTI Pharmacophore. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture useful in antibody-drug conjugates generally, directed toward bifunctional CTI-CTI and CBI-CTI dimers that can function as stand-alone drugs, payloads in ADCs, and linker-payload compounds useful in connection with the production or administration of such ADCs, that includes twenty-seven issued patents in Australia, Belgium, China, Denmark, Germany, Finland, France, Hong Kong, Ireland, Israel, India, Italy, Japan, Mexico, Netherlands, Norway, Russia, Singapore, South Korea, Spain, Sweden, Turkey, Taiwan, the United Kingdom, the United States and pending applications in Brazil and Canada. The 20-year term of the patents in this family runs through 2036, absent any available patent term adjustments or extensions.

Calicheamicin derivatives and antibody drug conjugates thereof. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture useful in antibody-drug conjugates generally, directed toward calicheamicin derivatives useful as payloads in antibody-drug-conjugates, that includes two issued patents in Canada and Japan, and pending applications in the United States and Europe. The 20-year term of the patents in this family runs through 2038, absent any available patent term adjustments or extensions.

Cysteine Engineered Antibody Drug Conjugate. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture useful in antibody-drug conjugates generally, directed toward anti-CD33 antibody-drug conjugates with an engineered cysteine residue, that includes one issued patent in the United States, and no pending applications. The 20-year term of the patent in this family runs through 2038, absent any available patent term adjustments or extensions.

Platform Patent Rights (Pyxis Oncology Managed)

Antibodies Specific for Trop-2 and Their Uses. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward antibodies and antibodies conjugates specific for Trop-2 in treating cancer, that includes four issued patents in the United States and Japan, and no pending applications. The 20-year term of the patents in this family runs through 2032, absent any available patent term adjustments or extensions.

Engineered Polypeptide Conjugates Using Transglutaminase. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward engineered polypeptide conjugates comprising specific acyl donor glutamine-containing tags and amine donor agents, that includes twelve issued patents in Canada, France, Germany, Ireland, Italy, Japan, Spain, the United Kingdom, and the United States, and a pending application in the United States. The 20-year term of the patents in this family runs through 2034, absent any available patent term adjustments or extensions.

Stability-Modulating Linkers For Use With Antibody Drug Conjugates. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward stability-modulating linker components used to make these stability-modulated antibody-drug conjugates, that includes thirty-five issued patents in Australia, Austria, Belgium, Bulgaria, Canada, China, Czech Republic, Denmark, Finland, France, Germany, Greece, Hong Kong, Hungary, India, Ireland, Israel, Italy, Japan, Luxembourg, Mexico, Netherlands, Poland, Portugal, Romania, Russia, Slovakia, Slovenia, South Korea, Spain, Sweden, Switzerland, Turkey, the United Kingdom, the United States, and pending applications in Brazil, Mexico, Russia, and the United States. The 20-year term of the patents in this family runs through 2035, absent any available patent term adjustments or extensions.

Synergistic Auristatin Combinations. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward combinations of an auristatin or an auristatin-based ADC with second active agents including PI3K/mTOR inhibitors, MEK inhibitors, taxanes, or other anti-cancer agents, that includes two issued patents in the United States and Japan, and pending applications in Canada and Europe. The 20-year term of the patents in this family runs through 2035, absent any available patent term adjustments or extensions.

Capped and Uncapped Antibody Cysteines, and Their Use in Antibody-Drug Conjugation. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward antibody production process in which engineered unpaired cysteine residues are post-translationally modified and capped with particular chemical entities, which capped antibodies are well suited to further site-specific conjugation steps to form antibody-drug conjugates, that includes thirty-six issued patents in Australia, Austria, Belgium, Bulgaria, China, Czech Republic, Denmark, Finland, France, Germany, Greece, Hong Kong, Hungary, India, Ireland, Israel, Italy, Japan, Luxembourg, Mexico, Netherlands, Poland, Portugal, Romania, Russia, Slovakia, Slovenia, South Korea, Spain, Sweden, Switzerland, Turkey, the United Kingdom, the United States, and pending applications in Brazil, Mexico, Russia, and the United States, and pending applications in Brazil, Canada, Europe, Russia and the United States. The 20-year term of the patents in this family runs through 2036, absent any available patent term adjustments or extensions.

Large Scale Production Process for Capped and Un-capped Antibody Cysteines and Their Use in Therapeutic Protein Conjugation. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward optimizing production of selectively capped, and uncapped, cysteines on antibodies by manipulation of cell growth conditions, that includes four issued patents in Canada, Japan, Russia, and South Korea, and pending applications in Australia, Brazil, China, Europe, Hong Kong, India, Israel, Mexico, and the United States. The 20-year term of the patents in this family runs through 2038, absent any available patent term adjustments or extensions.

Platform Patent Rights (Pfizer Managed)

Cytotoxic Peptides and Antibody Drug Conjugates Thereof. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family currently managed by Pfizer for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward cytotoxic pentapeptides, to antibody drug conjugates thereof, that includes seventy-six issued patents in Australia, Austria, Belgium, Bulgaria, Canada, China, Colombia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hong Kong, Hungary, Iceland, Indonesia, Ireland, Israel, Italy, Japan, Luxembourg, Malaysia, Mexico, Netherlands, New Zealand, Norway, Peru, Philippines, Poland, Portugal, Romania, Russia, Saudi Arabia, Singapore, Slovak Republic, Slovenia, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, Turkey, the United Kingdom, and the United States, and pending applications in Argentina, Brazil, India, Peru, and Venezuela. The 20-year term of the patents in this family runs through 2032, absent any available patent term adjustments or extensions.

Bifunctional Cytotoxic Agents. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family currently managed by Pfizer for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward cytotoxic dimers comprising CBI-based and/or CPI-based sub-units, antibody drug conjugates comprising such dimers, that includes forty-nine issued patents in Australia, Austria, Belgium, Brazil, Bulgaria, Canada, China, Colombia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hong Kong, Hungary, Iceland, India, Indonesia, Ireland, Israel, Italy, Japan, Luxembourg, Malaysia, Mexico, Netherlands, New Zealand, Norway, Peru, Philippines, Poland, Portugal, Romania, Russia, Saudi Arabia, Singapore, Slovak Republic, Slovenia, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, Turkey, the United Kingdom, and the United States, and pending applications in Argentina and Venezuela. The 20-year term of the patents in this family runs through 2035, absent any available patent term adjustments or extensions.

Antibodies and Antibody Fragments for Site-Specific Conjugation. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family currently managed by Pfizer for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward polypeptides, antibodies, and antigen-binding fragments thereof, that comprise a substituted cysteine for site-specific conjugation, that includes eight issued patents in China, Colombia, Japan, Russia, South Africa, South Korea, and Russia, and pending applications in Argentina, Australia, Brazil, Canada, Europe, Hong Kong, India, Indonesia, Israel, Malaysia, Mexico, New Zealand, Peru, Philippines, Saudi Arabia, Singapore, Taiwan, the United States, and Venezuela. The 20-year term of the patents in this family runs through 2036, absent any available patent term adjustments or extensions.

Engineered Antibody Constant Regions for Site-Specific Conjugation and Methods and Uses Therefor. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family currently managed by Pfizer for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward antibodies, and antigen-binding portions thereof, engineered to introduce amino acids for site-specific conjugation, that includes issued nine issued patents in Canada, France, Germany, Ireland, Italy, Japan, Spain, the United Kingdom, and the United States, and pending applications in Canada, Europe and Japan. The 20-year term of the patents in this family runs through 2032, absent any available patent term adjustments or extensions.

Engineered Polypeptide Conjugates and Methods for Making Thereof Using Transglutaminase. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family currently managed by Pfizer for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward engineered polypeptide conjugates comprising acyl donor glutamine-containing tags and amine donor agents, that includes six issued patents in Canada, Japan, and the United States, and pending applications in Europe and the United States. The 20-year term of the patents in this family runs through 2031, absent any available patent term adjustments or extensions.

Antibody-Drug Conjugates with High Drug Loading. We have exclusively licensed from Pfizer, subject to certain reservations, a patent family currently managed by Pfizer for compositions, methods of use, and/or methods of manufacture related to Pfizer's FACT Platform, directed toward transglutaminase-mediated antibody-drug conjugates with high anti-body-drug ratio, that includes thirty-six issued patents in Australia, Austria, Belgium, Bulgaria, Canada, China, Czech Republic, Denmark, Finland, France, Germany, Greece, Hong Kong, Hungary, India, Ireland, Israel, Italy, Japan, Luxembourg, Mexico, Netherlands, Poland, Portugal, Romania, Russia, Slovak Republic, Slovenia, South Korea, Spain, Sweden, Switzerland, Turkey, the United Kingdom, and the United States, and pending applications in Brazil, South Korea, and the United States. The 20-year term of the patents in this family runs through 2035, absent any available patent term adjustments or extensions.

Methods in Immuno-Oncology

Methods and compositions related to T-cell activity. We have exclusively licensed from the University of Chicago a patent family that includes two issued patents in the United States and pending applications in Europe and the United States that claim methods for treating patients with immunotherapy based on the identification of the patient as having non-anergic T cells after measuring expression levels of various genes. The 20-year term for patents in this family runs through March 2034, absent any available patent term adjustments or extensions.

Beta-catenin inhibitors in cancer immunotherapy. We have exclusively licensed from the University of Chicago a patent family that includes one issued patent and one pending application in the United States that claim methods for treating solid tumor cancers. The 20-year term for patents in this family runs through March 2036, absent any available patent term adjustments or extensions.

Dysfunctional antigen-specific CD8+ T cells in the tumor microenvironment. We have exclusively licensed from the University of Chicago a patent family that includes six pending applications in Canada, China, Europe, Japan, Hong Kong, and the United States that claim methods of treating cancer comprising administering an agent that specifically targets dysfunctional tumor antigen-specific CD8+ T cells. The 20-year term for patents in this family runs through January 2038, absent any available patent term adjustments or extensions.

Patent Term and Term Extensions

Individual patents have terms for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, utility patents issued for applications filed in the United States are granted a term of 20 years from the earliest effective filing date of a non-provisional patent application. In addition, in certain instances, the term of a U.S. patent can be extended to recapture a portion of the United States Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the restoration period cannot extend the patent term beyond 14 years from FDA approval. In addition, only one patent applicable to an approved drug is eligible for the extension, and only those claims covering the approved drug, a method for using it, or a method of manufacturing may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. We will, in general, pursue available patent term extensions in the U.S. and in foreign jurisdictions that provide for patent term extensions, however, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. All taxes, annuities or maintenance fees for a patent, as required by the USPTO and various foreign jurisdictions, must be timely paid in order for the patent to remain in force during this period of time.

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

Our patents and patent applications may be subject to procedural or legal challenges by others. We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see the section titled “Risk Factors—Risks Related to Our Intellectual Property.”

Trademarks and Know-How

In connection with the ongoing development and advancement of our product candidates in the United States and various international jurisdictions, we seek to create protection for our marks and enhance their value by pursuing trademarks where available and when appropriate. In addition to patent and trademark protection, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees and selected consultants. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and our trade secrets and other proprietary information may be disclosed. We may not have adequate remedies for any breach and could lose our trade secrets and other proprietary information through such a breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. In addition, we have licensed rights under proprietary technologies of third parties to develop, manufacture and commercialize specific aspects of our future products and services. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, alter our processes, obtain licenses or cease certain activities. The expiration of patents or patent applications licensed from third parties or our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future technology may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention.

For more information regarding the risks related to our intellectual property, please see “Risk Factors—Risks Related to Our Intellectual Property.”

Government Regulation

The research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, recordkeeping, serialization and tracking, promotion, advertising, distribution and marketing, post-approval or licensure monitoring and reporting, and export and import, among other things, of our product candidates are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates biological products under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and its implementing regulations, and the Public Health Service Act, or the PHSA, and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as the FDA's refusal to approve a Biologics License Application or BLA, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

Approval and Licensure Process for Biological Products

Biological products such as ours may not be commercially marketed without prior licensure from the FDA and approval or licensure from comparable regulatory agencies in other countries. In the United States, the process for receiving such licensure is long, expensive and risky, and includes the following steps:

- preclinical laboratory tests, animal studies, and formulation studies;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an Institutional Review Board, or IRB, at each clinical site before each trial may be initiated;
- adequate and well-controlled human clinical trials to establish the safety, purity, and potency of the drug for each indication;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the biological product is produced to assess compliance with cGMP;
- a potential FDA audit of the preclinical and clinical trial sites that generated the data in support of the BLA;
- the ability to obtain clearance or approval of companion diagnostic tests, if required, on a timely basis, or at all;
- FDA review and approval of the BLA prior to any commercial marketing or sale of the drug in the United States; and
- compliance with any post-approval requirements and/or commitments, including the potential requirement to implement a REMS, and the potential requirement to conduct post-approval studies.

In guidance, FDA has stated that it considers antibody-drug conjugates to be combination biological product-drug products for which a BLA should be submitted. FDA has also stated in guidance that it regulates monoclonal antibodies as biological products which require a BLA. FDA has issued guidance on product development considerations for antibody-drug conjugates, including dosing and clinical pharmacology testing recommendations.

Regulation by U.S. and foreign governmental authorities is a significant factor affecting our ability to commercialize any of our products, as well as the timing of such commercialization and our ongoing research and development activities. The commercialization of drug products requires regulatory approval by governmental agencies prior to commercialization. Various laws and regulations govern or influence the research and development, non-clinical and clinical testing, manufacturing, processing, packaging, validation, safety, labeling, storage, record keeping, registration, listing, distribution, advertising, sale, marketing and post-marketing requirements and/or commitments of our products. The lengthy process of seeking these approvals, and the subsequent compliance with applicable laws and regulations, require expending substantial resources.

The results of preclinical testing, which include laboratory evaluation of product chemistry, formulation, toxicity and carcinogenicity, animal studies to assess the potential safety, purity and potency of the product and its formulations, details concerning the drug manufacturing process and its controls, and a proposed clinical trial protocol and other information must be submitted to the FDA as part of an IND that must be reviewed and become effective before clinical testing can begin. The study protocol and informed consent information for patients in clinical trials must also be submitted to an independent IRB for approval covering each institution at which the clinical trial will be conducted. Once a sponsor submits an IND, the sponsor must wait 30 calendar days before initiating any clinical trials. If the FDA has comments or questions within this 30-day period, the issue(s) must be resolved to the satisfaction of the FDA before a clinical trial can begin. In addition, the FDA or an IRB may impose a clinical hold on ongoing clinical trials if, among other things, it believes that a clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable and significant risk to clinical trial patients. If the FDA imposes a clinical hold, clinical trials can only proceed under terms authorized by the FDA. If applicable, our preclinical and clinical studies must conform to the FDA's Good Laboratory Practice, or GLP, and Good Clinical Practice, or GCP, requirements, respectively, which are designed to ensure the quality and integrity of submitted data and protect the rights and well-being of study patients. Information for certain clinical trials also must be publicly disclosed within certain time limits on the clinical trial registry and results databank maintained by the National Institutes of Health, or NIH.

Typically, clinical testing involves a three-phase process; however, the phases may overlap or be combined:

- Phase 1 clinical trials typically are conducted in a small number of volunteers or patients to assess the early tolerability and safety profile, the pattern of drug absorption, distribution and metabolism, the mechanism of action in humans, and may include studies where investigational drugs are used as research to explore biological phenomena or disease processes;
- Phase 2 clinical trials typically are conducted in a limited patient population with a specific disease in order to assess appropriate dosages and dose regimens, expand evidence of the safety profile and evaluate preliminary efficacy; and
- Phase 3 clinical trials typically are larger scale, multicenter, well-controlled trials conducted on patients with a specific disease to generate enough data to statistically evaluate the efficacy and safety of the product, to establish the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug.

A therapeutic product candidate being studied in clinical trials may be made available for treatment of individual patients, intermediate-size patient populations, or for widespread treatment use under an expanded access protocol, under certain circumstances. Pursuant to the 21st Century Cures Act, or Cures Act, which was signed into law in December 2016, the manufacturer of one or more investigational products for the diagnosis, monitoring, or treatment of one or more serious diseases or conditions is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational product.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA authorization under an FDA expanded access program; however, manufacturers are not obligated to provide investigational new drug products under the current federal right to try law.

Disclosure of Clinical Trial Information

Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial are then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to therapeutic candidates (drugs or biological products) intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the U.S. or more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a therapeutic candidate for this type of disease or condition will be recovered from sales in the U.S. for that therapeutic candidate. Orphan drug designation must be requested before submitting a marketing application for the therapeutic candidate for that particular disease or condition. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. Among the other benefits of orphan drug designation are tax credits for certain research and an exemption from the BLA application fee. The FDA may revoke orphan drug designation, and if it does, it will publicly disclose that the product is no longer designated as an orphan drug.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the biological product was designated. Orphan drug exclusivity does not prevent the FDA from approving a different biological product for the same disease or condition, or the same biological product for a different disease or condition.

A designated orphan drug may not receive orphan drug exclusivity if it is licensed for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Expedited Development and Review Programs

The FDA has a number of programs intended to expedite the development and review of product candidates. These programs include Fast Track designation, Breakthrough Therapy designation, priority review designation, and accelerated approval. Fast Track designation is intended to expedite or facilitate the process for reviewing new biological products that meet certain criteria. Specifically, new biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biological product may request the FDA to designate the biological product as a Fast Track product at any time during the clinical development of the product. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application. FDA may revoke the Fast Track designation if it believes that the designation is no longer supported by data emerging in the clinical trial process.

Under the Breakthrough Therapy program, products intended to treat a serious or life-threatening disease or condition may be eligible for Breakthrough Therapy designation, which includes eligibility for the benefits of the Fast Track program, when preliminary clinical evidence demonstrates that such product may have substantial improvement on one or more clinically significant endpoints over existing therapies. Additionally, FDA will seek to ensure the sponsor of a Breakthrough Therapy product receives timely advice and interactive communications to help the sponsor design and conduct a development program as efficiently as possible.

A product is eligible for priority review if it is intended to treat a serious condition and, if approved or licensed, it would provide a significant improvement in safety or effectiveness. FDA intends to take action on a priority review marketing application within six months of receipt, compared to 10 months of receipt for regular review submissions.

Additionally, a product may be eligible for accelerated approval if it is intended to treat a serious or life-threatening disease or condition and would provide meaningful therapeutic benefit over existing treatments. Accelerated approval may be granted on the basis of adequate and well-controlled clinical studies establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality and is reasonably likely to predict an effect on irreversible morbidity, mortality, or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a biological product receiving accelerated approval diligently perform adequate and well-controlled clinical studies demonstrating clinical benefit, and may require that these studies by underway prior to approval under the Food and Drug Omnibus Reform Act of 2022, or FDORA. In addition, the FDA requires as a condition for accelerated approval the submission of promotional materials in advance, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, Breakthrough Therapy designation, priority review and accelerated approval do not change the standards for licensure but may expedite the review process.

Pediatric studies and exclusivity

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

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

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

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

FDA Review of BLAs

After completion of the required clinical testing, a BLA is prepared and submitted to the FDA. FDA approval of the BLA is required before marketing of the product may begin in the United States. The BLA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting a BLA is substantial. The submission of most BLAs is additionally subject to a substantial application user fee, currently $3,242,026 for BLAs requiring clinical data for fiscal year 2023, and the manufacturer and sponsor under an approved BLA are also subject to annual program fees, currently $393,933 for each prescription product. These fees are typically increased annually. Sponsors of applications for drugs granted Orphan Drug Designation are exempt from these user fees.

The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept a BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of BLAs to encourage timeliness. Applications for standard review biological products are meant to be reviewed within ten months; applications for priority review drugs are meant to be reviewed in six. Priority review can be applied to biological products that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by the FDA for three additional months ("major amendment") to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

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

Before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not license the product unless compliance with cGMPs is satisfactory, and the application meets the appropriate standard. A BLA must include data that demonstrate that the biological product is safe, pure, and potent.

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

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

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

Biosimilars and Reference Product Exclusivity

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

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

A biological product can also obtain pediatric market exclusivity in the United States. As stated above, pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, there has been discussion of whether Congress should reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate implementation of the BPCIA is subject to significant uncertainty.

Post-Licensure FDA Requirements

Biological products manufactured or distributed pursuant to FDA licenses 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 with the product. After licensure, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and licensure. 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.

Often times, even after a biological product has been licensed by the FDA for sale, the FDA may require that certain post-licensure requirements be satisfied, including the conduct of additional clinical studies. If such post-approval requirements are not satisfied, the FDA may withdraw its licensure of the biological product. In addition, holders of a biological product license are required to report certain adverse reactions to the FDA, comply with certain requirements concerning advertising and promotional labeling for their products, and continue to have quality control and manufacturing procedures conform to cGMP after approval. In addition, biological product manufacturers and their subcontractors 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 and other aspects of regulatory compliance. 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.

Among the conditions for BLA licensure is the requirement that the manufacturing operations conform on an ongoing basis with cGMP. In complying with cGMP, we must expend time, money and effort in the areas of training, production and quality control within our own organization and at our contract manufacturing facilities. A successful inspection of the manufacturing facility by the FDA is usually a prerequisite for final licensure of a biological product. Following licensure of the BLA, we and our manufacturers will remain subject to periodic inspections by the FDA to assess continued compliance with cGMP requirements and the conditions of licensure. We will also face similar inspections coordinated by foreign regulatory authorities. The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing facilities; this latter effort includes assessment of compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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

- Restrictions on the marketing or manufacturing of the product, including total or partial suspension of production, complete withdrawal of the product from the market or product recalls;
- Fines, warning letters or holds on post-licensure clinical trials;
- Refusal of the FDA to license pending BLAs or supplements, or suspension or revocation of product licensure;
- Product seizure or detention, or refusal to permit the import or export of products;
- Consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- Mandated modification of promotional materials and labeling and the issuance of corrective information;
- The issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- Injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates marketing, labeling, advertising and promotion of products that are placed on the market. Biological products may be promoted only for the licensed indications and in accordance with the provisions of the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

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

Patent term extension

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

FDA approval and regulation of companion diagnostics

A therapeutic product may rely upon an *in vitro* companion diagnostic for use in selecting the patients that will be more likely to respond to that therapy. If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

If FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication contemporaneously, except for the high unmet medical need. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of *in vitro* companion diagnostics in conjunction with the review of our therapeutic product candidates will, therefore, likely involve coordination of review by the FDA's Center for Biologics Evaluation and Research and the FDA's Center for Devices and Radiological Health.

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The three primary types of FDA marketing authorization applicable to a medical device include premarket notification, also called 510(k) clearance, premarket approval, or PMA, and De Novo classification requests. The FDA has generally required *in vitro* companion diagnostics intended to select the patients who will respond to cancer treatment to obtain a PMA for that diagnostic simultaneously with approval of the drug.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee of $441,547 for most PMAs for fiscal year 2023. Medical device establishments are also subject to annual registration fees, currently $6,493, and class III devices are subject to annual fees for periodic reporting, currently $15,454. FDA requires lower fee amounts for businesses certified by the Center for Devices and Radiological Health as a small business. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution, and the requirement for post approval studies as well as post-marketing surveillance. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained, or problems are identified following initial marketing.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Manufacturers are also subject to medical device reporting requirements as well as reporting certain requirements related to device corrections and removals. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the U.S.

Foreign Regulation

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

Other Healthcare Laws

Among others, the FDA, U.S. Department of Health and Human Services, or HHS, Office of Inspector General, the Centers for Medicare and Medicaid Services, or CMS, and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the preclinical and clinical development, manufacture, marketing, and distribution of drugs such as those we are developing. These agencies and other federal, state, and local entities regulate, among other activities, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, sales, commercialization, marketing, advertising and promotion, distribution, post-approval monitoring and reporting, sampling, and export and import of our product candidates. Any drug candidates that we develop must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in those foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in the European Union, or EU, are addressed in a centralized way, but country-specific regulation remains essential in many respects.

Although we do not currently have any products on the market, in addition to FDA restrictions on marketing of pharmaceutical products, we are also subject to healthcare statutory and regulatory requirements and enforcement by the U.S. federal and state governments. Pharmaceutical companies like us are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such regulation may constrain the financial arrangements and relationships through which we research, develop, and, ultimately, sell, market, and distribute any products for which we obtain marketing approval. Such laws include, without limitation:

- The federal Anti-Kickback Statute, an intent-based criminal statute that prohibits, among other activities, persons and entities from knowingly and willfully soliciting, offering, paying, receiving, or providing any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, or recommendation of, any item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare or Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. A conviction for violation of the federal Anti-Kickback Statute can result in criminal fines and/or imprisonment and requires mandatory exclusion from participation in federal health care programs. Exclusion may also be imposed if the government determines that an entity has committed acts that are prohibited by the federal Anti-Kickback Statute.

- The federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which prohibit individuals or entities from, among other activities, knowingly presenting, or causing to be presented, to the federal government claims for payment or approval that are false, fictitious, or fraudulent; knowingly making, using, or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. Moreover, pharmaceutical manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring *qui tam* actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery or settlement. FCA liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per false or fraudulent claim or statement for violations. Criminal penalties, including imprisonment and criminal fines, are also possible for making or presenting a false, fictitious or fraudulent claim to the federal government.

- The federal civil monetary penalties laws, which prohibit, among other activities (1) arranging for or contracting with an individual or entity that is excluded from participation in federal healthcare programs to provide items or services reimbursable by a federal healthcare program, (2) failing to report and return a known overpayment, or (3) offering or transferring any remuneration to a Medicare or Medicaid beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of items or services reimbursable by Medicare or Medicaid, unless an exception applies.

- The federal criminal statutes enacted under the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which impose criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program; knowingly and willfully embezzling or stealing from a healthcare benefit program; willfully preventing, obstructing, misleading, or delaying a criminal investigation of a healthcare offense; and knowingly and willfully falsifying, concealing, or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items, or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- The federal Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, which imposes annual reporting requirements for "applicable manufacturers," meaning certain manufacturers of drugs, devices, biological products, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program. The law requires applicable manufacturers to disclose certain payments and other "transfers of value" provided to "covered recipients," which include U.S.-licensed physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists, anesthesiologist assistants, certified nurse midwives, and U.S. teaching hospitals. The law also requires applicable manufacturers to disclose certain ownership and investment interests held by U.S.-licensed physicians and their immediate family members.
- The FDCA and PHSA, which regulate licensure of biological products and prohibit the misbranding and adulteration of biological products.
- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply with respect to healthcare items or services reimbursed by non-governmental third-party payors and may be broader than their federal equivalents; state and foreign laws requiring pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and/or the relevant compliance guidance promulgated by the federal government or otherwise restricting payments that may be made to healthcare providers; state laws and regulations requiring drug manufacturer disclosures to state agencies and/or commercial purchasers with respect to certain price increases; state and foreign laws requiring drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers and restricting marketing practices or requiring disclosure of marketing expenditures and pricing information; and state and local laws that requiring registration of pharmaceutical sales representatives.

Violations of any of these laws or any other applicable laws or regulations may result in significant penalties, including, without limitation, administrative, civil, and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations to resolve allegations of noncompliance; exclusion from participation in federal and state healthcare programs, such as Medicare and Medicaid; and imprisonment. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

Coverage and Reimbursement

Sales of any pharmaceutical product depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement for such product by third-party payors. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a payor-by-payor basis. These third-party payors are increasingly reducing coverage and reimbursement for healthcare items (including drugs) and services. Moreover, for products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself may or may not be available. Instead, the hospital or administering physician may be reimbursed only for providing the treatment or procedure in which our product is used.

In addition, the U.S. government, states, and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of lower-cost or generic products. Adoption of price controls and cost-containment measures and adoption of more restrictive policies in jurisdictions with existing controls and measures could further limit sales of any drug product. Decreases in third-party reimbursement for any drug product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product and also have a material adverse effect on sales.

Moreover, as a condition of participating in, and having products covered under, certain federal healthcare programs, such as Medicare and Medicaid, we may become subject to federal laws and regulations that require pharmaceutical manufacturers to calculate and report certain pricing metrics to the government, including the Average Manufacturer Price, or AMP, and Best Price under the Medicaid Drug Rebate Program, the Medicare Average Sales Price, the 340B Ceiling Price, and Non-Federal AMP reported to the Department of Veteran Affairs, and with respect to Medicaid, pay statutory rebates on utilization of manufacturers' products by Medicaid beneficiaries. Compliance with these laws and regulations will require significant resources and may have a material adverse effect on our revenues.

Healthcare Reform

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the ACA, was enacted in the United States, which made a number of substantial changes in the way healthcare is financed by both governmental and private insurers. Among other ways in which it may affect our business, the ACA established a new Patient-Centered Outcomes Research Institute to oversee and identify priorities in comparative clinical effectiveness research in an effort to coordinate and develop such research; implemented payment system reforms including a national pilot program on payment bundling to encourage hospitals, physicians and other healthcare providers to improve the coordination, quality and efficiency of certain healthcare services through bundled payment models; implemented the federal Physician Payments Sunshine Act; and expanded the eligibility criteria and rebates for Medicaid programs.

Since its enactment, there have been executive, judicial and legislative branch challenges to certain aspects of the ACA. For example, while Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, 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. Prior to the Supreme Court's decision, President Biden had issued an executive order that instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, policies that create barriers to obtaining access to health insurance coverage through the ACA marketplaces. It is unclear how healthcare reform measures enacted by Congress or implemented by the Biden administration or other efforts to challenge, repeal or replace the ACA, if any, will impact the ACA.

Other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other changes, led to aggregate reductions in Medicare payments to providers of up to 2% per fiscal year that started in April 2013 and, due to subsequent legislation, will continue into 2031 (with the exception of a temporary suspension instituted during the COVID-19 pandemic that halted the sequestration from May 1, 2020 to March 31, 2022, and later reduced the reductions to 1% from April 1, 2022 until July 1, 2022). To offset the temporary suspension during the COVID-19 pandemic, in 2030, reductions in Medicare payments will be 2.25% for the first half of the year, and 3% in the second half of the year. In addition, the American Rescue Plan Act of 2021 eliminated the statutory cap on drug manufacturers' MDRP rebate liability effective January 1, 2024. Under current law, enacted as part of the ACA, drug manufacturers' MDRP rebate liability is capped at 100% of AMP for a covered outpatient drug. However, beginning in 2024, drug manufacturers' MDRP rebate liability may exceed 100% of AMP if the price of a covered outpatient increases faster than the rate of inflation.

Moreover, in August 2022, President Biden signed into law the Inflation Reduction Act of 2022, or the IRA, which implements substantial changes to the Medicare program, including drug pricing reforms and the creation of new Medicare inflation rebates. Namely, the IRA (1) imposes inflation rebates on drug manufacturers for products reimbursed under Medicare Parts B and D if the prices of those products increase faster than inflation; (2) implements changes to the Medicare Part D benefit that, beginning in 2025, will cap beneficiary annual out-of-pocket spending at $2,000, while imposing new discount obligations for pharmaceutical manufacturers; and, (3) beginning in 2026, establishes a "maximum fair price" for a fixed number of high expenditure pharmaceutical and biological products covered under Medicare Parts B and D following a price negotiation process with CMS.

On February 2, 2022, the Biden Administration signaled its continued commitment to the Cancer Moonshot initiative, which was initially launched in 2016. In its announcement, the administration noted that its new goals under the initiative include addressing inequities in order to ensure broader access to cutting-edge cancer therapeutics and investing in a robust pipeline for new treatments. Additionally, on October 14, 2022, President Biden also issued an Executive Order on Lowering Prescription Drug Costs for Americans, which instructed the Secretary of the HHS to consider whether to select for testing by the CMS Innovation Center new health care payment and delivery models that would lower drug costs and promote access to innovative drug therapies for beneficiaries enrolled in the Medicare and Medicaid programs. Most recently, on February 14, 2023, the HHS issued a report in response to the October 14, 2022 Executive Order, which, among other things, selects three potential drug affordability and accessibility models to be tested by the CMS Innovation Center. Specifically, the report addresses: (1) a model that would allow Part D Sponsors to establish a "high-value drug list" setting the maximum co-payment amount for certain common generic drugs at $2; (2) a Medicaid-focused model that would establish a partnership between CMS, manufacturers, and state Medicaid agencies that would result in multi-state outcomes-based agreements or certain cell and gene therapy drugs; and (3) a model that would adjust Medicare Part B payment amounts for Accelerated Approval Program drugs to advance the developments of novel treatments.

Meanwhile, individual states in the U.S. have increasingly passed legislation and implemented 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. In some cases, states have also encouraged importation of pharmaceutical and biological products from other countries and employed bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could adversely affect our business prospects, financial condition, and results of operations. In addition, regional healthcare 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 healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

We expect that additional state and federal healthcare reform and/or drug pricing measures will be adopted in the future, any of which could affect the pricing and/or availability of drug products, the amounts that federal and state governments and other third-party payors will pay for healthcare products and services, and/or our ability to generate revenue, attain or maintain profitability, or commercialize products for which we may receive regulatory approval in the future.

Data Privacy & Security

Numerous state, federal and foreign laws and regulations govern the collection, dissemination, use, access to, privacy and security of personal information (including health-related information). Such laws and regulations that could apply to our operations or the operations of our partners include health information privacy and security laws (e.g., HIPAA), federal and state consumer protection laws and regulations (e.g., Section 5 of the Federal Trade Commission Act), state privacy laws (e.g., the California Consumer Privacy Act, or CCPA, as modified by the California Consumer Privacy Rights Act, or CPRA, in 2023; the Virginia Consumer Data Protection Act which went into effect in 2023), data breach notification laws, and the EU General Data Protection Regulation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Employees and Human Capital Management

Overview

We view our values of "Be Clever," "Be of Service," "Be Gutsy," "Be Tenacious," and "Be You," as a mandate for excellence and the foundation for our success. These values create a culture that focuses on science and patients and promotes trust, teamwork, and celebration. As of March 22, 2023, we employed 75 full-time permanent employees. Of these employees, approximately 49% have advanced degrees including Ph.D., M.D., M.B.A., J.D. and approximately 69% were engaged in research and development activities. More than half of our workforce and our executive leadership is comprised of women. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

We consider the intellectual capital of our employees to be an essential driver of our business. Our workforce expanded during fiscal year 2022; new employees were hired to support our clinical and preclinical work, with additions in our research, clinical development, clinical operations and general and administrative functions. We continually evaluate our business needs and opportunities and strive to balance inhouse expertise and capacity with outsourced expertise and capacity.

Strategy

Our human capital resource objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our employees. We believe that our continued success is directly due to the commitment, engagement and performance of our employees. We strive to attract and retain experienced operators, oncology experts, clinicians, and biopharma veterans with deep market knowledge and insights with an uncompromising vision of delivering solutions for patients. In order to achieve this, we provide an inclusive and empowering work environment, foster a culture built on diversity, equity and inclusion, reward performance and leadership skills, and by offering competitive compensation and benefits programs.

Culture and Employee Engagement

We also place a high value on the diversity of our team, including gender, background and expertise, to foster our culture of innovation. Our employees are guided by our Code of Conduct, which sets basic requirements for business conduct and serves as a foundation for our policies, procedures and guidelines, all of which provide additional guidance on expected employee behaviors.

Compensation and Benefits

Drug development is a complex endeavor which requires deep expertise and experience across a broad array of disciplines. Biotechnology and pharmaceutical companies both large and small compete for a limited number of qualified applicants to fill specialized positions. As part of our total rewards philosophy, we offer competitive compensation and benefits to attract and retain top talent. We are committed to fair and equitable treatment in our compensation and benefits for employees at all levels. Our total rewards offerings include an array of programs to support our employees' financial well-being, including annual performance incentive opportunities, retirement savings programs, health and welfare benefits, paid time off and flexible work schedules. We also allow our employees to participate in equity incentive plans. The principal purposes of our equity incentive plans are to align the interests of our stockholders and those eligible for awards, to retain and incentivize officers, directors, employees, and other service providers and to encourage them to act in our long-term best interests.

Ongoing Professional Development

We focus on attracting, retaining and cultivating talented individuals. We provide reimbursement and time for employees to attend professional development courses ranging from technical training, competency-based workshops, and leadership development programs. Direct managers also take an active role in identifying individualized development plans to assist their employees in realizing their full potential and creating opportunities for promotions and added responsibilities that enhance the engagement and retention of our workforce. We are committed to maintaining and increasing our investment in our workforce as we grow, including improvements in the way we hire, develop, motivate and retain employees.

Safety and Well-Being

Employee health and safety in the workplace is one of our main priorities. As a result of the new challenges the COVID-19 pandemic brought, we took various steps to support our employees, including transitioning to remote work and offering flexible schedules. At the same time, we protected our facility-dependent employees, including those needed to maintain our research and development activities, by instituting strict protocols designed to ensure a healthy environment.

Board of Directors Oversight

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

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

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

Corporate Information

We were incorporated in the state of Delaware on June 11, 2018 and launched with our first employee and Series A funding in July 2019. Our principal executive offices are located at 150 Cambridgepark Drive, Cambridge, Massachusetts 02140, and our telephone number is (617) 221-9059. Our website address is www.pyxisoncology.com.

The information in, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 12(a) or 15(d) of the Exchange Act are available, free of charge, on or through our website as soon as reasonably practicable after such reports and amendments are electronically filed with or furnished to the SEC. The SEC maintains an Internet site that contains, reports, proxy and information statements and other information regarding our filings at sec.gov. The contents of these websites are not incorporated into this filing. Further, references to the URLs for these websites are intended to be inactive textual references only.

Item 1A. Risk Factors.

Our business involves a high degree of risk. You should consider and read carefully all of the risks and uncertainties described below, as well as other information included in this Annual Report on Form 10-K, including our financial statements and related notes appearing at the end of this Annual Report on Form 10-K. The risks described below are not the only ones facing us. The occurrence of any of the following risks or additional risks and uncertainties not presently known to us or that we currently believe to be immaterial could materially and adversely affect our business, financial condition or results of operations. In such case, the trading price of our common stock could decline, and you may lose all or part of your investment. This Annual Report on Form 10-K also contains forward-looking statements and estimates that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of specific factors, including the risks and uncertainties described below.

Risks Related to Our Financial Position and Need for Additional Capital

We are a clinical stage biopharmaceutical company with a limited operating history and have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.

We are a clinical stage biopharmaceutical company with a limited operating history. Since our inception, we have incurred significant operating losses. We reported net losses of $120.7 million and $76.0 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $212.4 million. To date, we have not generated any revenue from product sales and have financed our operations primarily through sales of our equity interests. As such, we expect that it will be several years, if ever, before we have a product candidate ready for regulatory licensure and commercialization. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. To become and remain profitable, we must succeed in developing, obtaining marketing licensure for and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including, without limitation, procuring clinical- and commercial-scale manufacturing, successfully completing preclinical studies and clinical trials of our product candidates, establishing arrangements with third parties for the conduct of our clinical trials, obtaining marketing licensure for our product candidates, manufacturing, marketing and selling any products for which we may obtain marketing licensure, discovering or obtaining rights to additional product candidates, identifying collaborators to develop product candidates we identify or additional uses of existing product candidates and successfully completing development of product candidates for our collaboration partners.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially if and as we:

- manufacture product candidates and continue to develop and conduct clinical trials for our ADC product candidate, PYX-201, and our IO product candidate, PYX-106;
- select antibody programs to take into development, manufacture product candidates, conduct IND enabling studies and submit INDs and initiate Phase 1 clinical trials;
- initiate, conduct and successfully complete later-stage clinical trials;
- scale up external manufacturing capabilities for later stage trials and to commercialize our products;
- seek marketing licenses for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure for which we may obtain marketing licensure;
- leverage the FACT Platform to identify and then advance additional product candidates into preclinical and clinical development;
- expand, maintain and protect our intellectual property portfolio;
- hire additional clinical, regulatory, scientific, operational, financial and management information personnel; and
- continue to operate as a public company.

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

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses we will incur or when, if ever, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts or continue operations. A decline in the value of our company, or in the value of our common stock, could also cause investors to lose all or part of their investment.

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

We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce or eliminate one or more of our research and product development programs or future commercialization efforts.

The development of biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we continue our clinical trials of our product candidates PYX-201 and PYX-106 and advance our other preclinical research and development programs. For example, to refocus development efforts and spending towards our two most advanced programs, PYX-201 and PYX-106, we have elected to pause preclinical development of PYX-203 and PYX-102. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other comparable regulatory authorities to perform clinical trials or preclinical studies in addition to those that we currently anticipate. Other unanticipated costs may also arise. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of any product candidate we develop. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

As of December 31, 2022, we had approximately $179.3 million in cash and cash equivalents. Based on our current operating plan, we estimate that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the first half of the calendar year 2025. Our estimate as to how long we expect to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

We intend to use our cash and cash equivalents for development and regulatory activities relating to our product candidates, discovery programs, business development activities and other general corporate purposes. Advancing the development of our product candidates will require a significant amount of capital. Our cash and cash equivalents will not be sufficient to fund any of our product candidates through regulatory licensure. Because the length of time and activities associated with successful research and development of any individual product candidate are highly uncertain, we are unable to estimate the actual funds we will require for development, marketing licensure and commercialization activities. The timing and amount of our operating expenditures will depend largely on:

- the manufacture of product candidates and conduct of Phase 1 clinical trials for PYX-201 and PYX-106;
- the timing and progress of our other preclinical and clinical development activities;
- the number and scope of other preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we have entered or may in the future enter into in-licensing, collaborations and research and development agreements;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing licensure;
- our ability to maintain our current licenses and research and development programs and to establish new collaboration arrangements;
- the costs involved in prosecuting, maintaining and enforcing patent and other intellectual property rights;
- any delays or interruptions that we experience in our preclinical studies, future clinical trials and/or supply chain;
- the cost and timing of regulatory licenses; and
- our efforts to hire additional clinical, regulatory, scientific, operational, financial and management personnel.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue on our own. We do not expect to realize revenue from sales of products or royalties from licensed products in the foreseeable future, if at all, and not until our product candidates are clinically tested, licensed for commercialization and successfully marketed. To date, we have primarily financed our operations through the sale of equity securities. We will be required to seek additional funding in the future and our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. For example, market volatility resulting from global economic developments, political unrest, high inflation, the COVID-19 pandemic and other factors could adversely impact our ability to access capital as and when needed. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders.

Adverse developments affecting the financial services industry, including events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our business, financial condition or results of operations.

Events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. Most recently, on March 10, 2023, Silicon Valley Bank ("SVB") was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although we assess our banking and customer relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our business, financial condition or results of operations

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

We incorporated in 2018 and staffing and meaningful operations commenced in mid-2019 and our operations to date have been focused on developing and conducting preclinical and, since the first quarter of 2023, initiating Phase 1 clinical trials of our product candidates. To date, we have not yet demonstrated our ability to successfully complete a clinical trial, obtain marketing licenses, manufacture a commercial scale product directly or through a third party, or conduct sales, marketing, and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or if we had already successfully completed some or all of these types of activities

In addition, as a clinical stage biopharmaceutical company, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities and we may not be successful in making that transition.

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

Risks Related to the Discovery and Development of our Product Candidates

We are heavily dependent on the success of PYX-201 and PYX-106, which are in the early stages of development, and if PYX-201 and/or PYX-106 are not successful in clinical trials or do not receive regulatory approval or licensure or are not successfully commercialized, our business will be materially and adversely affected.

To date, we have invested a significant portion of our efforts and financial resources in the development of PYX-201 and PYX-106. Our future success is substantially dependent on our ability to successfully initiate and complete clinical development for, obtain regulatory licensure for, and successfully commercialize PYX-201 and PYX-106 which may never occur. We currently have no products that are approved or licensed for commercial sale and may never be able to develop a marketable product. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to PYX-201 and PYX-106 which will require clinical development, management of clinical and manufacturing activities, regulatory licensure, establishing commercial scale manufacturing, and significant sales, marketing, and distribution efforts before we can generate any revenues from any commercial sales. We cannot be certain that we will be able to successfully complete any of these activities or that, even if PYX-201 and PYX-106 receive regulatory licensure, such products will be able to successfully compete against therapies and technologies offered by other companies.

The research, testing, manufacturing, labeling, licensure, sale, packaging, marketing, and distribution of biological products are subject to extensive regulation by the FDA and comparable regulatory authorities in other countries. We are not permitted to market PYX-201 and PYX-106 in the United States until we receive licensure of a Biologics License Application, or BLA, from the FDA for such product candidates, as appropriate. Further, we are not permitted to market PYX-201 and PYX-106 in any foreign countries until we receive the requisite licensure or approvals from such countries. We have not submitted a BLA to the FDA or comparable applications to any other comparable regulatory authorities for PYX-201 and PYX-106. We will not be in a position to do so for several years, if ever. If we are unable to obtain the necessary regulatory licensure or approvals for PYX-201 and PYX-106 in a country, we will not be able to commercialize such product candidate in that country. As a result, our financial position will be materially adversely affected, and we may not be able to generate sufficient revenue to continue our business.

Our product candidates may fail in development or suffer delays that materially and adversely affect their commercial viability. If we or our existing or future collaborators are unable to initiate and complete clinical development of, obtain regulatory approval or licensure for or commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have no products on the market and only two of our product candidates are currently in early stages of clinical development. As a result, their risk of failure is high. Our ability to achieve and sustain profitability depends on obtaining regulatory licensure for and successfully commercializing our product candidates, either alone or with third parties. Before obtaining regulatory licensure for the commercial distribution of our product candidates, we or an existing or future collaborator must conduct extensive preclinical studies and clinical trials to demonstrate the safety, purity and potency in humans of our product candidates. In addition, the development of novel antibodies is complex and difficult. Although our discovery and preclinical programs may initially show promise in identifying potential product candidates, they may not translate into product candidates for clinical development for a number of reasons, including that the target selection methodology we use may not be successful due to our inability to generate an applicable antibody candidate. In addition, several of our product candidates are in-licensed and we continue to look for additional product candidates to in-license or acquire. Our preclinical studies or clinical trials may not replicate or advance the results of the research programs and pre-clinical studies that were completed prior to our in-licensing or acquisition of product candidates.

We may not have the financial resources to continue development of, or to modify existing or enter into new collaborations for, a product candidate if we experience any issues that delay or prevent regulatory licensure of, or our ability to commercialize, product candidates, including:

- negative or inconclusive results from preclinical studies or clinical trials leading to a decision or requirement to conduct additional preclinical studies or clinical trials or abandon a program;
- product-related side effects experienced by participants in our clinical trials or by individuals using therapeutic biological products similar to our product candidates;
- failure in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA, EMA or other comparable authorities regarding the scope or design of our clinical trials;
- delays in enrolling patients in clinical trials;
- high drop-out rates of patients;
- inadequate supply or quality of product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness of our product candidates during clinical trials;
- unfavorable FDA or other comparable regulatory agency inspection and review of a clinical trial site;
- failure of our third party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of data by the FDA, the EMA and other comparable foreign regulatory authorities.

If any of the foregoing circumstances occur, we could experience significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business. Moreover, if we do not receive regulatory approvals, we may not be able to continue our operations.

We have no experience as a company completing a clinical trial or submitting a BLA or NDA and may be unable to successfully do so for PYX-201 and PYX-106.

The conduct of a clinical trial is a long, expensive, complicated and highly regulated process. Although our employees have conducted successful clinical trials and made regulatory submissions in the past across many therapeutic areas while employed at other companies, we, as a company, have not completed any clinical trials, or submitted a BLA or New Drug Application, or NDA, and as a result may require more time and incur greater costs than we anticipate. Failure to commence or complete, or delays in, our clinical trials or planned regulatory submissions would prevent us from, or delay us in, obtaining regulatory approval of and commercializing PYX-201 and PYX-106, which would adversely impact our financial performance. Large-scale clinical trials would require significant additional financial and management resources and reliance on third-party clinical investigators and consultants. Relying on third-party clinical investigators, contract research organizations, or CROs, and consultants may cause us to encounter delays that are outside of our control. In addition, relying on third parties in the conduct of our preclinical studies or clinical trials exposes us to a risk that they may not adequately comply with good laboratory practice, or GLP, or good clinical practice, or GCP, as required for any studies or trials we plan to submit to a regulatory authority. We may be unable to identify and contract with sufficient investigators, CROs and consultants on terms that are acceptable to us on a timely basis or at all.

We may not be able to submit INDs to commence additional clinical trials on the timelines we expect and, even if we are able to, the FDA may not permit us to proceed.

We may submit additional INDs in the future. We may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing us to commence clinical trials or that, once begun, issues will not arise that lead to the suspension or termination of our clinical trials. Additionally, even if the applicable regulatory authorities agree with the design and implementation of the clinical trials set forth in our INDs, we cannot guarantee that those regulatory authorities will not change their requirements in the future, or that circumstances will not arise under which FDA or other regulatory authorities may place our clinical trials on partial or full clinical hold. These considerations apply to the INDs described above and also to new clinical trials we may submit as amendments to existing INDs or as part of new INDs in the future. Any failure to submit INDs on the timelines we expect or to obtain authorization to proceed with our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

Our preclinical studies and clinical trials may fail to demonstrate adequately the safety, purity and potency of any of our product candidates, which would prevent or delay development, regulatory approval or licensure and commercialization.

Before obtaining regulatory licensure for the commercial sale of any of our product candidates, including PYX-201 and PYX-106, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are safe, pure, and potent, as required under a BLA. Preclinical and clinical testing is expensive and can take many years to complete and the outcome of these activities is inherently uncertain. Failure can occur at any time during the preclinical study and clinical trial processes and, because our product candidates are in an early stage of development and have never been tested in humans, there is a high risk of failure. In addition, any failures or adverse outcomes in preclinical or clinical testing seen by other developers of similar product candidates could materially impact the success of our programs. We may never succeed in developing marketable products.

It is also possible that the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Although product candidates may demonstrate promising results in preclinical studies and early clinical trials, they may not prove to be effective in subsequent clinical trials. For example, testing on animals occurs under different conditions than testing in humans and, therefore, the results of animal studies may not accurately predict human experience. There is typically an extremely high rate of attrition from the failure of product candidates proceeding through preclinical studies and clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety, purity, and potency profile despite having progressed successfully through preclinical studies and/or initial clinical trials. Likewise, early, smaller-scale clinical trials may not be predictive of eventual safety, purity and potency in large-scale pivotal clinical trials. Many companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of potency, insufficient durability of potency or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence preclinical studies and clinical trials are never approved or licensed for commercialization. In addition, preclinical studies or clinical trials we conduct may contradict, undermine or otherwise not replicate or advance the results of the research programs and pre-clinical studies that were completed prior to our in-licensing or acquisition of product candidates, which may materially and adversely affect our business, results of operations and prospects.

Additionally, we expect that the first clinical trials for our product candidates may be open-label studies, where both the patient and investigator know whether the patient is receiving the investigational product candidate or an existing licensed biological product. Most typically, open-label clinical trials test only the investigational product candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. FDA may also not consider open-label clinical trials to be adequate and well controlled trials sufficient to support BLA licensure.

Any preclinical studies or clinical trials that we may conduct may not demonstrate the safety, purity, and potency necessary to obtain regulatory licensure to market our product candidates. If the results of our ongoing or future preclinical studies and clinical trials are inconclusive with respect to the safety, purity, and potency of our product candidates, if we do not meet the clinical endpoints with statistical and clinically meaningful significance or if there are safety concerns associated with our product candidates, we may be prevented or delayed in obtaining marketing licensure for those product candidates. In some instances, there can be significant variability in safety, purity, and potency results between different preclinical studies and clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. If that were to occur, or if other developers of similar products were to find an unacceptable severity or prevalence of side effects with their candidates, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny licensure of our product candidates for any or all targeted indications. Product-related side effects could also affect patient recruitment or the ability of enrolled patients to complete an ongoing trial or result in potential product liability claims. Any of these occurrences may significantly harm our business, financial condition and prospects.

Further, our product candidates could cause undesirable side effects in clinical trials related to on-target toxicity. If on-target toxicity is observed or if our product candidates have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in early-stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approval or licensure or commercialize these programs on a timely basis or at all.

In order to obtain FDA, European Commission (based on the opinion of the EMA's Committee for Human Medicinal Products, or CHMP) or other comparable licensure to market a new biological product we must demonstrate proof of safety, purity and potency or efficacy in humans. To meet these requirements, we will have to conduct adequate and well-controlled clinical trials. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical studies that support our planned INDs or similar applications in foreign countries. We cannot be certain of the timely completion or outcome of our preclinical studies and cannot predict if the FDA or other comparable foreign authorities and independent ethics committees will accept our proposed clinical programs or if the outcome of our preclinical 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 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 or independent ethics committees allowing clinical trials to begin.

Conducting preclinical studies is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. Any delays in preclinical studies conducted by us or potential future partners may cause us to incur additional operating expenses. The commencement and rate of completion of preclinical studies for a product candidate may be delayed by many factors, including, for example:

- inability to generate sufficient preclinical or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- the COVID-19 pandemic, which may result in delays; and
- delays in reaching a consensus with regulatory agencies on study design.

Moreover, because standards for preclinical assessment are evolving and may change rapidly, even if we reach an agreement with the FDA on a pre-IND proposal, the FDA may not accept the IND submission as presented. Even if clinical trials do begin for our preclinical programs, our clinical trials or development efforts may not be successful.

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

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to the timing and outcome. A failure of one or more clinical trials can occur at any stage of the process. We may experience numerous unforeseen events during or as a result of clinical trials, which could delay or prevent our ability to receive marketing licensure or commercialize our product candidates, including:

- delays in reaching, or the failure to reach, a consensus with regulators on clinical trial design;
- 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, including as a result of delays in the testing, validation, manufacturing and delivery of product candidates to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- delays in reaching, or the failure to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- the failure of regulators or institutional review boards to authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- difficulty in designing clinical trials and in selecting endpoints for diseases that have not been well studied and for which the natural history and course of the disease is poorly understood;
- the selection of certain clinical endpoints that may require prolonged periods of clinical observation or analysis of the resulting data;
- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or fail to return for post-treatment follow-up or the failure to recruit suitable patients to participate in our clinical trials;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate our clinical trials;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- the third parties with whom we contract may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the requirement from regulators or institutional review boards that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or unacceptable safety risks;
- clinical trials of our product candidates may produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product candidate development and discovery programs;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations, trial sites or manufacturing facilities;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- delays in developing and validating any companion diagnostic to be used in the trial, to the extent we are required to do so.

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

- be delayed in obtaining marketing licenses for our product candidates;
- not obtain marketing licensure at all;
- obtain licensure for indications or patient populations that are not as broad as intended or desired;
- obtain licensure with labeling that includes significant use or distribution restrictions or safety warnings;
- be required to perform additional clinical trials to support marketing licensure;
- have regulatory authorities withdraw or suspend their license, or impose restrictions on distribution of a product candidate in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to additional post-marketing testing requirements or changes in the way the product is administered;
- the FDA or comparable foreign regulatory authorities may fail to approve any companion diagnostics that may be required in connection with approval of our therapeutic product candidates; or
- have our product removed from the market after obtaining marketing licensure.

For example, the FDA launched *Project Optimus* in 2021 as an initiative to reform the dose optimization and dose selection paradigm in oncology drug development, which was driven by the FDA's concerns that the current paradigm for dose selection may result in doses and schedules of molecularly targeted therapies that are inadequately characterized before initiating pivotal trials. Through collaboration with the biopharmaceutical industry, academia and other stakeholders, the FDA's goal for this initiative is to advance an oncology dose-finding and dose optimization paradigm that emphasizes dose selections that maximize efficacy as well as safety and tolerability. In support of this initiative, the FDA may request sponsors of oncology product candidates to conduct dose optimization studies pre- or post-approval. The FDA also continues to develop and finalize guidance documents and implement initiatives regarding the development and clinical research of oncology product candidates.

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

Further, cancer therapies sometimes are characterized as first-line, second-line or third-line. The FDA often approves or licenses new oncology therapies initially only for third-line or later use, meaning for use after two or more other treatments have failed. When cancer is detected early enough, first-line therapy, usually hormone therapy, surgery, radiation therapy, immunotherapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second-line and third-line therapies are administered to patients when prior therapy is not effective. Our clinical trials will be with patients who have received one or more prior treatments and we expect that we would initially seek regulatory licensure for use of these product candidates as second-line or third-line therapy. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek licensure potentially as a first-line therapy, but any product candidates we develop, even if approved for second-line or third-line therapy, may not be approved for first-line therapy and, prior to seeking and/or receiving any licensures for first-line therapy, we may have to conduct additional clinical trials.

Any failures or setbacks involving the FACT Platform, including adverse events, could have a detrimental impact on our research pipeline and future success.

We use the FACT Platform in our ADC product candidate, PYX-201. Any failures or setbacks involving the FACT Platform, including adverse events, could have a detrimental impact on our research pipeline and future success. For example, we may uncover a previously unknown risk associated with the FACT Platform or other issues that may be more problematic than we currently believe, which may prolong the period of observation required for obtaining regulatory approval, necessitate additional clinical testing or result in the failure to obtain regulatory licensure. If the FACT Platform or any of its components that is used in our ADC product candidate is not safe, we would be required to abandon or redesign other product candidates we develop via the FACT Platform, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be successful in our efforts to use and expand the FACT Platform to continue to build a pipeline of product candidates and develop marketable products.

We are using the FACT Platform to develop PYX-201, as well as continuing to build our pipeline of product candidates. Our business depends not only on our ability to successfully develop, obtain regulatory licensure for, and commercialize our product candidates, but to continue to generate new product candidates through our platform. Even if we are successful in continuing to build our pipeline and further progress the development of our current product candidates, any additional product candidates may not be suitable for clinical development, including as a result of harmful side effects, manufacturing issues, limited potency or other characteristics that indicate that they are unlikely to be products that will succeed in clinical development, receive marketing licensure or achieve market acceptance. If we cannot validate our technology platform by successfully commercializing product candidates, we may not be able to obtain product, licensing or collaboration revenue in future periods, which would adversely affect our business, financial condition, results of operations and prospects.

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

As a result of our limited financial and managerial resources, we must make strategic decisions as to which targets and product candidates to pursue and may forego or delay pursuit of opportunities with other targets or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Failure to properly assess potential product candidates could result in our focus on product candidates with low market potential, which would harm our business, financial condition, results of operations and prospects. Our spending on current and future research, product candidates and discovery programs for specific targets or indications may not yield any commercially viable products. 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 royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

If the market opportunities for any product candidate that we develop are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.

The potentially addressable patient population for our current programs or future product candidates may be limited and the number of patients who have the cancers we are targeting may turn out to be lower than expected. Potentially addressable patient populations for our product candidates are only estimates. These estimates could prove to be incorrect, and the estimated number of potential patients in the United States and elsewhere could be lower than expected. It may also be that such patients may not be otherwise amenable to treatment with our product candidates, or patients could become increasingly difficult to identify and access, any of which could materially adversely affect our business, financial condition, results of operations and growth prospects.

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

The market may not be receptive to our product candidates because they are based on our novel therapeutic modality, and we may not generate any future revenue from the sale or licensing of product candidates.

Even if regulatory licensure is obtained for a product candidate, we may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and whether the product is otherwise accepted in the market. Some product candidates that we are developing are based on the FACT Platform, which is a new technology and therapeutic approach. Our future success depends on the successful development of this novel therapeutic approach. Additionally, the regulatory licensure process for novel product candidates such as ours can be more expensive and take longer than for other, better-known or extensively-studied product candidates. No regulatory authority has granted licensure for any therapeutic using the FACT Platform. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the FACT Platform will result in the development and marketing licensure of any products. Any development problems we experience in the future related to any of our programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Advancing our products creates significant challenges for us, including:

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

Any of these factors may prevent us from commercializing any of our product candidates we may develop on a timely or profitable basis, if at all.

Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payors, may not adopt a product or treatment based on the FACT Platform and technologies, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for, any product candidates developed by us or our existing or future collaborators. Market acceptance of our product candidates will depend on, among other factors:

- the timing of our receipt of any marketing and commercialization licensures;
- the terms of any licensures and the countries in which licensures are obtained;
- the safety, purity, and potency of our product candidates;
- the prevalence and severity of any adverse side effects associated with our product candidates;
- limitations or warnings contained in any labeling approved by the FDA, or other comparable foreign regulatory authorities;
- relative convenience and ease of administration of our product candidates;
- the willingness of patients to accept any new methods of administration;
- the success of our physician education programs;
- the availability of adequate government and third-party payor reimbursement;
- the pricing of our products, particularly as compared to alternative treatments; and
- availability of alternative effective treatments for the disease indications our product candidates are intended to treat and the relative risks, benefits and costs of those treatments.

If any product candidate we commercialize fails to achieve market acceptance, it could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We are early in our development efforts. Our lead product candidates, PYX-201 and PYX-106, are in the early stages of clinical development. The results of preclinical studies and early-stage clinical trials may not be predictive of future results in later studies or trials. Initial success in clinical trials may not be indicative of results obtained when these trials are completed or in later-stage clinical trials.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials that are continuing may not be predictive of the results of the later-stage clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed on in later stage clinical trials. In particular, the small number of patients in our planned early clinical trials may make the results of these trials less predictive of the outcome of later clinical trials. For example, even if successful, the results of our Phase 1 clinical trials of our product candidates PYX-201 and PYX-106 and other product candidates may not be predictive of the results of further clinical trials of these product candidates or any of our other product candidates. Moreover, preclinical and clinical data often are susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless have failed to obtain marketing licensure of their products. Our future clinical trials may not ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for product candidates proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving encouraging results in earlier studies. Any such setbacks in our clinical development could materially harm our business, results of operations, financial condition and prospects.

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

If we experience delays or difficulties in the enrollment of patients in our clinical trials, our timelines for submitting applications for and receiving necessary marketing authorizations, if any, could be delayed or prevented.

We may not be able to initiate clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials, as required by the FDA or similar regulatory authorities outside of the United States. While we believe that we will be able to enroll a sufficient number of patients into each of these clinical trials, we cannot predict with certainty how difficult it will be to enroll patients for trials in these rare indications generally and during the COVID-19 pandemic, specifically. Our ability to identify and enroll eligible patients for clinical trials may turn out to be limited or we may be slower in enrolling these trials than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates and, as a result, patients who would otherwise be eligible for our clinical trials may instead elect to enroll in clinical trials of our competitors' product candidates. Patient enrollment in clinical trials is also affected by other factors including:

- the severity of the disease under investigation;
- the size and nature of the patient population;
- the eligibility criteria for the trial in question;
- competing clinical trials or approved therapies which present an attractive alternative to patients and their physicians;
- perceived risks and benefits of the product candidate under study, including as a result of adverse effects observed in similar or competing therapies;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the burden on patients due to the scope and invasiveness of required procedures under clinical trial protocols, some of which may be inconvenient and/or uncomfortable;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients;

- the impact of the current COVID-19 pandemic, which may affect the conduct of a clinical trial, including by slowing potential enrollment or reducing the number of eligible patients for clinical trials;
- the risk that enrolled subjects will drop out or die before completion of the trial;
- patients failing to complete a clinical trial or returning for post-treatment follow-up; and
- our ability to manufacture the requisite materials for a patient and clinical trial.

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

Our product candidates may cause undesirable and unforeseen side effects or have other properties impacting safety that could halt their clinical development, delay or prevent their regulatory licensure, limit their commercial potential or result in significant negative consequences.

Undesirable side effects caused by our product candidates could cause regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory licensure or approval by the FDA or other regulatory authorities. As is the case with oncology drugs, it is likely that there may be side effects associated with their use. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny licensure or approval of our product candidates for any or all targeted indications. Such 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 materially and adversely affect our business, financial condition, results of operations and prospects.

Further, clinical trials by their nature utilize 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 with a significantly larger number of patients exposed to the product candidate.

In the event that any of our product candidates receive regulatory licensure or approval and we or others identify undesirable side effects caused by one of our products, any of the following adverse events could occur, which could result in the loss of significant revenue to us and materially and adversely affect our results of operations and business:

- regulatory authorities may withdraw their licensure or approval of the product or seize the product;
- we may be required to recall the product or change the way the product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

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

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

We face competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.

The development and commercialization of therapeutic biological products is highly competitive. We compete with a variety of multinational biopharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will develop product candidates and processes competitive with our product candidates. Competitive therapeutic treatments include those that have already been approved or licensed and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop product candidates. The biotechnology and pharmaceutical industries, including the oncology subsector, are characterized by rapidly evolving technologies, intense competition, and a strong defense of intellectual property and proprietary technologies. Any product candidates that we successfully commercialize may not be competitive with currently marketed therapies and any new therapies commercialized in the future.

We are aware of several companies that are developing cancer immunotherapies and ADCs. Many of these companies are well-capitalized and, in contrast to us, have significant clinical experience, and may include our existing or future collaborators. In addition, these companies compete with us in recruiting scientific and managerial talent and the patient pool available for participation in clinical trials.

Our success will partially depend on our ability to develop and protect therapeutics that are more safe, pure, and potent than competing products. Our commercial opportunity and success will be reduced or eliminated if competing products that are safer, more effective, or less expensive than the therapeutics we develop are commercialized.

If our product candidates are licensed, they will compete with a range of therapeutic treatments that are either in development or currently marketed. Many companies are active across various stages of development in the oncology subsector and are marketing and developing products that employ similar ADC and immunotherapy approaches. As of April 2021, there were approximately 275 ADCs in clinical or preclinical development worldwide, of which the vast majority are being developed for the treatment of various cancer indications. Additionally, there are several large and small companies working on various immunotherapy approaches for treatment of cancer. Multiple companies are also involved in the marketing of ADC therapeutics and Immunotherapy which include, but are not limited to, ADC Therapeutics SA, Astellas Pharma, Inc., AstraZeneca plc, Daiichi Sankyo Company, Ltd., Genentech, Inc., Gilead Sciences, Inc, GlaxoSmithKline, plc, Pfizer Inc., Rakuten Medical, Inc., Seagen, Inc., Nextcure, Inc. and Abcure, Inc.

Our preclinical ADC and immunotherapy candidates may face substantial competition from alternative therapeutic modalities, such as CAR-T therapies, bispecific antibodies, and small molecules that are being developed for the same cancer types that we are targeting with our pipeline candidates. These approaches could prove to be more effective, safer, or convey other advantages over any products resulting from our technology. In addition, we also face competition on specific targets, including the target of our PYX-201 candidate, EDB, from Philogen S.p.A., the target of our PYX-203 product candidate, CD123, from ImmunoGen, Inc., Vincerx Pharma, Inc., Macrogenics and Byondis B.V., the target of our PYX-106 product candidate, BSI-060T, from Nextcure, Inc. lead program - NC318 and the target of our PYX-102 product candidate, Anti-KLRG1, from Abcuro, Inc. Additionally, there is a wide array of activity in the development of immunotherapies for oncology which may be competitive with our preclinical discovery programs. Furthermore, if any of our product candidates are approved in oncology indications such as lung, hematological and other cancers, they may compete with existing approaches to treating cancer including surgery, radiation, and drug therapy, including conventional chemotherapy, biological products, and targeted drug small molecule therapies.

Many of our competitors have significantly greater scientific, research and development capabilities, as well as greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain licensure for any product candidate, we will face competition based on many different factors, including the safety, purity and potency of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory licenses for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

Our biological product candidates for which we intend to seek licensure may face competition sooner than anticipated.

The Affordable Care Act, or ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which created an abbreviated licensure pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the 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 market a competing version of the reference product if the FDA approves a full BLA for the competing 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 law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have an adverse effect on the future commercial prospects for our product candidates.

There is a risk that any product candidates we may develop that are licensed as a biological product under a BLA would not qualify for the 12-year period of exclusivity or that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider any product candidates we may develop to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation, including litigation challenging the constitutionality of the ACA.

For example, in December 2018, a federal district court ruled that the ACA, without the "individual mandate" penalty (which was repealed by Congress as part of the Tax Cuts and Jobs Act), is unconstitutional in its entirety. In December 2019, the U.S. Court of Appeals for the 5th Circuit upheld the district court ruling that the individual mandate provisions are unconstitutional and remanded the case back to the district court for further analysis of whether such provisions could be severed from the remainder of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the case without specifically ruling on the constitutionality of the ACA. There may, however, be other efforts to challenge, repeal, or replace the ACA in the future. We continue to evaluate the effect that the ACA and its possible repeal and replacement has (or may have) on our business and exclusivity under the BPCIA. It is uncertain the extent to which any such changes may impact our business or financial condition.

Our business entails a significant risk of product liability, and if we are unable to obtain sufficient insurance coverage, such failure could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We expect to be exposed to significant product liability risks inherent in the development, testing and manufacturing of our product candidates and products, if approved. Product liability claims could delay or prevent completion of product candidate development programs. If we succeed in marketing products, such claims could result in an FDA investigation of the safety and effectiveness of our products, our third-party manufacturer's manufacturing processes and facilities or our marketing programs and potentially a recall of our products or more serious enforcement action, including limitations on the approved indications for which our product candidates may be used or suspension or withdrawal of licenses. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources, substantial monetary awards to trial participants or patients and a decline in our stock price. In addition, we may be subject to liability based on the actions of our existing or future collaborators in connection with their development of products using the FACT Platform. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to maintain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Licensure or Approval and Other Legal Compliance Matters

The regulatory licensure and approval processes of the FDA and other comparable regulatory authorities are lengthy, time-consuming and inherently unpredictable and, if we are ultimately unable to obtain marketing licensure or approval for our product candidates, our business will be substantially harmed.

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

Our product candidates could fail to receive marketing licensure in the United States for many reasons, including the following:

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

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

In addition, even if we were to obtain licensure, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant a license contingent on the performance of costly post-marketing clinical trials, or may approve or license a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we obtain FDA licensure for any of our product candidates in the United States, we may never obtain approval or licensure for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential.

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety, purity, potency and efficacy.

Licensure by the FDA in the United States does not ensure approval or licensure by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval or licensure in one jurisdiction may negatively impact our ability to obtain approval or licensure elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval or licensure in one country does not guarantee regulatory approval or licensure in any other country.

Approval or licensure processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval or licensure could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved or licensed for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval or licensure in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals or licensures, or if regulatory approvals or licensures in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

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

If any of our product candidates are licensed or approved by regulatory authorities, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, track and trace, serialization, post-market adverse event reporting, and submission of safety, purity, potency, efficacy and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-licensure.

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

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

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

- regulatory authorities may withdraw their licensure of the biological product or seize the biological product;
- we, or any future collaborators, may be required to recall the biological product, change the way the biological product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular biological product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we, or any future collaborators, may be required to create a medication guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the biological product may become less competitive in the marketplace; and
- our reputation may suffer.

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

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety, purity, or potency of the product, including the adoption and implementation of REMS. The FDA and other agencies, including the United States Department of Justice, or DOJ, closely regulate and monitor the post-licensure marketing and promotion of biological products to ensure they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products only for the approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug and Cosmetic Act, or FDCA, and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

We, and any collaborators, must comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing licensure. Promotional communications with respect to prescription biological products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we, and any collaborators, will not be able to promote any products we develop for indications or uses for which the biological product is not licensed. 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. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments, but the FDA does restrict manufacturer's communications on the subject of off-label use of their products. The policies of the FDA and of comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory licensure of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing licensure that we may have obtained and we may not achieve or sustain profitability.

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

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

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

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA and similar foreign authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of licenses;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population (as explained further below), also can result in significant financial penalties, and non-compliance with pediatric requirements may prevent regulatory approvals from being granted. Similarly, failure to comply with the European Union and United Kingdom's, or UK, requirements regarding the protection of personal information can lead to significant penalties and sanctions.

A Breakthrough Therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or licensure process and it does not increase the likelihood that our product candidates will receive marketing licensure.

We may seek Breakthrough Therapy designation for our product candidates and some or all of our future product candidates. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs or biological products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biological products 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 product candidates 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. Drugs designated as Breakthrough Therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval, if they meet requirements for those other programs.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or licensure compared to candidate products considered for licensure under non-expedited FDA review procedures and does not assure ultimate licensure by the FDA. In addition, even if one or more of our product candidates qualify as Breakthrough Therapies, the FDA may later decide that the product no longer meets the conditions for qualification. For example, in June 2022, FDA published a draft guidance document outlining considerations for the FDA in rescinding Breakthrough Therapy designation for products that no longer meet the requirements for that designation. Thus, even though we intend to seek Breakthrough Therapy designation for some or all of our future product candidates for the treatment of various cancers, there can be no assurance that we will receive Breakthrough Therapy designation.

Fast Track designation by the FDA, even if granted for other current or future product candidates, may not lead to a faster development or regulatory review, licensure process and does not increase the likelihood that our product candidates will receive marketing licensure.

We may seek Fast Track designation for one or more of our future product candidates. If a drug or biological product is intended 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, the drug sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for our product candidates, but there is no assurance that the FDA will grant this designation to any of our proposed product candidates. Marketing applications submitted by sponsors of products in Fast Track development may qualify for priority review under the policies and procedures offered by the FDA, but the Fast Track designation does not assure any such qualification or ultimate marketing licensure by the FDA. The FDA has broad discretion whether or not to grant Fast Track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or licensure compared to conventional FDA procedures or pathways and receiving a Fast Track designation does not provide assurance of ultimate FDA licensure. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any Fast Track designation at any time.

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

We may seek Orphan Drug Designation for one or more of our current or future product candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs or biological products for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug or biological product. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants Orphan Drug Designation, the identity of the drug or biological product and its potential orphan use are disclosed publicly by the FDA. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and licensure process.

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

We may seek Orphan Drug Designation for our product candidates in additional orphan indications in which there is a medically plausible basis for the use of these product candidates. Even if we obtain Orphan Drug Designation, exclusive marketing rights in the United States may be limited if we seek licensure for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if we, through our manufacturer, are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, although we intend to seek Orphan Drug Designation for other product candidates, we may never receive these designations.

Congress is also considering updates to the orphan drug provisions of the FDCA in response to a recent 11th Circuit decision. Any changes to the orphan drug provisions could change our opportunities for, or likelihood of success in obtaining, orphan drug exclusivity and would materially adversely affect our business, financial condition, results of operations, cash flows and prospects.

Accelerated approval by the FDA, even if granted, 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 licensure. If we are unable to obtain licensure of our products through the Accelerated Approval Program in the United States, we may be required to conduct additional nonclinical and clinical studies and trials beyond those that we currently contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing licensure. Even if we receive accelerated approval from the FDA through the Accelerated Approval Program, if our confirmatory post-marketing trial does not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We plan to seek accelerated approval of PYX-201 and PYX-106 and may seek approval of future product candidates using the FDA's accelerated approval pathway. For any licensure to market a biological product, we must provide the FDA and foreign regulatory agencies with clinical data that adequately demonstrate the safety, purity, and potency of the product for the indication applied for in the NDA or BLA or other respective regulatory filings. The Accelerated Approval Program is one of several approaches used by the FDA to make prescription drugs or biological products more rapidly available for the treatment of serious or life-threatening diseases. Section 506(c) of the FDCA provides that the FDA may grant accelerated approval to "a product for a serious or life-threatening condition upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments." Licensure through the Accelerated Approval Program is subject, however, to the requirement that a sponsor perform adequate and well controlled post-marketing clinical trials to verify and describe the drug's clinical benefit, where there is uncertainty as to the relationship of the surrogate endpoint to the clinical benefit, or of the observed clinical endpoint to ultimate outcome. Typically, clinical benefit is verified when post-marketing clinical trials show that the biological products provide a clinically meaningful positive therapeutic effect, that is, an effect on how a patient feels, functions, or survives. These confirmatory trials must be completed with due diligence and may require that such studies be underway prior to approval under FDORA. If such confirmatory post-marketing trial fails to confirm the product's clinical profile or risks and benefits, the FDA may withdraw accelerated approval of the product.

The FDA has broad discretion with regard to licensure through the Accelerated Approval Program, and even if we believe that the Accelerated Approval Program is appropriate for one of our products, we cannot assure you that the FDA will ultimately agree. Furthermore, even if we do obtain licensure through the Accelerated Approval Program, we may not experience a faster development process, review, or licensure compared to conventional FDA procedures.

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

Even if we receive licensure for one of our products through the Accelerated Approval Program, we will be subject to rigorous post-marketing requirements, including the completion of one or more confirmatory post-marketing trials as the FDA may require, to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. These requirements could adversely impact the timing of the commercial launch of the product. Even if we do receive accelerated approval, we may not experience a faster development or regulatory review or licensure process. Further, receiving accelerated approval does not provide assurance of ultimate full FDA licensure.

The FDA could seek to withdraw accelerated approval for multiple reasons, including if we fail to conduct any required confirmatory post-marketing trial with due diligence, our confirmatory post-marketing trial does not confirm the predicted clinical benefit, other evidence shows that the product is not safe, pure, or potent under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false and misleading.

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

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

In the European Union and the UK, innovative medicinal products are authorized based on a full marketing authorization application and conditional authorization (as opposed to an application for marketing authorization that relies on data in the marketing authorization dossier for another, previously approved medicinal product). Applications for marketing authorization for innovative medicinal products must contain, *inter alia*, the results of pharmaceutical tests, preclinical tests and clinical trials conducted with the medicinal product for which marketing authorization is sought (and where applicable the results of the pediatric studies unless a waiver or a deferral has been obtained— as described further below).

A marketing authorization can be obtained via the centralized procedure or the national procedure. The centralized procedure results in a single marketing authorization, issued by the European Commission (based on the opinion of the EMA), which is valid across the entire European Economic Area, or EEA, which comprises the EU, Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human drugs that are (i) derived from biotechnology processes, such as genetic engineering; (ii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases; (iii) designated orphan medicines; and (iv) advanced-therapy medicines, such as gene therapy, somatic cell therapy or tissue-engineered medicines. The centralized procedure may at the request of the applicant also be used in certain other cases. Therefore, the centralized procedure would be mandatory for the product candidates we are developing.

Where an applicant for a marketing authorization submits a full dossier containing its own pharmaceutical, preclinical tests and clinical trials data, and where the application does not fall within the 'global marketing authorization' of an existing medicinal product, reference product candidates may receive eight years of data exclusivity and an additional two years of market exclusivity, upon grant of the marketing authorization. If granted, during the data exclusivity period, applicants for approval of biosimilars cannot rely on data contained in the marketing authorization dossier submitted for the already authorized, or reference product candidate, to support their application. The market exclusivity period prevents a successful biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from the initial marketing authorization of the reference product in the EU, but a biosimilar marketing authorization application can be submitted during this time. The overall 10-year market exclusivity period can further be extended by one more year if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, even if a compound is considered to be a new active substance and the innovator is able to gain the period of data and market exclusivity, provided that no other IP or regulatory exclusivities apply, another unrelated company could also apply for a marketing authorization and market another competing medicinal product for the same therapeutic indication if such company obtained its own marketing authorization based on a separate marketing authorization application based on a full self-standing scientific data package supporting the application.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical testing or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological products. There are currently no such guidelines for complex biological products such as gene or cell therapy medicinal products, and so in the short term it is unlikely that biosimilars of those products will be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time.

In the EU, marking authorization applications for new medicinal products must include the results of clinical trials conducted in pediatric population, in compliance with a pediatric investigation plan, or PIP, agreed with the EMA's Pediatric Committee, or PDCO. The PDCO can grant waivers or deferrals to these requirements in certain circumstances (for example, a waiver may be obtained if the condition only occurs in adult populations). Where required, pediatric studies must cover all sub-sets of the pediatric population for both existing and new indications, pharmacological forms and route of administrations. Limited further exclusions apply, including in relation to biosimilar applications. Certain incentives may be available for completion of pediatric studies. For example, once the marketing authorization is obtained in all European Union Member States and study results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

In the EU, the criteria for designating an "orphan medicinal product" are similar in principle to those in the United States. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition (2) either (a) such condition affects no more than five in 10,000 persons in the EU when the application is made or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. The application for Orphan Drug Designation must be submitted before the marketing authorization application. Orphan Drug Designations entitle a party to financial incentives such as reduction of fees or fee waivers and are, upon grant of a marketing authorization, entitled to 10 years of market exclusivity. During the 10-year market exclusivity period, the EMA cannot accept another marketing authorization application, or grant a marketing authorization or accept an application to extend an existing marketing authorization, for the same therapeutic indication, in respect of a similar medicinal product. An orphan medicinal product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for Orphan Drug Designation, for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. At any time, a marketing authorization may be granted to a similar product for the same indication if:

1. the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
2. the holder of the marketing authorization for the original orphan medicinal product has given his consent to the second applicant; or
3. the holder of the marketing authorization for the original orphan medicinal product is unable to supply sufficient quantities of the medicinal product.

Although the UK has left the EU, its regulatory legal framework provides for similar periods of protection (namely regulatory data exclusivity, marketing protection and market exclusivity).

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

The failure to obtain required regulatory clearances or approvals for any companion diagnostic tests that we may pursue may prevent or delay approval of any of our product candidates. Moreover, the commercial success of any of our product candidates that require a companion diagnostic will be tied to the receipt of any required regulatory clearances or approvals and the continued availability of such tests.

In connection with the clinical development of our product candidates for certain indications, we may work with collaborators to develop or obtain access to companion diagnostic tests to identify appropriate patients for our product candidates. We may rely on third parties for the development, testing and manufacturing of these companion diagnostics, the application for and receipt of any required regulatory clearances or approvals, and the commercial supply of these companion diagnostics. The FDA and foreign regulatory authorities regulate companion diagnostics as medical devices that will likely be subject to clinical trials in conjunction with the clinical trials for product candidates, and which will require separate regulatory clearance or approval prior to commercialization. This process could include additional meetings with health authorities, such as a pre-submission meeting and the requirement to submit an investigational device exemption, or IDE. In the case of a companion diagnostic that is designated as "significant risk device," approval of an IDE by the FDA and IRB is required before such diagnostic is used in conjunction with the clinical trials for a corresponding product candidate. We or our third-party collaborators may fail to obtain the required regulatory clearances or approvals, which could prevent or delay approval of our product candidates. In addition, the commercial success of any of our product candidates that requires a companion diagnostic will be tied to and dependent upon the receipt of required regulatory clearances or approvals and the continued ability of such third parties to make the companion diagnostic commercially available to us on reasonable terms in the relevant geographies.

If we are required to in the future and if we are unable to successfully develop companion diagnostic tests for our product candidates that require such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these product candidates.

We may be required by the FDA to develop, either by ourselves or with collaborators, companion diagnostic tests for our product candidates for certain indications. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. We have no prior experience with medical device or diagnostic test development. If we choose to develop and seek FDA clearance or approval for companion diagnostic tests on our own, we will require additional personnel with medical device knowledge and expertise. We may rely on third parties for the design, development and manufacture of companion diagnostic tests for our therapeutic product candidates that require such tests. If these parties are unable to successfully develop companion diagnostics for these therapeutic product candidates, or experience delays in doing so, we may be unable to enroll enough patients for our current and planned clinical trials, the development of these therapeutic product candidates may be adversely affected, these therapeutic product candidates may not obtain marketing approval, and we may not realize the full commercial potential of any of these therapeutics that obtain marketing approval. Any failure to successfully develop this companion diagnostic may cause or contribute to delayed enrollment of this trial and may prevent us from initiating or completing further clinical trials to support marketing approval for our product candidates. As a result, our business, results of operations and financial condition could be materially harmed.

Our relationships with customers, physicians and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and other healthcare laws and regulations. If we are unable to comply or have not fully complied with these laws, we could face substantial penalties.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing licensure. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws that may constrain the business or financial arrangements and relationships through which we research, develop, sell, market and distribute our product candidates, if we obtain marketing licensure. In particular, the research of our product candidates, as well as the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business or financial arrangements.

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements. 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, disgorgement, imprisonment, or exclusion from participating in government-funded healthcare programs, such as Medicare and Medicaid; additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws; contractual damages; reputational harm; and/or the curtailment or restructuring of our operations.

If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusion from government-funded healthcare programs. Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have an adverse effect on our ability to compete in the marketplace.

The successful commercialization of our product candidates in the United States and elsewhere will depend in part on the extent to which third-party payors, including governmental authorities and private health insurers, provide coverage and adequate reimbursement levels, as well as implement pricing policies favorable for our product candidates. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory licensure. In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (e.g., Medicare, Medicaid or TRICARE), managed care providers, private health insurers, health maintenance organizations and other organizations is essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates. Third-party payors decide which medications they will pay for and establish reimbursement levels.

Our ability to successfully commercialize our product candidates will depend, in part, on the extent to which coverage and adequate reimbursement for any products for which we obtain marketing authorization will be available from third-party payors. In the United States, no uniform policy for coverage and reimbursement for pharmaceutical products exists among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting reimbursement policies, but also have their own methods and approval processes apart from Medicare coverage and reimbursement determinations. Therefore, coverage and reimbursement for products for which we may obtain marketing authorization could differ significantly from payor to payor. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product. Payors consider a number of factors when determining whether to cover a new product, including, for example, whether the product is a covered benefit under its health plan; safe, effective and medically necessary; appropriate for the specific patient; cost-effective; and neither experimental nor investigational. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication.

Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. A decision by a third-party payor not to cover or not to separately reimburse for any products for which we may obtain marketing authorization could reduce physician utilization of such products. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our product candidates. We cannot be sure that coverage and reimbursement in the United States will be available for our current or future product candidates or for any procedures using our current or future product candidates, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future. Moreover, for products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself may or may not be available. Instead, the hospital or administering physician may be reimbursed only for providing the treatment or procedure in which our product is used.

Further, increasing efforts by third-party payors in the United States and abroad to cap or reduce healthcare costs may cause payor organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable marketing authorizations or approvals. Additionally, we may also need to provide permissible discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after marketing authorization or approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates.

Lastly, in some foreign countries, the proposed pricing for a drug must be approved before the drug may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, countries in the European Union Member States can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and they can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these Member States may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A European Union Member State may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Approaches between European Union Member States are diverging. For example, in France, effective market access will be supported by agreements with hospitals and products may be reimbursed by the Social Security Fund. The price of medicines is negotiated with the Economic Committee for Health Products, or CEPs. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices in the European Union tend to be significantly lower than prices in the United States.

Enacted and future healthcare legislation may increase the difficulty and cost for us to progress our clinical programs and obtain marketing licensure or approval of and commercialize our product candidates and may affect the prices we may set.

In the United States and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect results of our future operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. See Part I, Item 1, Government Regulation – Other Healthcare Laws - Healthcare Reform for additional detail on recent healthcare reform efforts that could affect our operations.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the extent to which state and federal governments cover particular healthcare products and services and could limit the amounts that federal and state governments will pay for healthcare items and services. This could result in reduced demand for any product candidate we develop or could result in additional pricing pressures.

In markets outside of the United States, reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. The price control regulations outside of the United States can have a significant impact on the profitability of a given market, and further uncertainty is introduced if and when these laws change. For example, in Canada, price control legislation for patented medicines is currently undergoing significant change that may have significant effects on profitability for companies selling products in Canada.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or these third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory licensure or approval that may have been obtained and we may not achieve or sustain profitability.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, operations, and financial condition.

The global data protection landscape is rapidly evolving, and we may be or become subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, transfer, security and processing of personal information, such as information that we collect about participants and healthcare providers in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, which may create uncertainty in our business, affect our or our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal data, result in liability or impose additional compliance or other costs on us. Any failure or perceived failure by us to comply with federal, state or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, most healthcare providers, including certain research institutions from which we may obtain patient health information, are subject to privacy and security regulations promulgated under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which we collectively refer to as HIPAA. We are not currently acting as a covered entity or business associate under HIPAA and therefore are not directly regulated under HIPAA. However, any person may be prosecuted under HIPAA's criminal provisions either directly or under aiding-and-abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has disclosed individually identifiable health information in a manner that is not authorized or permitted under HIPAA. In addition, in the future, we may maintain sensitive personal information, including health-related information, that we receive throughout the clinical trial process, in the course of our research collaborations and/or directly from individuals (or their healthcare providers) who may enroll in patient assistance programs if we choose to implement these types of programs. As a result, we may be subject to data privacy and security laws protection such information, including state laws requiring notification of affected individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

The Federal Trade Commission, or the FTC and many state attorney generals are interpreting existing federal and state consumer protection laws to impose evolving standards for the collection, use, dissemination and security of health-related and other personal information. Privacy laws require us to publish statements that describe how we handle personal information and choices individuals may have about the way we handle their personal information. Violating individuals' privacy rights, publishing false or misleading information about security practices, or failing to take appropriate steps to keep individuals' personal information secure may constitute unfair or deceptive acts or practices in violation of Section 5 of the FTC Act. Additionally, the FTC recently published an advance notice of proposed rule making on "commercial surveillance" and data security, and is seeking comment on whether it should implement new trade regulation rules or other regulatory alternatives concerning the ways in which companies (2) collect, aggregate, protect, use, analyze, and retain consumer data, as well as (2) transfer, share, sell, or otherwise monetize that data in ways that are unfair or deceptive. Federal regulators, state attorneys general and plaintiffs' attorneys have been and will likely continue to be active in this space, and if we do not comply with existing or new laws and regulations related to patient health information, we could be subject to criminal or civil sanctions. Further, the California Consumer Privacy Act of 2018, or the CCPA, went into effect in January 2020, which creates individual data privacy rights for consumers and operational requirements for companies, including placing increased privacy and security obligations on entities handling certain personal information of consumers or households. These requirements could increase our compliance costs and potential liability. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. While there is currently an exception for protected health information maintained by a business associate or covered entity as well as an exception for clinical trial data, as currently written, the CCPA may impact certain of our business activities. Further, the California Privacy Rights Act, or CPRA, recently passed in California and modifies the CCPA. The CCPA (as modified by the CPRA) imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. The majority of the provisions went into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Similar laws have been adopted in other states or proposed in other states and at the federal level, and if passed, such laws may have potentially conflicting requirements that would make compliance challenging. For example, on March 2, 2021, the Nevada Privacy of Information Collected on the Internet from Consumers Act went into effect on October 1, 2021, the Virginia Consumer Data Protection Act went into effect on January 1, 2023, the Colorado Privacy Act goes into effect on July 1, 2023, the Connecticut Data Privacy Act goes into effect July 1, 2023, and the Utah Consumer Privacy Act goes into effect December 31, 2023. In the event that we are subject to or affected by HIPAA, the CCPA and CPRA, or other privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In addition, the European Union General Data Protection Regulation, or EU GDPR, went into effect on May 2018 and imposes strict requirements for processing the personal data (i.e., data which identifies an individual or from which an individual is identifiable) of individuals within the EEA and grants individuals various data protection rights (e.g., the right to erasure of personal data).

Companies that must comply with the EU GDPR face increased compliance obligations including *inter alia*: (i) accountability and transparency requirements, and enhanced requirements for obtaining valid consent; (ii) obligations to consider data protection as any new products or services are developed, including to limit the amount of personal data processed; (iii) obligations to implement appropriate technical and organizational measures to safeguard personal data and to report certain personal data breaches to the relevant supervisory authority without undue delay (and, in any event, no later than 72 hours, where feasible); and (iv) additional more onerous requirements around the processing of special categories of personal data (including health data and genetic data).

The EU GDPR also prohibits transfers of personal data subject to the EU GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, unless specific safeguards are implemented. Historically of the primary safeguards allowing U.S. companies to import personal data from the EEA was certification to the EU-U.S. Privacy Shield framework. However, the Court of Justice of the European Union, or the CJEU, issued a decision in July 2020 invalidating the EU-U.S. Privacy Shield framework as a data transfer mechanism (*Schrems II*) and imposing further restrictions on the use of standard contractual clauses, or SCCs, including a requirement for companies to carry out a transfer privacy impact assessment, which, among other things, assesses laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under the SCCs will need to be implemented to ensure an "essentially equivalent" level of data protection to that afforded in the EU. Subsequently, the European Commission published new EU SCCs in June 2022 to account for the decision in *Schrems II* and which place onerous obligations on the contracting parties. At present, there are few, if any, viable alternatives to the SCCs. However, on October 7, 2022, the U.S. President introduced an Executive Order to facilitate a new U.S.-EU Data Privacy Framework which will act as a successor to the invalidated Privacy Shield. On December 13, 2022, the European Commission also published its draft adequacy decision to reflect its view that the new executive order and U.S.-EU Data Privacy Framework, is able to meet the concerns raised in *Schrems II*. If the draft adequacy decision is approved and implemented, the agreement will facilitate the transatlantic flow of personal data and provide additional safeguards to data transfer mechanisms (including EU SCCs and Binding Corporate Rules) for companies transferring personal data from the EU to the U.S. However, before parties rely on the new framework, there are still legislative and regulatory steps that must be undertaken both in the U.S. and in the EU.

Companies subject to the EU GDPR may be subject to robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global turnover of the noncompliant company, whichever is greater. In addition, the EU GDPR confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the EU GDPR.

Further, from January 1, 2021, companies may have to comply with the EU GDPR and also the United Kingdom GDPR, or the UK GDPR, which, together with the amended United Kingdom Data Protection Act 2018, retains the EU GDPR in United Kingdom national law. The UK GDPR mirrors the fines under the EU GDPR, i.e., fines up to the greater of €20 million (£17.5 million) or 4% of annual global turnover. The European Commission has adopted an adequacy decision in favor of the UK, enabling data transfers from EU Member States to the UK without additional safeguards. However, the UK adequacy decision will automatically expire in June 2025 unless the European Commission re-assesses and renews/extends that decision, and remains under review by the Commission during this period. These changes may lead to additional costs and increase our overall risk exposure. It should also be noted that the UK Government published its own form of SCCs, known as the International Data Transfer Agreement and International Data Transfer Addendum to the new EU SCCs. The UK Information Commissioner's Office has also published its version of the transfer impact assessment and revised guidance on international transfers, although entities may choose to adopt either the EU or UK style transfer impact assessment. In terms of international data transfers between the UK and U.S., it is understood that the UK and the U.S. are negotiating an adequacy agreement to be known as a "Data Bridge".

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

If we or our third-party manufacturers and suppliers 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 an adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development activities involve the use of biological and hazardous materials and produce hazardous waste products. 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, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. Upon an event of this nature, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Further, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of any changes of this nature and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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 or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can 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 Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act of 2001 and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors and other collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties for clinical trials outside of the United States, to sell our products abroad once we enter a commercialization phase and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We may also have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors and other collaborators, even if we do not explicitly authorize or have actual knowledge of these activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

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

If we fail to attract and retain qualified senior management and key scientific personnel, our business may be materially and adversely affected.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management and clinical and scientific personnel. We are highly dependent upon members of our senior management, including Lara Sullivan, M.D., our President and Chief Executive Officer, Pamela Connealy, our Chief Financial Officer and Chief Operating Officer, and Jay Feingold M.D., Ph.D., our Chief Medical Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, the initiation and completion of our planned clinical trials or the commercialization of product candidates or any future product candidates.

Competition for qualified personnel in the pharmaceutical, biopharmaceutical and biotechnology field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and if we initiate commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, 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.

If our product candidates advance into clinical trials, we may experience difficulties in managing our growth and expanding our operations.

As of March 22, 2023, we had 75 full-time employees. As our development and commercialization plans and strategies develop, and as we continue to operate as a public company, we expect to expand our employee base for managerial, operational, financial and other resources. In addition, we have limited experience in product development. As our product candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. Our inability to successfully manage our growth and expand our operations could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We currently have no marketing, sales, or distribution infrastructure and we intend to either establish a sales and marketing infrastructure or outsource this function to a third party. Either of these commercialization strategies carries substantial risks to us.

We currently have no marketing, sales, and distribution capabilities because all our product candidates are still in preclinical development. If any of our product candidates complete clinical development and are approved, we intend to either establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates in a legally compliant manner, or to outsource this function to a third party. There are risks involved if we decide to establish our own sales and marketing capabilities or enter into arrangements with third parties to perform these services. To the extent that we enter into collaboration agreements with respect to marketing, sales or distribution, our product revenue may be lower than if we directly marketed or sold any approved products. Such collaborative arrangements with partners may place the commercialization of our products outside of our control and would make us subject to a number of risks, including that we may not be able to control the amount or timing of resources that our collaborative partner devotes to our products or that our collaborator's willingness or ability to complete its obligations, and our obligations under our arrangements may be adversely affected by business combinations or significant changes in our collaborator's business strategy.

If we are unable to enter into these arrangements on acceptable terms or at all, we may not be able to successfully commercialize any approved products. If we are not successful in commercializing any approved products, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses, which would have a material adverse effect on our business, financial condition, and results of operations.

Our internal computer systems, or those of any of our existing or future CROs, manufacturers, other contractors, consultants, or collaborators, may fail or suffer security or data privacy breaches or other unauthorized or improper access to, use of or destruction of our proprietary and confidential data, employee data or personal data, which could result in additional costs, significant liabilities, harm to our reputation and material disruption of our operations.

In the ordinary course of our business, we collect, process, and store proprietary, confidential, and sensitive information, including personal information (including health information), intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other parties.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs, manufacturers, other contractors, consultants, existing or future collaborators and other third-party service providers are vulnerable to damage from various methods, including cybersecurity attacks, breaches, intentional or accidental mistakes or errors, or other technological failures, which can include, among other things, computer viruses, unauthorized access attempts, including third parties gaining access to systems using stolen or inferred credentials, ransomware attacks, denial-of-service attacks, phishing attempts, service disruptions, natural disasters, fire, terrorism, war and telecommunication and electrical failures. As the cyber-threat landscape evolves, these attacks are growing in frequency, sophistication and intensity, and are becoming increasingly difficult to detect. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period.

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, it could result in a material disruption of our product candidate development programs and our business operations including without limitation, disruptions of our drug development programs, delays in our regulatory approval efforts, regulatory investigations or enforcement actions, litigation, indemnity obligations, negative publicity, and financial loss and significant liabilities. In addition, system failures could cause the loss, theft, exposure, or unauthorized access or use of valuable clinical trial data as a result of accidents, errors or malfeasance by our employees, independent contractors or others working with us or on our behalf or otherwise disrupt our clinical activities and be expensive and time-consuming to remedy. Some of the federal, state and foreign government legal 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 and cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed, ongoing or future clinical trials involving our product candidates could result in delays in our regulatory licensure efforts and significantly increase our costs to recover or reproduce the lost data. Any breach of our computer systems may result in a loss of data or compromised data integrity across many of our programs in various stages of development.

We may be required to expend resources, modify our business activities and practices, or modify our operations (including our development program activities) or information technology in an effort to comply with applicable data protection laws, privacy policies and data protection obligations.

While we have implemented security measures designed to protect against security breaches, there can be no assurance that our security measures or those of our service providers, partners and other third parties, will be effective in protecting against all security breaches and material adverse effects on our business that may arise from such breaches. The recovery systems, security protocols, network protection mechanisms and other security measures that we (and our third parties) have integrated into our platform, systems, networks and physical facilities, which are designed to protect against, detect and minimize security breaches, may not be adequate to prevent or detect service interruption, system failure, or data loss.

We will also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information, we could be exposed to litigation and governmental investigations, the further development and commercialization of our product candidates could be delayed and we could be subject to significant fines or penalties for any noncompliance with certain state, federal or international privacy and security laws.

Our insurance policies may not be adequate to compensate us for the potential losses arising from any such disruption, failure or security breach. In addition, such insurance may not be available to us in the future on economically reasonable terms, or at all. Further, our insurance may not cover all claims made against us and could have high deductibles in any event, and defending a suit, regardless of its merit, could be costly and divert management attention.

We or the third parties upon whom we depend on may be adversely affected by earthquakes, wildfires or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

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

Our business is subject to economic, political, regulatory and other risks associated with conducting business internationally.

We may seek regulatory approval or licensure of our product candidates outside of the United States. Accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals or licenses, including:

- differing regulatory requirements and reimbursement regimes in foreign countries;
- 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;
- 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 Foreign Corrupt Practices Act, or FCPA, or 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 geo-political actions, including war and terrorism.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

We face risks related to health epidemics and outbreaks, including the COVID-19 pandemic, which could significantly disrupt our preclinical studies and clinical trials, and therefore our receipt of necessary regulatory licensure or approvals could be delayed or prevented.

In December 2019, the coronavirus disease, COVID-19, was identified in Wuhan, China. Since then, COVID-19 has spread globally. In March 2020, the World Health Organization declared COVID-19 a global pandemic and the United States declared a national emergency with respect to COVID-19. In response to the COVID-19 pandemic, "shelter in place" orders and other public health guidance measures have been implemented across much of the United States, including in the locations of our offices and those of key vendors and partners. As a result of the COVID-19 pandemic, or similar pandemics, and related "shelter in place" orders and other public health guidance measures, we may in the future experience disruptions that could materially and adversely impact our preclinical studies and development, any clinical trials we subsequently commence, and our business, financial condition, and results of operations. Potential disruptions to our preclinical development efforts include, but are not limited to:

- delays or disruptions in preclinical experiments and IND-enabling studies due to restrictions of on-site staff, limited or no access to animal facilities, and unforeseen circumstances at CROs and vendors;
- limitations on employee or other resources that would otherwise be focused on the conduct of our preclinical work and any clinical trials we subsequently commence, including because of sickness of employees or their families, the desire of employees to avoid travel or contact with large groups of people, an increased reliance on working from home, school closures, or mass transit disruptions;
- delays in necessary interactions with regulators, ethics committees, and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel; and
- limitations in maintaining our corporate culture that facilitates the transfer of institutional knowledge within our organization and fosters innovation, teamwork, and a focus on execution.

Potential disruptions of clinical activities as a result of COVID-19 or similar pandemics including, but are not limited to:

- interruption of key clinical trial activities, such as clinical trial site data monitoring and efficacy, safety and translational data collection, processing and analyses, due to limitations on travel imposed or recommended by federal, state, or local governments, employers and others or interruption of clinical trial subject visits, which may impact the collection and integrity of subject data and preclinical study endpoints;
- delays or difficulties in initiating or expanding clinical trials, including delays or difficulties with clinical site initiation and recruiting clinical site investigators and clinical site staff;
- delays or difficulties in enrolling and retaining patients in our clinical trials;
- increased rates of patients withdrawing from our clinical trials following enrollment as a result of contracting COVID-19 or other health conditions or being forced to quarantine;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns, or stoppages and disruptions in materials and reagents;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies;
- changes in regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- interruption of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;

- refusal of the FDA or comparable regulatory authorities to accept data from clinical trials in affected geographies; and
- additional delays, difficulties or interruptions as a result of current or future shutdowns due to the COVID-19 pandemic in countries where we or our third-party service providers operate.

The COVID-19 global pandemic continues to rapidly evolve. Although many countries, including certain countries in Europe and the United States, have re-opened, rises in new cases have caused certain countries to re-initiate restrictions. The extent to which the outbreak may affect our preclinical studies, clinical trials, business, financial condition, and results of operations will depend on future developments, which are highly uncertain and cannot be predicted at this time, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions, and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures, or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease. Additionally, we are unable to predict if a different pandemic could have similar or different impacts on our business, financial condition, or share price. Future developments in these and other areas present material uncertainty and risk with respect to our clinical trials, business, financial condition, and results of operations.

Disruptions at the FDA, the SEC 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, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA 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. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the Securities and Exchange Commission, or the SEC, and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/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 SEC, had to furlough critical employees and stop critical activities. If a prolonged government shutdown 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. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. On July 10, 2020, the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites. According to the guidance, the FDA intends to request such remote interactive evaluations in situations where an in-person inspection would not be prioritized, deemed mission-critical, or where direct inspection is otherwise limited by travel restrictions, but where the FDA determines that remote evaluation would still be appropriate.

FDA has since adjusted its inspection activities in response to the ongoing COVID-19 pandemic. On December 29, 2021, the agency implemented temporary changes to its inspectional activities to ensure the safety of its employees and regulated firms. On February 2, 2022, FDA announced that it would resume domestic surveillance inspections across all product areas on February 7, 2022. We cannot predict whether, and when, FDA will decide to pause or resume inspections due to the COVID-19 pandemic.

Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Our Dependence on Third Parties

If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates or we could lose certain rights to grant sublicenses.

We are a party to license agreements with Pfizer Inc., or Pfizer, Biosion USA, Inc., or Biosion, and the University of Chicago, pursuant to which we in-license patents and technology for certain of our product candidates, and we are also party to a collaboration agreement with Alloy Therapeutics, Inc., or Alloy, and Voxall Therapeutics, LLC, or Voxall, pursuant to which we may license patents and technology for future product candidates. Our current license agreements and our collaboration agreement impose, and any future license agreements or collaboration agreements we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement and/or other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. 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. 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, 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.

We have already entered into collaborations with third parties for the research, development and commercialization of certain of the product candidates we may develop. We may form or seek additional collaborations or strategic alliances or enter into additional licensing arrangements in the future. If any of these collaborations, strategic alliances or additional licensing arrangements are not successful, we may not be able to capitalize on the market potential of those product candidates.

We entered into a three-year collaboration with Alloy to finance and operate Voxall, a joint venture company formed in collaboration with Alloy to leverage our site-specific target catalog and Alloy's ATX-Gx platform and antibody discovery services. We additionally may seek other third-party collaborators for the research, development and commercialization of our current or future product candidates. The collaboration with Alloy and Voxall and any other collaboration agreements we enter into will likely limit our control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of any product candidates we may seek to develop with them. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration in which we have entered or may enter.

We may in the future form or seek strategic alliances, create joint ventures or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. Any of these relationships 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 face significant competition in seeking appropriate strategic partners and the negotiation process for these sorts of transactions is time-consuming, complex and expensive. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety, potency, purity and efficacy and obtain marketing approval. Additionally, our existing partners may decide to acquire or partner with other companies developing oncology therapeutics, which may have an adverse impact on our business prospects, financial condition and results of operations.

As a result, if we enter into additional collaboration agreements and strategic partnerships or license our product candidates, we may not be able to realize the benefit of those transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business prospects, financial condition and results of operations. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies the entry into the transaction in the first place. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations.

We rely on third parties to manufacture our product candidates. Any failure by a third party manufacturer to produce acceptable raw materials or product candidates for us or to obtain authorization from the FDA or comparable foreign regulatory authorities relating thereto may delay or impair our ability to initiate or complete our clinical trials, obtain regulatory licensure or approvals or commercialize approved products.

We rely on third-party contract manufacturers to manufacture our preclinical trial product supplies and clinical product supplies, and if we receive authorization to market our product candidates, for commercial supplies. We do not own or operate manufacturing facilities for producing such supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements and could take a significant amount of time to complete.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as cGMPs. In the event that any of our manufacturers fail to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third party manufacturers if we receive regulatory licensure for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMP or similar foreign requirements could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory licenses, for product candidates;
- loss of the cooperation of an existing or future collaborators;
- subjecting third party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- the inability to commercialize a product candidate, and an inability to meet commercial demands for such products.

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

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

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

The CMOs we retain may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our CMOs, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of license, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or the European Union Member States in coordination with the EMA pursuant to inspections that will be conducted after we submit our BLA to the FDA or our marketing authorization application to the EMA. We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacturing. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or comparable foreign regulatory bodies, they will not be able to secure and/or maintain marketing licensure for their manufacturing facilities. In addition, we do not have complete control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, European Union Member States and the EMA or other comparable regulatory authorities does not approve these facilities for the manufacture of our product candidates or if it withdraws any such licensure in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing licensure for or market our product candidates, if approved or licensed.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of licensure, license revocation, seizures or recalls of products or product candidate, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and harm our business and results of operations. Our product candidates and any products that we may develop may compete with other product candidates and products for access to suitable manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

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

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

A portion of our manufacturing of our product candidates takes place in China, through third-party manufacturers. A significant disruption in the operation of those manufacturers could materially adversely affect our business, financial condition and results of operations.

We currently contract manufacturing operations to third parties, and large quantities of our product candidates are manufactured by these third parties outside the U.S., including in China. Any disruption in production or inability of our manufacturers to produce adequate quantities to meet our needs could impair our ability to operate our business on a day-to-day basis and to continue our development of our product candidates. Furthermore, since certain of these manufacturers are located 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 conditions in China. For example, a trade war could lead to tariffs on the chemical intermediates we use that are manufactured in China. Any of these matters could materially and adversely affect our business and results of operations. Any recall of the manufacturing lots or similar action regarding our product candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings.

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

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

Some of our suppliers may experience disruption to their respective supply chain due to the effects of the COVID-19 pandemic, which could delay, prevent or impair our development or commercialization efforts.

We obtain certain chemical or biological intermediates in the synthesis of our product candidates in countries affected by the COVID-19 pandemic. If we are unable to obtain these chemical or biological intermediates in sufficient quantity and in a timely manner, the development, testing and clinical trials of that product candidate may be delayed or infeasible, and regulatory licensure or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

If we are unable to obtain sufficient raw and intermediate materials on a timely basis or if we experience other manufacturing or supply difficulties, our business may be adversely affected.

The manufacture of certain of our product candidates requires the timely delivery of sufficient amounts of raw and intermediate materials. We work closely with our suppliers to ensure the continuity of supply but cannot guarantee these efforts will always be successful. Further, while efforts are made to diversify our sources of raw and intermediate materials, in certain instances we acquire raw and intermediate materials from a sole supplier. While we believe that alternative sources of supply exist where we rely on sole supplier relationships, there can be no assurance that we will be able to quickly establish additional or replacement sources for some materials. A reduction or interruption in supply, and an inability to develop alternative sources for such supply, could adversely affect our ability to manufacture our product candidates in a timely or cost-effective manner.

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

We will rely on third-party CROs, to conduct clinical trials for our biological product candidates. We currently do not plan to conduct any clinical trials independently. Agreements with these CROs might terminate for a variety of reasons, including for their failure to perform. Entry into alternative arrangements, if necessary, could significantly delay our product development activities.

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

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

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our product candidates, or if the scope of the patent protection obtained is not sufficiently broad, or if our patents are insufficient to protect our product candidates for an adequate amount of time, or if we are unable to obtain adequate protection for our proprietary know-how, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, proprietary know-how, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates and discovery programs. 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 current and any future product candidates. We seek to protect our proprietary position by, among other methods, licensing and filing patent applications in the United States and abroad related to our current and future product candidates and discovery programs. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We in-license and file patent applications directed to our product candidates in an effort to establish intellectual property positions directed to their compositions of matter as well as uses of these product candidates in the treatment of diseases. Our intellectual property includes patents and patent applications that we own, as well as patents and patent applications that we in-license. For example, our license agreements with Pfizer and Biosion grant us exclusive rights to certain patents and patent applications relating to our product candidates.

We or our licensors have not pursued or maintained, and may not pursue or maintain in the future, patent protection for our product candidates in every country or territory in which we may sell our products, if approved. In addition, we cannot be sure that any of our pending patent applications will issue or that, if issued, they have or will issue in a form that will be advantageous to us. The United States Patent and Trademark Office, or the USPTO, international patent offices or judicial bodies may deny, or significantly narrow claims made under our patent applications and our issued patents may be successfully challenged, may be designed around, or may otherwise be of insufficient scope to provide us with protection for our commercial products.

It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, patent prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the USPTO may be significantly narrowed by the time they issue, or claims may not issue at all. The claims of our issued patents or patent applications when issued may not cover our current or future product candidates, or even if such patents provide coverage, the coverage obtained may not provide any competitive advantage. The patent applications that we own, or in-license may fail to result in issued patents with claims that cover our current or any future product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our current or any future product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory licensure or approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

If the patent applications we own or have in-licensed with respect to our product candidates and discovery programs fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our current or any future product candidates, it could dissuade companies from collaborating with us to develop and commercialize product candidates and future drugs and threaten our ability to commercialize future drugs. Any such outcome could have a negative effect on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our intellectual property rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Furthermore, other parties may have developed or may develop technologies that may be related to, or competitive with, our technologies, and such parties may have filed, or may file, patent applications, or may have received, or may receive, patents, claiming inventions that may overlap or conflict with those claimed in our patent applications or issued patents, and that we may rely upon to establish exclusivity for our products in the market. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or drugs, in whole or in part, or which effectively prevent others from commercializing competitive technologies and drugs. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

We may be subject to a third-party submission of prior art to the USPTO, or other patent offices, in our pending patent applications. Such a submission may preclude the granting of any of our pending patent applications, or may result in patents granting with narrow claims, which could limit our ability to stop others from using or commercializing similar or identical technology and products. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patent rights may be challenged in the courts or patent offices in the United States and abroad. For example, we may become involved in opposition, derivation, reexamination, inter partes review, post-grant review, or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such proceeding, or in litigation, could reduce the scope of our patent claims, result in our patent rights being held invalid, in whole or in part, or unenforceable, or limit the duration of the patent protection of our technology and products, and allow third parties to commercialize our technology or products and compete directly with us without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. 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 our current or any future product candidates.

Moreover, patents have a limited lifespan. In the United States, a patent generally expires 20 years after the earliest filing date of a non-provisional patent application. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our current or any future product candidates, we may be open to competition from generic and/or biosimilar versions of such products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent rights may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

Even if our patent rights are unchallenged, our issued patents and our 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 owned patent rights by developing similar or alternative technologies or products in a non-infringing manner. For example, a third-party may develop a competitive product that provides benefits similar to one or more of our product candidates, but that has a different composition that falls outside the scope of our patent protection. If the protection provided by our patent rights with respect to our product candidates is not sufficiently broad to impede such competition, or if the breadth, strength or term (including any extensions or adjustments) of protection provided by our patent rights with respect to our product candidates or any future product candidates is successfully challenged, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates or any future product candidates under patent protection would be reduced.

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

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. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or patent applications will have to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our owned and licensed patents and/or applications and any patent rights we may own or license in the future. We rely on our service providers or our licensors to pay these fees. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, 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. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our products or technologies, we may not be able to stop a competitor from marketing products that are the same as, or similar to, our product candidates, which would have a material adverse effect on our business. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance 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. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

In addition, if we fail to apply for applicable patent term extensions or adjustments, we will have a more limited time during which we can enforce our granted patent rights. In addition, if we are responsible for patent prosecution and maintenance of patent rights in-licensed to us, any of the foregoing could expose us to liability to the applicable patent owner.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates such as PYX-201 and PYX-106, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we have or will obtain patent rights. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, provided that the patent is not enforceable for more than 14 years from the date of licensure, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their drug earlier than might otherwise be the case.

Intellectual property rights do not necessarily address all potential threats to our business.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds or formulations that are similar to our product candidates but that are not covered by the claims of any patents, should they issue, that we own or license;
- we or our licensors might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or license;
- we or our licensors might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability and the ability of others with whom we may collaborate to develop, manufacture, market and sell our current and any future product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and any future product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our current and any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Other companies and research institutions have filed, and may file in the future, patent applications related to antibodies or antibody-drug conjugates and their therapeutic use. Some of these patent applications have already been allowed or issued, and others may issue in the future. While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third-party patents or patent applications, or we may incorrectly conclude that a third-party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes our product candidate infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the therapeutic or product candidate that is the subject of the actual or threatened suit.

If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidate(s) and technology. Under any such license, we would most likely be required to pay various types of fees, milestones, royalties or other amounts. Moreover, we may not be able to obtain any required license on commercially reasonable terms or at all.

The licensing or acquisition of third-party intellectual property rights is a competitive area, and more established companies may also pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate(s), which could have a material adverse effect on our business, financial condition, results of operations and prospects. Furthermore, even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. We may be required to indemnify collaborators or contractors against such claims. A finding of infringement could prevent us from manufacturing and commercializing our current or any future product candidates or force us to cease some or all of our business operations, which could materially harm our business. Even if we are successful in defending against such claims, litigation can be expensive and time consuming and would divert management's attention from our core business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. If we breach our University of Chicago, Pfizer, or Biosion license agreements or any of the other agreements under which we acquired, or will acquire, intellectual property rights covering our product candidates, we could lose the ability to continue the development and commercialization of the related product candidates(s).

The licensing of intellectual property is of critical importance to our business and to our current and future product candidates, and we expect to enter into additional such agreements in the future.

In particular, the rights to the intellectual property covering PYX-201 are in-licensed from Pfizer and the rights to the intellectual property covering our product candidate PYX-106 are in-licensed from Biosion. We may acquire the rights to the intellectual property covering future product candidates from other third-party licensors.

If we fail to meet our obligations under any of our in-license agreements, including the Pfizer License Agreement (as amended and restated by the A&R License Agreement), or the Biosion License Agreement, then the licensor may terminate the license agreement. If one of our material in-license agreements is terminated, we will lose the right to continue to develop and commercialize the product candidate(s) covered by such in-license agreement. While we would expect to exercise all rights and remedies available to us, including seeking to cure any breach by us, and otherwise seek to preserve our rights under our in-license agreements, we may not be able to do so in a timely manner, at an acceptable cost or at all.

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

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors 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 owned or licensed patents at risk of being invalidated or interpreted narrowly and could put our owned or licensed patent applications at risk of not issuing. The initiation of a claim against a third party might also cause the third party to bring counter claims against us, such as claims asserting that our patent rights are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte reexaminations, inter partes review, or post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is or will be no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business.

We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license, and such a license may not be on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

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. There could also 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 an adverse effect on the price of our common stock.

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

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our current and any future product candidates.

The United States has recently enacted and implemented wide ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we own, have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we own or have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting and defending patents covering our current and any future product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we or our licensors have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims, or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

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

In addition to seeking patent and trademark protection for our product candidates, we may also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us.

Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Since we rely on third parties to help us discover, develop, manufacture or commercialize our current and any future product candidates, or if we collaborate with third parties for the development, manufacturing or commercialization of our current or any future product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third-party illegally or unlawfully obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. We have not yet selected trademarks for our product candidates and have not yet begun the process of applying to register trademarks for our current or any future product candidate. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with our current or any other product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

Risks Related to Our Common Stock

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

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

- results of preclinical studies, IND submissions, clinical trials, or the addition or termination of clinical trials or funding support by us, or existing or future collaborators or licensing partners;
- variations in the level of expense related to the ongoing development of the FACT Platform, our product candidates or future development programs;
- our execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our product candidates receive regulatory licensure, the terms of such licensure and market acceptance and demand for such product candidates;
- regulatory developments affecting our product candidates or those of our competitors; and
- changes in general market and economic conditions.

If our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Our stock price is volatile, and you could lose all or part of your investment.

Our stock price is highly volatile. As a result of this volatility, investors may not be able to sell their common stock at or above the price they purchased their common stock. The market price for our common stock may be influenced by many factors, including the other risks described in this section of the Annual Report on Form 10-K titled “Risk Factors” and the following:

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

- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us, our insiders or our other stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;
- the impact of any natural disasters or public health emergencies, such as the COVID-19 pandemic, and other calamities; and
- general economic, industry and market conditions.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has been often unrelated to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

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

We will need to raise additional capital in the future. To the extent we raise additional capital through the issuance of equity or convertible debt securities in the future, there will be dilution to our existing investors and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or equity securities. We may choose to raise additional capital through the issuance of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. No prediction can be made as to the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

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

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us, our business or our market. If no or few securities or industry analysts commence or maintain coverage of us, the trading price for our stock would be negatively impacted. If any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval and their interests may conflict with your interests as an owner of our common stock.

As of March 22, 2023, our executive officers and directors, together with holders of five percent or more of our outstanding common stock and their respective affiliates, beneficially own approximately 56.2% of our outstanding common stock. As a result, these stockholders, if acting together, have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with interests of our other stockholders. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Our common stock price could decline as a result of sales of a large number of shares of common stock or the perception that these sales could occur. These sales, or the possibility that these sales may occur, might also make it more difficult for us to sell equity securities in the future at a time and price that we deem appropriate.

Shares issued upon the exercise of stock options and warrants outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules, market stand-off agreements and/or lock-up agreements, as well as Rules 144 and 701 under the Securities Act.

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," as defined in the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenue of at least $1.235 billion or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeded $700 million as of the prior June 30th and (ii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

An emerging growth company may take advantage of specified reduced reporting requirements and other burdens that are otherwise applicable generally to public companies. These provisions include:

- being permitted to present only two years of audited financial statements and only two years of related management's discussion and analysis of financial condition and results of operations in this Annual Report on Form 10-K;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act;
- an exemption from compliance with any new requirements adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotations;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirement to hold a nonbinding advisory vote on executive compensation and to obtain stockholder approval of any golden parachute payments not previously approved.

We have elected to take advantage of certain reduced disclosure obligations and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our investors may be different from the information you might receive from other public reporting companies that are not emerging growth companies in which you hold equity interests. 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 applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected not to avail itself of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are also a "smaller reporting company," and will continue to be a smaller reporting company as long as (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. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation, and, similar to emerging growth companies, if we are a smaller reporting company with less than $100 million in annual revenue, we would not be required to obtain an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

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

Provisions in the amended and restated certificate of incorporation and our amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. In addition, 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. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a prohibition on actions by our stockholders by written consent;
- a requirement that special meetings of stockholders be called only by the chairman of our board of directors, our chief executive officer, or our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors;
- advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings;
- a requirement that directors may only be removed "for cause" and only with 66 2/3% voting stock of our stockholders;
- a requirement that only the board of directors may change the number of directors and fill vacancies on the board;
- division of our board of directors into three classes, serving staggered terms of three years each; and
- the authority of the board of directors to issue preferred stock with such terms as the board of directors may determine.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, as amended, 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. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices. Additionally, if we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

As a public company, and particularly after we are no longer an emerging growth company or a smaller reporting company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of Nasdaq and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Also, the Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or to incur substantial costs to maintain the same or similar coverage. These rules and regulations could also make it more difficult for us to attract and retain qualified members of our board of directors or our board committees or as executive officers. However, 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.

In addition, as a public company, we will incur additional costs and obligations in order to comply with SEC rules that implement Section 404 of the Sarbanes-Oxley Act. Under these rules, we are required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be an emerging growth company or a smaller reporting company, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, 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 our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively, and implement a continuous reporting and improvement process for internal control over financial reporting.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act. Our internal control over financial reporting will not prevent or detect all errors and all fraud.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and 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 controls and procedures, 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 facts 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 due to error or fraud may occur and not be detected.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, your ability to achieve a return on your investment will depend on appreciation of the value of our common stock.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of our common stock, which is not certain.

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

In the past, companies that have experienced volatility in the market price of their securities have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Regardless of the merits or the ultimate results of such litigation, securities litigation brought against us could result in substantial costs and divert our management's attention from other business concerns.

Our certificate of incorporation and bylaws designate the Court of Chancery of the State of Delaware 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 or employees.

Our amended and 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, another state court located within the State of Delaware, or the federal district court for the District of Delaware) shall be the sole and exclusive forum for the following types of proceedings: (1) any derivative action or proceeding brought on our behalf under Delaware law, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or bylaws, (4) any other action asserting a claim that is governed by the internal affairs doctrine or (5) any other action asserting an "internal corporate claim," as defined in Section 115 of the Delaware General Corporation Law. This provision would not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. Our amended and restated bylaws further provide that the federal district courts of the United States of America will be the exclusive forum to the fullest extent permitted by law, for resolving any complaint asserting a cause of action arising under the Securities Act or the Exchange Act. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation and amended and restated bylaws inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation and amended and restated bylaws described above.

Our ability to use net operating loss carryforwards and other tax attributes may be subject to limitations.

We have incurred substantial losses during our history, do not expect to become profitable in the near future and may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, subject to certain limitations (including the limitations described below) until such unused losses expire (if at all). As of December 31, 2022, our federal and state net operating losses, or NOL, in the United States were $10.1 million ($48.0 million before tax) and $3.0 million ($48.1 million before tax) respectively. The federal net operating loss carryforwards in the United States can be carried forward indefinitely but may be subject to annual usage limitations to the extent certain substantial changes our ownership occur. The state net operating loss carryforwards begin expiring in 2039. In addition, as of December 31, 2022, we had $2.5 million and $1.2 million of federal and state credit carryovers which begin to expire in 2039. These loss and credit carryforwards are subject to review and possible adjustment by the appropriate taxing authorities.

Our NOL and credit carryforwards are subject to review and possible adjustment by the IRS, and state tax authorities. Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, our federal NOL and credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership of our company. An "ownership change" pursuant to Section 382 of the Code generally occurs if one or more stockholders or groups of stockholders who own at least 5% of a company's stock increase their ownership by more than 50 percentage points over their lowest ownership percentage within a rolling three-year period. Our ability to utilize our NOL carryforwards and other tax attributes to offset future taxable income or tax liabilities may be limited as a result of ownership changes, including potential changes in connection with our IPO. Similar rules may apply under state tax laws. We have not yet determined the amount of the cumulative change in our ownership resulting from our IPO or other transactions, or any resulting limitations on our ability to utilize our NOL carryforwards and other tax attributes. In addition, we may experience ownership changes in the future due to subsequent shifts in our stock, some of which are outside of our control. If we earn taxable income, such limitations could result in increased future income tax liability to us, and our future cash flows could be adversely affected. We have recorded a full valuation allowance related to our NOL carryforwards and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our headquarters are located at 150 Cambridgepark Drive, Cambridge, MA 02140, where we lease approximately 8,955 rentable square feet of office and laboratory space under a lease that terminates on March 31, 2023. On September 29, 2021, we entered into a new lease agreement for approximately 31,659 square feet of an office and laboratory space at 321 Harrison Avenue, Boston, MA 02118. The lease will end on December 31, 2032, with an additional five-year option to extend the lease beyond December 31, 2032. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. As of the date of this Annual Report on Form 10-K, we were not a party to any material legal matters or claims and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results or financial condition.

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 trading on The Nasdaq Global Select Market under the symbol "PYXS".

Holders of Our Common Stock

Broadridge Corporate Issuer Solutions, Inc is our transfer agent and registrar for our common stock. As of the close of business on March 21, 2023, there were approximately 34 holders of record of shares of our common stock. These numbers were derived from our stockholder records and do not include beneficial owners of our common stock whose shares are held in "street" name with various dealers, clearing agencies, banks, brokers and other fiduciaries.

Dividends

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, for use in the operation of our business and do not anticipate paying any cash dividends on our common stock in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, our financial condition, our capital requirements, general business conditions, our future prospects and other factors that our board of directors may deem relevant. Our ability to pay cash dividends on our capital stock in the future may also be limited by the terms of any preferred securities we may issue or agreements governing any additional indebtedness we may incur.

Recent Sales of Unregistered Equity Securities

On March 16, 2023, or the Effective Date, we entered into the first amendment, or Amendment No. 1, to the Amended and Restated License Agreement, or the A&R License Agreement, dated October 14, 2022 between Pfizer Inc. or Pfizer, and the Company, which amends and restates certain terms of the A&R License Agreement. The A&R License Agreement amends and restates the previously executed license agreement dated December 8, 2020, effective as of March 12, 2021 between Pfizer and the Company, as amended to date. Pursuant to Amendment No. 1, we agreed to issue such number of shares of common stock equivalent to $5.0 million at a per share price equal to the closing price of our common stock on the business day when the closing price of our common stock on the Nasdaq Global Select Market is at or above $2.46 per share on any day from the Effective Date to a date that is within 180 days following October 6, 2022, or the A&R Effective Date. If, within 180 days following the A&R Effective Date, the share price for our common stock has not closed at or above $2.46 per share, then we agreed to issue such number of shares of common stock 180 days following the effective date, or the Issuance Date, equivalent to $5.0 million at a per share price equal to the closing price of our common stock on the business day prior to the Issuance Date, such that Pfizer's ownership interest in us shall not exceed nineteen and a half percent (19.5%) with any difference in value between the value of shares and $5.0 million being payable in cash.

On March 17, 2023, the closing price of our common stock on the Nasdaq Global Select Market was $2.76 per share. In accordance with the terms of Amendment No. 1, we issued 1,811,594 shares of our common stock to Pfizer, which is an amount equivalent to $5.0 million.

The shares of common stock issued pursuant to Amendment No. 1 are not registered under the Securities Act of 1933, as amended, or the Securities Act, in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act.

A copy of Amendment No. 1 is filed as Exhibit 10.24 to this Annual Report on Form 10-K. The foregoing description of the terms of Amendment No. 1 is qualified in its entirety by reference to the full text of Amendment No. 1.

Use of Proceeds from Initial Public Offering

Our initial public offering of common stock, or the IPO, was affected through a Registration Statement on Form S-1 (File No. 333-259627) that was declared effective by the SEC on October 7, 2021. We issued and sold in aggregate 10,500,000 shares of common stock, at a public offering price of $16.00 per share, for net proceeds of $152.3 million after deducting underwriting discounts, commissions and other offering costs of $15.7 million. BofA Securities, Inc., Jefferies LLC, Credit Suisse Securities (USA) LLC and William Blair & Company, L.L.C. and LifeSci Capital LLC acted as underwriters for the offering. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any of our affiliates. We have invested the net proceeds from the IPO in a money market fund. There has been no material change in our planned use of the net proceeds from the IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on October 8, 2021.

Securities authorized for issuance under equity incentive plans

The following table summarizes information about our equity incentive plans as of December 31, 2022. All outstanding awards relate to our common stock.

	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights[1] (b)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (c)
Equity compensation plans approved by security holders:			
2021 Equity Incentive Plan(1)(3)	5,117,872	$ 14.28	360,924
2019 Equity Incentive Plan(1)	2,745,402	$ 6.22	657,484
2021 Employee Stock Purchase Plan(4)	—	$ —	752,524
Restricted Common Stock pursuant to Separate Agreements(5)	151,286	$ 0.01	—
Equity compensation plans not approved by security holders:			
2022 Inducement Plan(1)(2)	721,242	$ 1.95	678,758
Total	**8,735,802**	**$ 9.43**	**2,449,690**

(1) Restricted Stock Units issued under the 2022 Inducement Plan, 2021 Equity Incentive Plan and 2019 Equity Incentive Plan, which do not have an exercise price, are excluded in the calculation of weighted-average exercise price.

(2) On July 1, 2022, the Company's board of directors approved the 2022 Equity Inducement Plan (the "2022 Plan"), which became effective on that date.

(3) The number of shares of common stock reserved for issuance under the 2021 Equity Incentive Plan will automatically increase annually on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021, and continuing until (and including) the fiscal year ending December 31, 2031 by the lesser of (i) 5% of the total number of shares of common stock outstanding on December 31st of the immediately preceding fiscal year and (ii) the number of shares as may be determined by our board of directors. As a result of the evergreen provision of the 2021 Plan, the Company added an additional 1,639,643 shares of common stock to the 2021 Plan as of January 1, 2022.

[4] On September 27, 2021, our board of directors and stockholders approved the 2021 Employee Stock Purchase Plan (the "2021 ESPP"), which became effective on the date immediately preceding the date on which our registration statement declared effective by the SEC. The 2021 ESPP initially reserved and authorized the issuance of up to a total of 424,595 shares of common stock to participating employees. The number of shares of common stock reserved for issuance under the ESPP will automatically increase annually on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2022, and continuing until (and including) the fiscal year ending December 31, 2031 by the lesser of (i) 1% of the total number of shares of common stock outstanding on December 31st of the immediately preceding fiscal year and (ii) the number of shares as may be determined by the board of directors. As a result of the evergreen provision of the 2021 ESPP, the Company added an additional 327,929 shares of common stock to the 2021 ESPP as of January 1, 2022.

[5] In 2019, we issued certain shares of restricted common stock to the employee co-founders and certain non-employee consultants. The shares of restricted common stock were issued pursuant to standalone restricted stock purchase agreements that are independent of the 2019 Plan. The shares of restricted common stock carried a purchase price equivalent of $0.01 per share.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. [Reserved].

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

You should read the following discussion and analysis of our financial condition and results of operations together with our audited consolidated financial statements and related notes thereto included elsewhere in this Annual Report on Form 10-K. Unless the context requires otherwise, references in this Annual Report on Form 10-K to "Pyxis Oncology," the "Company," "we," "us," and "our" refer to Pyxis Oncology, Inc. and its subsidiary.

We are a clinical-stage oncology company focused on developing a multi-modality portfolio of next-generation therapeutics to target difficult-to-treat cancers and improve quality of life for patients. We develop our product candidates with the objective to directly kill tumor cells, and to address the underlying pathologies created by cancer that enable its uncontrollable proliferation and immune evasion. We consider multi-modality as a variety of technologies, either stand-alone or in combination with others, to build effective cancer therapeutics for patients. Since our launch in 2019, we have developed a broad portfolio that includes novel antibody drug conjugate, or ADC, product candidates, immuno-oncology, or IO, product candidates, and monoclonal antibody, or mAb, preclinical discovery programs that we are developing as monotherapies and in combination with other therapies.

We have assembled a team with deep experience and proficiency in oncology research and development and plan to leverage our team's decades of experience in drug development to bring a variety of innovative therapies through the clinic. The collective experience across our team spans the spectrum of both pharmaceuticals and biotechnology.

Our portfolio consists of both ADC and IO product candidates. Our pipeline is balanced across programs with an emphasis on solid tumors. We in-licensed two ADC programs in March 2021 from Pfizer and one IO program from Biosion USA, Inc. in March 2022. We have additional preclinical mAb discovery programs derived from work at the laboratory of Dr. Thomas Gajewski. We retain full worldwide development and commercialization rights to all our product candidates, with the exception of PYX-106 in Greater China (mainland China, Hong Kong, Macau and Taiwan). In December 2022, we announced clearance of our investigation new drug applications, or IND, by the U.S. Food and Drug Administration, or FDA, for PYX-201 and PYX-106. We are enthusiastic to have transitioned to a clinical stage oncology company and look forward to leveraging our team's experience to execute our clinical trials with the aim of providing patients with safer and more efficacious treatment options.

The following is our current clinical development pipeline:

Program	Potential Indications	Discovery	Preclinical	Phase 1	Most Recent Milestone Achieved	Next Milestone
Antibody-drug Conjugates (ADC)						
Anti-EDB (PYX-201)	e.g., breast, head and neck, lung, and thyroid cancer				Dosing Initiated in 1Q23	Preliminary Data in Early 2024
Immuno-oncology (IO)						
Anti-Siglec-15 (PYX-106)	e.g., bladder, cholangio-carcinoma, colorectal, and kidney cancer				IND Clearance November 2022	First Subject Dosing Early 2Q23

PYX-201

Our lead ADC product candidate is PYX-201, an investigational, novel ADC consisting of an Immunoglobulin G1, or IgG1, anti-fibronectin Extradomain-B, or EDB, mAb site-specifically conjugated to an auristatin derivative via a cathepsin B-cleavable linker. Fibronectin is a glycoprotein found in the extracellular matrix. Fibronectin EDB regulates blood vessel morphogenesis, which provides the tumor access to nutrition and oxygen, a means to remove waste, and a pathway for metastasizing cells. EDB is overexpressed in many malignancies and is minimally expressed in most normal adult tissues, making it a potentially attractive means to target tumors while sparing healthy cells. In preclinical models of patient-derived xenograft, or PDX models, we observed tumor regression with single agent PYX-201. In addition, we observed that the treatment of preclinical syngeneic tumor models with PYX-201 resulted in enhanced T-cell infiltration into the TME, which is a hallmark of immunogenic cell death, or ICD, enabling synergistic activity in combination with a checkpoint inhibitor.

In December 2022, we announced clearance of our IND by the FDA for PYX-201 to initiate a Phase 1 clinical trial. During the first quarter of 2023, we announced dosing of the first subject in a Phase 1 trial of PYX-201, referred to as PYX-201-101. PYX-201-101 is an open-label, multicenter, dose-escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary efficacy of PYX-201 and identify recommended doses for further study. Patients with relapsed or refractory solid tumors, including non-small cell lung cancer, or NSCLC, hormone receptor positive breast cancer, ovarian cancer, thyroid cancer, pancreatic ductal adenocarcinoma, or PDAC, soft tissue sarcoma, or STS, hepatocellular carcinoma, or HCC, and kidney cancer are eligible to enroll. We anticipate reporting preliminary data from this Phase 1 clinical trial, including biomarker results and early signs of potential clinical activity, in early 2024.

PYX-106

Our lead IO product candidate is PYX-106, an investigational, fully human IgG1 isotype Siglec-15-targeting antibody designed to block Siglec-15 mediated suppression of T-cell proliferation and function. We plan to initially develop this asset for the treatment of solid tumors. We licensed worldwide rights, other than in Greater China (mainland China, Hong Kong, Macau and Taiwan), to PYX-106 from Biosion USA, Inc.

In December 2022, we announced clearance of our IND by the FDA for PYX-106 to initiate a Phase 1 clinical trial. During the first quarter of 2023, we began activating clinical trial sites and are currently screening patients for enrollment in the Phase 1 trial, referred to as PYX-106-101. PYX-106-101 is a first-in-human, Phase 1, multicenter, open-label dose escalation trial designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PYX-106 in patients with relapsed or refractory solid tumors. This Phase 1 dose escalation trial includes patients who have developed solid tumors and disease progression through standard therapy and patients for whom standard of care therapy that prolongs survival is unavailable or unsuitable. This trial will enroll patients with solid tumors including non-small cell lung cancer without driver mutations/translocations, breast cancer, endometrial cancer, thyroid cancer, kidney cancer, cholangiocarcinoma, bladder cancer, colorectal cancer, and head and neck squamous cell carcinoma, or HNSCC. We anticipate dosing patients in early second quarter of 2023. We anticipate reporting preliminary data from this Phase 1 clinical trial, including biomarker results and early signs of potential clinical activity, in late 2023.

Paused / terminated programs

In August 2022, we paused preclinical development of our anti-CD123 ADC, PYX-203, and anti-KLRG1 IO program, PYX-102. Although these programs remain important to our diversified portfolio of therapeutic candidates, pausing preclinical development efforts currently will allow us to increase the resources available to advance clinical development of PYX-201 and PYX-106. Further, we elected to pause the continued development of our anti-DLK1 ADC, PYX-202, based upon review and analysis of data from preclinical toxicity studies, and the anticipated clinical use and commercial prospects of PYX-202 if approved.

Discovery

In addition to the programs identified above, we are conducting research and development activities on various targets, leveraging our expertise in monoclonal antibodies, ADC conjugation, linker and payload selection, and understanding of immuno-oncology.

Since our inception, we have focused substantially all of our resources on conducting research and development activities, undertaking preclinical studies and clinical trials, organizing and staffing our company, business planning, raising capital, establishing and maintaining our intellectual property portfolio and identifying potential product candidates. We do not have any products approved for sale and have not generated any revenue from product sales or from any other sources. We have incurred significant operating losses since our inception. We reported net losses of $120.7 million and $76.0 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $212.4 million, net equity of $160.8 million, and cash and cash equivalents of $179.3 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We expect that our expenses and capital expenditures will increase substantially in connection with our ongoing activities. Our operations to date have been financed primarily through sales of convertible preferred stock and sale of equity securities and additional funding may be necessary to fund future clinical and preclinical activities.

Licensing and Collaboration Agreements

License Agreement with Pfizer Inc.

In December 2020, we entered into a license agreement, as amended, or the Pfizer License Agreement, with Pfizer Inc., or Pfizer, for worldwide development and commercialization rights to antibody drug conjugate product candidates directed to certain licensed targets, including PYX-201 and PYX-203, and products containing the ADC product candidates. Our rights are exclusive with respect to certain patents owned or controlled by Pfizer covering the licensed ADCs. Pfizer has also granted us a non-exclusive license to use Pfizer's ADC technology, or FACT, platform. The initial licensed targets include CD123 and extra domain B (EDB of fibronectin) and we have the option to expand the scope of its license to add additional licensed targets that have not been licensed to a third party or are not the subject of a Pfizer ADC development program. The Pfizer License Agreement became effective in March 2021 and we paid a combined $25.0 million for the license fee, consisting of an upfront cash payment of $5.0 million and issued 12,152,145 shares of Series B convertible preferred stock, which was converted into 1,911,015 shares of its common stock upon the initial public offering in October 2021, with a value of $20.0 million to Pfizer.

On October 6, 2022, we entered into an amended and restated license agreement, or the A&R License Agreement, with Pfizer, which amends and restates the Pfizer License Agreement. Pursuant to the A&R License Agreement, Pfizer granted us exclusive worldwide rights under Pfizer's FACT Platform technology to develop and commercialize ADC product candidates directed to certain licensed targets, including PYX-201 and PYX-203, and products containing the ADC product candidates. Additional ADC targets may be licensed for a nominal upfront payment and milestones. Further, we granted the right of first negotiation to Pfizer, on an exclusive basis, to purchase or to develop, manufacture and commercialize licensed ADCs and licensed products in one or more countries directed to EDB and CD123. In accordance with the terms of the A&R License Agreement, we agreed to pay $8.0 million to Pfizer (which was paid in January 2023) and issued 2,229,654 shares of our common stock. Additionally, we will issue such number of shares of common stock 180 days following the effective date, or the Issuance Date, equivalent to $5.0 million at a per share price equal to the closing price of our common stock on the business day prior to the Issuance Date, such that Pfizer's ownership interest in us shall not exceed nineteen and a half percent (19.5%) with any difference in value between the value of shares and $5.0 million being payable in cash.

We are also obligated to pay future contingent payments including development, regulatory and commercial milestones up to an aggregate of $665 million for the first four licensed ADCs. In addition, we are required to pay future contingent payments including development, regulatory and commercial milestones for ADCs to each additional licensed target beyond the first four licensed ADCs developed and commercialized via the FACT Platform. Additionally, if ADC licensed products are launched, we will pay Pfizer tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to mid-teens. Our royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. We are also obligated to pay Pfizer a percentage of certain sublicensing revenue ranging from twenty percent to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

License Agreement with the University of Chicago

In April 2020, we entered into a license agreement, or the University License Agreement, as well as a sponsored research agreement, with the University of Chicago, or the University. Under the terms of the license, we have the exclusive global right to develop and commercialize products that are covered by a valid claim of a licensed patent, incorporate or use the licensed know-how and materials or are known to assess, modulate or utilize the activity of certain specified biological targets.

In partial consideration for the license from the University, we issued to the University 48,919 shares of our common stock in 2020. Pursuant to the University License Agreement, we are obligated to pay potential development and commercial milestones of up to an aggregate of $7.7 million as well as running royalties on net sales of licensed products at varying rates ranging from less than one percent to the low single digits, subject to a minimum annual royalty of up to $3.0 million during certain years following the first commercial sale of a licensed product. We are also obligated to pay the University a percentage of certain sublicensing revenue ranging from low- to mid-teens based on the date of entering into the applicable sublicense.

Agreements with LegoChem Biosciences, Inc.

In December 2020, we entered into a license agreement, or the LegoChem License Agreement, and an opt-in, investment and additional consideration agreement, or the Opt-In Agreement, with LegoChem Biosciences, Inc., or LegoChem. Pursuant to the LegoChem License Agreement, we obtained worldwide (other than Korea) development and commercialization rights for LCB67, an ADC product candidate targeting DLK-1, and products containing the licensed compound. We paid $9.0 million in March 2021 to LegoChem, which was recorded as research and development expenses. Additionally, we may purchase certain initial quantities of licensed products from LegoChem for an estimated cost of $7.0 million and are also obligated to make future contingent payments including development, regulatory and commercial milestones as well as running royalties on net sales of licensed products at varying rates. In the third quarter of the calendar year 2022, we stopped the continued development of LCB67, based on review and analysis of data from the toxicity studies, and anticipated clinical use and commercial prospects of anti-DLK1 ADC.

In addition, as part of the Opt-in Agreement, LegoChem exercised an option to pay $8.0 million to us, in exchange for the right to receive a milestone payment, or the Extra Milestone Payment, of $9.6 million upon the earliest to occur of certain events, including the date of pricing or offer of the first public offering of its common stock or if we are the subject of a change in control transaction. Upon our IPO in October 2021, the extra milestone payment event triggered, and we paid $9.6 million in January 2022 to LegoChem. We have no further obligations under the Opt-In Agreement.

License Agreement with Biosion USA, Inc.

On March 28, 2022, we entered into a license agreement, or the Biosion License Agreement, with Biosion USA, Inc., or Biosion, pursuant to which we obtained an exclusive, worldwide (other than Greater China (mainland China, Hong Kong, Macau and Taiwan)) license for development, manufacture and commercialization rights for BSI-060T, a Siglec-15 targeting antibody, an IO product candidate (now referred to as PYX-106), and products containing the licensed compound. Under the terms of the Biosion License Agreement, each party granted to the other party a right of first offer to obtain an exclusive license in the other party's territory (Greater China for Biosion, and the rest of the world for Pyxis) to develop, manufacture and commercialize any bi-specific or multi-specific antibody any antibody-drug conjugate controlled by a party or its affiliate that inhibits, modulates or binds to Siglec-15 as an intended mechanism of action.

Pursuant to the Biosion License Agreement, we paid an upfront fee of $10.0 million and are also obligated to pay future contingent payments including development, regulatory and commercial milestones up to an aggregate of $217.5 million in case of normal approval and $222.5 million in case of accelerated approval. Additionally, if products are launched, we will pay Biosion tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to low teens. Our royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. We are also obligated to pay Biosion a percentage of certain sublicensing revenue ranging from mid-double to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

The Voxall Joint Venture with Alloy Therapeutics, Inc.

In March 2021, we entered into definitive transaction agreements with Alloy to finance and operate Voxall, a joint venture company formed in collaboration with Alloy to leverage Pyxis Oncology's site-specific target catalog and Alloy's ATX-Gx™platform and antibody discovery services. Voxall granted to both Pyxis Oncology and Alloy 50% of the voting membership units of Voxall in exchange for certain initial contributions.

In connection with the formation of Voxall, we entered into a three-year research collaboration with Alloy and Voxall to identify and select certain biological targets and create development candidate antibodies directed to those targets for further preclinical development, clinical development and commercialization. Under the collaboration agreement, the parties will conduct research under a mutually agreed research plan and budget for up to six research programs focused on mutually selected targets. Each of us and Alloy will provide research support for the collaboration through separate services agreements with Voxall, which services will be paid in the form of promissory notes issued by Voxall. Voxall will own all intellectual property arising from the collaboration, subject to certain exceptions for intellectual property relating to Alloy's ATX-Gx™ platform.

If a development candidate antibody under a research program meets certain mutually agreed selection criteria, we will have the exclusive option to obtain an exclusive license from Voxall to further develop and commercialize all the development candidate antibodies discovered under that research program. We may in-license one research program on certain pre-agreed financial terms. For all other in-licensed research programs, we will be obligated to pay fair market value as determined by a third-party valuation. Any research program that we do not in-license may be licensed by Voxall to a third party.

Components of Our Results of Operations

Operating Expenses

Research and Development Expenses

Research and development expenses consist of costs incurred for our research activities, including our discovery efforts, and the development of our programs. These expenses include:

- employee-related expenses, including salaries, payroll taxes, related benefits, severance and stock-based compensation expense for employees engaged in research and development activities;
- expenses incurred under agreements with clinical research organizations, or CROs, investigative sites that conduct our clinical trials, and other clinical trial-related vendors, and consultants;
- the costs of acquiring, developing, and manufacturing and testing clinical and preclinical materials, including costs incurred under agreements with contract manufacturing organizations, or CMOs;
- costs associated with preclinical activities and regulatory operations;
- license fees and milestone payments related to the acquisition and retention of certain licensed technology and intellectual property rights; and
- facilities, depreciation, market research, and other expenses, which include allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory supplies.

We expense research and development costs as incurred. Non-refundable advance payments that we make 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, or when it is no longer expected that the goods will be delivered, or the services rendered.

Our direct external research and development expenses consist of costs that include fees, reimbursed materials and other costs paid to consultants, contractors, CMOs and CROs in connection with our preclinical and clinical activities. We do not allocate employee costs, costs associated with our discovery efforts, laboratory supplies, and facilities expenses, including depreciation or other indirect costs, to specific product development programs because these costs are deployed across multiple programs and our platform and, as such, are not separately classified.

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 increase substantially in connection with our ongoing and planned preclinical and clinical development activities in the near term and in the future. The successful development of our product candidates is highly uncertain. At this time, we cannot accurately estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates and we may never succeed in obtaining regulatory approval for any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and personnel-related costs, including stock-based compensation, and severance for our personnel in executive, legal, finance and accounting, human resources and other administrative functions. General and administrative expenses also include professional fees for auditing, tax, and legal services, as well as insurance, board of director compensation, consulting, other administrative expenses and facility costs not otherwise included in research and development expenses.

Other Income (Expense)

Interest income consists primarily of interest earned on our invested cash and cash equivalent balances.

The change in fair value of derivative liability represents the increase in the fair value of the derivative liability recorded as a result of an opt-in, investment and additional consideration agreement with LegoChem.

Income Taxes

Since our inception, we have not recognized any income tax benefits for the net losses we have incurred or for the research and development tax credits earned in each year and interim period, as we believe, based upon the weight of available evidence, that it is more likely than not that all of our net operating losses, or NOLs, carryforwards and tax credit carryforwards will not be realized.

As of December 31, 2022, our federal and state net operating losses in the United States were $10.1 million ($48.0 million before tax) and $3.0 million ($48.1 million before tax) respectively. The federal net operating loss carryforwards in the United States can be carried forward indefinitely but may be subject to annual usage limitations to the extent certain substantial changes our ownership occur. The state net operating loss carryforwards begin expiring in 2039. In addition, as of December 31, 2022, we had $2.5 million and $1.2 million of federal and state credit carryovers which begin to expire in 2039. These loss and credit carryforwards are subject to review and possible adjustment by the appropriate taxing authorities.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Operating expenses:			
Research and development	$ 86,129	$ 51,054	$ 35,075
General and administrative	37,352	18,663	18,689
Total operating expenses:	123,481	69,717	53,764
Loss from operations	(123,481)	(69,717)	(53,764)
Other income (expense):			
Interest income	2,764	23	2,741
Service fee income from related party	—	181	(181)
Change in fair value of derivative liability	—	(6,231)	6,231
Total other income (expense)	2,764	(6,027)	8,791
Loss from equity method investment in joint venture	—	(231)	231
Net loss	**$ (120,717)**	**$ (75,975)**	**$ (44,742)**

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Research and development program expenses	$ 60,967	$ 40,363	$ 20,604
Personnel-related expenses including stock-based compensation	18,975	7,836	11,139
Other research and development expenses	6,187	2,855	3,332
Total research and development expenses	**$ 86,129**	**$ 51,054**	**$ 35,075**

Research and development expenses increased by $35.1 million, from $51.0 million for the year ended December 31, 2021, to $86.1 million for the year ended December 31, 2022. The program expenses increased by $20.6 million, which was primarily due to increases in contract manufacturing costs of $13.7 million, preclinical costs of $6.2 million primarily related to toxicity studies and preclinical work towards IND filings related to PYX-201 and PYX-106, and clinical trial costs of $3.0 million, offset by a decrease in licensing fees of $2.3 million. The increases in both personnel-related expenses by $8.6 million and stock-based compensation by $2.5 million were primarily due to an increase in headcount to support our research and development activities. Other research and development expenses increased by $3.3 million which was primarily related to the increase in laboratory supplies, allocated cost for laboratory space and higher professional and consulting costs.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,		
	2022	2021	Change
Personnel-related expenses including stock-based compensation	$ 18,732	$ 8,622	$ 10,110
Professional and consultant fees	13,061	7,606	5,455
Facilities, insurance and other costs	5,559	2,435	3,124
Total general and administrative expenses	**$ 37,352**	**$ 18,663**	**$ 18,689**

General and administrative expenses increased by $18.7 million, from $18.7 million for the year ended December 31, 2021, to $37.4 million for the year ended December 31, 2022. Personnel-related expenses including stock-based compensation increased by $10.1 million primarily due to higher personnel-related expenses of $3.3 million and higher stock-based compensation of $6.8 million, both of which were due to an increase in headcount. Professional and consultant fees increased by $5.4 million primarily due to an overall increase in legal, professional, and consulting fees to support our growth and operations. Facilities, insurance and other costs increased by $3.1 million mainly due to an increase in rent expense by $1.6 million and directors and officers insurance expense of $1.5 million.

Other Income (Expense)

Interest income for the years ended December 31, 2022 and 2021 was $2.8 million and $23 thousand, respectively, consisting of interest earned on invested cash and cash equivalent balances. The increase during the year ended December 31, 2022 was primarily due to higher interest rates on our deposits and money market funds.

Other expense consists of change in fair value of the derivative liability of $6.2 million for the year ended December 31, 2021 as a result of the Opt-In Agreement. Service fee income from related party consists of income from services provided to the Voxall joint venture of $0.2 million for the year ended December 31, 2021.

Liquidity and Capital Resources

We had cash and cash equivalents of $179.3 million as of December 31, 2022. For the years ended December 31, 2022 and 2021, we had net losses of $120.7 million and $76.0 million, respectively. As of December 31, 2022, we had an accumulated deficit of $212.4 million.

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the clinical trials for our product candidates in development. The timing and amount of our funding requirements will depend on many factors, including:

- the cost associated with Phase 1 clinical trials for PYX-201 and PYX-106;
- the manufacture of product candidates for PYX-201 and PYX-106;
- the timing and progress of our other preclinical and clinical development activities;
- the number and scope of other preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we have entered or may in the future enter into in-licensing, collaborations and research and development agreements;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing licensure;
- our ability to maintain our current licenses and research and development programs and to establish new collaboration arrangements;
- the costs involved in prosecuting, maintaining and enforcing patent and other intellectual property rights;
- the costs of maintaining, expanding and protecting our intellectual property portfolio;
- the cost and timing of regulatory licenses;
- our efforts to hire additional clinical, regulatory, scientific, operational, financial and management personnel; and
- incur insurance, legal and other regulatory compliance expenses to operate as a public company.

Until such time, if ever, we can generate substantial product revenue, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions, engaging in acquisition, merger or collaboration transactions, selling or licensing our assets, making capital expenditures, redeeming our stock, making certain investments or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Shelf Registration Statement and "At-the-Market" Program

On November 1, 2022, we filed a registration statement on Form S-3 with the SEC for the issuance of common stock, preferred stock, warrants, debt securities, rights and units up to an aggregate of $250.0 million. On November 14, 2022, the registration statement was declared effective by the SEC. The registration statement includes an at-the-market, or ATM, offering program for the sale of up to $125.0 million of shares of our common stock. We have not sold any shares of our common stock or received any proceeds from the ATM offering program as of the date of this report.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2022 and 2021 (in thousands):

	Year Ended December 31,	
	2022	2021
Net cash used in operating activities	$ (89,335)	$ (35,326)
Net cash used in investing activities	(6,399)	(590)
Net cash provided by financing activities	183	304,044
Net (decrease) increase in cash, cash equivalents and restricted cash	**$ (95,551)**	**$ 268,128**

Operating Activities

Net cash used in operating activities was $89.3 million for the year ended December 31, 2022 and consisted of our net loss of $120.7 million, partially offset by non-cash charges of $26.9 million and a net change in our operating assets and liabilities of $4.6 million. The non-cash charges primarily consisted of $9.3 million related to license fees for Pfizer FACT Platform settled and payable in common stock, stock-based compensation expenses of $15.8 million, and amortization of operating lease right-of-use assets of $1.1 million. The change in our operating assets and liabilities was primarily due an increase in operating lease liabilities of $4.3 million as a result of the operating lease for our new headquarters and an increase in prepaid expenses and other current assets of $3.4 million primarily related to prepayment of clinical and contract manufacturing costs and directors and officers insurance policy costs, offset by an increase in accrued expenses and other current liabilities of $12.0 million and a decrease in accounts payable of $8.3 million related to timing of routine vendor payments.

Net cash used in operating activities was $35.3 million for the year ended December 31, 2021 and consisted of our net loss of $76.0 million, partially offset by non-cash charges of $34.0 million and a net change in our operating assets and liabilities of $6.7 million. The non-cash charges of $34.0 million was primarily due to the $20.0 million of research and development license fees for Pfizer settled in Series B convertible preferred stock, the $6.2 million change in the fair value of derivative liability and $6.4 million in stock-based compensation. The change in our operating assets and liabilities was primarily due to an increase of $9.7 million in accounts payable and accrued expenses and other current liabilities, partially offset by changes in prepaid and other current assets and lease payments of $3.0 million, all of which were due to growth in our business, the advancement of our research programs, and the timing of vendor invoicing and payments.

Investing Activities

Net cash used in investing activities for the years ended December 31, 2022 and 2021 was $6.4 million and $0.6 million, respectively, primarily due to purchases of property and equipment. The purchases of property and equipment consists of laboratory equipment, furniture and fixtures and leasehold improvements for our new headquarters. During the year ended December 31, 2021, we also made an investment in our joint venture, Voxall Therapeutics, LLC, for $0.1 million.

Financing Activities

Net cash provided by financing activities was $0.2 million for the year ended December 31, 2022 and consisted primarily of net proceeds from stock option exercises.

Net cash provided by financing activities was $304.0 million for the year ended December 31, 2021 and consisted primarily of net proceeds of $152.3 million from the sale of our common stock in the initial public offering and net proceeds of $151.6 million from the sale of our Series B convertible preferred stock.

Based on our existing cash balance as of December 31, 2022 of $179.3 million and our research and development and business development plans, we expect to be able to fund our operating expenses and capital expenditure requirements into the first half of the calendar year 2025. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. In addition, we could utilize our available capital resources sooner than we expect.

Contractual Obligations and Commitments

The following summarizes our contractual obligations as of December 31, 2022, and the effects that such obligations are expected to have on our liquidity and cash flows in future periods.

We lease an office and laboratory space in Boston, Massachusetts. The lease payments on from December 22, 2022 and will continue through December 31, 2032, and have scheduled rent increases each year of 3%. The remaining contractual fixed lease payments over the term of the lease net of tenant improvement allowance aggregate to $31.8 million.

In addition, we entered into licensing and related agreements in the normal course of business. In accordance with the agreements, we are obligated to pay, among other items, future contingent payments, royalties, and sublicensing revenue in the future, as applicable. We have not included potential future payments due under these licensing and collaboration agreements in contractual obligations because the payment obligations under the agreements are contingent upon future events.

Pursuant to the A&R License Agreement with Pfizer, we are obligated to pay future contingent payments including development, regulatory and commercial milestones up to an aggregate of $665 million for the first four licensed ADCs. In addition, we are required to pay future contingent payments including development, regulatory and commercial milestones for ADCs to each additional licensed target beyond the first four licensed ADCs developed and commercialized via the FACT Platform. Additionally, if products are launched, we will pay Pfizer tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to mid-teens. Our royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. We are also obligated to pay Pfizer a percentage of certain sublicensing revenue ranging from twenty percent to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

Additionally, pursuant to the A&R License Agreement with Pfizer, we agreed to issue such number of shares of common stock in April 2023, equivalent to $5.0 million at a per share price equal to the closing price of our common stock on the business day prior to the date of issuance, such that Pfizer's ownership interest in us shall not exceed nineteen and a half percent (19.5%) with any difference in value between the value of shares and $5.0 million being payable in cash.

Pursuant to the LegoChem License Agreement, we are obligated to pay up to an aggregate of $284.5 million to LegoChem if certain development, regulatory and sales milestones are achieved, as well as tiered royalties on net sales of licensed products ranging from mid-single digit to high single digit royalty rates. As part of our pipeline reprioritization, we have elected to stop the continued development of the PYX-202, which was licensed from LegoChem.

Pursuant to the University License Agreement with the University of Chicago, or the University, we are obligated to pay potential development and commercial milestones of up to an aggregate of $7.7 million as well as running royalties on net sales of licensed products at varying rates ranging from less than one percent to the low single digits, subject to a minimum annual royalty ranging up to $3.0 million during certain years following the first commercial sale of a licensed product. We are also obligated to pay the University a percentage of certain sublicensing revenue ranging from low- to mid-teens based on the date of entering into the applicable sublicense.

Pursuant to the Biosion License Agreement, we are obligated to pay future contingent payments including development, regulatory and commercial milestones up to an aggregate of $217.5 million in case of normal approval and $222.5 million in case of accelerated approval. Additionally, if products are launched, we will pay Biosion tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to low teens. Our royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. We are also obligated to pay Biosion a percentage of certain sublicensing revenue ranging from mid-double to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

We also enter into contracts in the normal course of business with CMOs, CROs, and other third parties for preclinical work and clinical development related work. These contracts do not contain minimum purchase commitments and are cancelable by us upon prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation. These payments are not included in the contractual obligations above as the amount and timing of such payments are not known.

Off-Balance Sheet Arrangements

We did not have during the years presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission.

Critical Accounting Policies and Significant Judgments and Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events, and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are the critical accounting policies used in the preparation of our consolidated financial statements that require significant estimates and judgments.

Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves 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 actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. At each period end, we corroborate the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include those related to fees paid to:

- CROs in connection with performing research and development services on our behalf;
- CMOs in connection with manufacturing of drug substance and drug products to be used in clinical trials on our behalf;
- other providers in connection with clinical trials;
- vendors in connection with non-clinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We record the expense and accrual related to contract research and manufacturing based on our estimates of the services received and efforts expended considering a number of factors, including our knowledge of the progress towards completion of the research, development and manufacturing activities; invoicing to date under contracts; communication from the CROs, CMOs and other companies of any actual costs incurred during the period that have not yet been invoiced; and the costs included in the contracts and purchase orders. In accruing service fees, we estimate the 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 the estimate, we adjust the accrual or the amount of prepaid expense accordingly. There have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We maintain equity incentive plans as a long-term incentive for employees, consultants, and directors. We account for all stock-based awards granted to employees and non-employees based on their fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. The grant date fair value of the stock-based awards with graded vesting is recognized on a straight-line basis over the requisite service period. We recognize forfeitures related to stock-based compensation awards as they occur and reverse any previously recognized compensation cost associated with forfeited awards in the period the forfeiture occurs.

We value stock options with service conditions using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model uses various inputs and we make certain assumptions regarding the fair value of our common stock, the expected volatility of our common stock, the expected term of stock options, the risk-free interest rate for a period that approximates the expected term of our common stock options and our expected dividend yield. The following summarizes the inputs used and assumptions made:

Expected Volatility—We lack company-specific historical and implied volatility information. Therefore, we estimate the expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expect to continue to do so until we have adequate historical data regarding the volatility of our traded stock price.

Expected Term—We use the simplified method described in the SEC's Staff Accounting Bulletin No. 107, *Share-Based Payment* ("SAB 107"), to determine the expected life of the option grants.

Risk-Free Interest Rate—The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award.

Dividends—Expected dividend yield is zero because we have not paid cash dividends on shares of common stock and do not expect to pay any cash dividends in the foreseeable future.

Determination of Fair Value of Common Stock

Prior to the our IPO on October 8, 2021, the estimated fair value of our common stock has been determined by our board of directors as of the date of grant of each option award, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Our common stock valuations were prepared using either an option pricing method, or OPM, or a hybrid method, both of which used market approaches to estimate our enterprise value.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Following our IPO, we determined the fair value of our common stock based on the quoted market price of our common stock on the Nasdaq Global Select Market.

Recent Accounting Pronouncements

For information with respect to recently issued accounting standards and the impact of these standards on our consolidated financial statements, refer to "Note 2 — Summary of Significant Accounting Policies" in our consolidated financial statements in Part II, Item 8 of this Annual Report on Form 10-K.

Jumpstart Our Business Startups Act

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an "emerging growth company" to take advantage of an extended transition period to comply with new or revised accounting standards. We are an "emerging growth company," as defined in the JOBS Act. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

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 rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation, and, similar to emerging growth companies, if we are a smaller reporting company with less than $100 million in annual revenue, we would not be required to obtain an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Under SEC rules and regulations, because we are considered to be a "smaller reporting company", we are not required to provide the information required by this item in this report.

Item 8. Financial Statements and Supplementary Data.

The financial information required by Item 8 is located beginning on page F-1 of this report.

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 Securities Exchange Act of 1934, as amended, or the Exchange Act), that are designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Disclosure controls and procedures include, without limitation, controls and procedures designed to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2022, the end of the period covered by this Annual Report. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2022, at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting.

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with United States GAAP. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately, and fairly reflect our transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with United States GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in its 2013 Internal Control - Integrated Framework. Based on our assessment, our management has concluded that, as of December 31, 2022, our internal control over financial reporting is effective based on those criteria.

Changes in Internal Control Over Financial Reporting.

There was no change 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 fiscal quarter ended December 31, 2022, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitation on the Effectiveness of Internal Control.

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures, or our internal controls, will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within our Company have been detected.

Attestation Report of the Registered Public Accounting Firm.

This Annual Report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting due to an exemption established by the JOBS Act for "emerging growth companies."

Item 9B. Other Information.

On March 16, 2023, or the Effective Date, we entered into the first amendment, or Amendment No. 1, to the Amended and Restated License Agreement, or the A&R License Agreement, dated October 14, 2022 between Pfizer Inc. or Pfizer, and the Company, which amends and restates certain terms of the A&R License Agreement. The A&R License Agreement amends and restates the previously executed license agreement dated December 8, 2020, effective as of March 12, 2021 between Pfizer and the Company, as amended to date. Pursuant to Amendment No. 1, we agreed to issue such number of shares of common stock equivalent to $5.0 million at a per share price equal to the closing price of our common stock on the business day when the closing price of our common stock on the Nasdaq Global Select Market is at or above $2.46 per share on any day from the Effective Date to a date that is within 180 days following October 6, 2022, or the A&R Effective Date. If, within 180 days following the A&R Effective Date, the share price for our common stock has not closed at or above $2.46 per share, then we agreed to issue such number of shares of common stock 180 days following the effective date, or the Issuance Date, equivalent to $5.0 million at a per share price equal to the closing price of our common stock on the business day prior to the Issuance Date, such that Pfizer's ownership interest in us shall not exceed nineteen and a half percent (19.5%) with any difference in value between the value of shares and $5.0 million being payable in cash.

On March 17, 2023, the closing price of our common stock on the Nasdaq Global Select Market was $2.76 per share. In accordance with the terms of Amendment No. 1, we issued 1,811,594 shares of our common stock to Pfizer, which is an amount equivalent to $5.0 million.

The shares of common stock issued pursuant to Amendment No. 1 are not registered under the Securities Act of 1933, as amended, or the Securities Act, in reliance on the exemption from registration provided by Section 4(a)(2) of the Securities Act.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item will be included in our definitive proxy statement to be filed with the SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item will be included in our definitive proxy statement to be filed with the SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item will be included in our definitive proxy statement to be filed with the SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item will be included in our definitive proxy statement to be filed with the SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item will be included in our definitive proxy statement to be filed with the SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) For a list of the financial statements included herein and report of independent registered public accounting firm (PCAOB ID: 42), see *Index to the Consolidated Financial Statements* on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(3) Exhibits:

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation of Pyxis Oncology, Inc.	10-Q	001-40881	3.1	November 15, 2021	
3.2	Amended and Restated Bylaws of Pyxis Oncology, Inc.	10-Q	001-40881	3.1	November 15, 2021	
4.1	Description of registrant's securities	10-K	001-40881	4.1	March 22, 2023	
10.1	Amended and Restated Investor Rights Agreement, dated March 5, 2021	S-1/A	333-259627	10.1	October 1, 2021	
10.2+	Form of Indemnification Agreement	S-1/A	333-259627	10.2	October 4, 2021	
10.3+	Employment Agreement between Pyxis Oncology, Inc. and Lara Sullivan, M.D.	S-1/A	333-259627	10.3	October 4, 2021	
10.4+	Pyxis Oncology, Inc. 2019 Equity Incentive Plan	S-8	333-260441	4.3	October 22, 2021	
10.5+	Pyxis Oncology, Inc. 2021 Equity Incentive Plan	S-8	333-260441	4.4	October 22, 2021	
10.6+	Pyxis Oncology, Inc. Employee Stock Purchase Plan	S-8	333-260441	4.5	October 22, 2021	
10.7†	License Agreement by and between Pyxis Oncology, Inc. and Pfizer Inc., dated December 8, 2020	S-1	333-259627	10.7	September 17, 2021	
10.8†	Amendment No. 1 to License Agreement by and between Pyxis Oncology, Inc. and Pfizer Inc., dated March 22, 2021	S-1	333-259627	10.8	September 17, 2021	
10.9†	Exclusive License Agreement between the University of Chicago and Pyxis Oncology for Cancer Immunotherapy Technology, dated April 16, 2020	S-1	333-259627	10.9	September 17, 2021	
10.10†	License Agreement between Pyxis Oncology, Inc. and LegoChem Biosciences Inc., dated December 1, 2020	S-1	333-259627	10.10	September 17, 2021	
10.11†	First Amendment to License Agreement between Pyxis Oncology, Inc. and LegoChem Biosciences Inc., dated February 25, 2021	S-1	333-259627	10.11	September 17, 2021	
10.12†	Opt-In, Investment and Additional Consideration Agreement between Pyxis Oncology, Inc. and LegoChem Biosciences, Inc., dated December 1, 2020	S-1	333-259627	10.12	September 17, 2021	
10.13	Amendment to Opt-In, Investment and Additional Consideration Agreement between Pyxis Oncology, Inc. and LegoChem Biosciences, Inc., dated August 2, 2021	S-1/A	333-259627	10.13	October 1, 2021	
10.14†	Collaboration Agreement by and among Pyxis Oncology, Inc., Alloy Therapeutics, Inc. and Voxall Therapeutics, LLC., dated March 30, 2021	S-1/A	333-259627	10.14	October 1, 2021	
10.15	Lease by and between B9 LS Harrison & Washington LLC and Pyxis Oncology, Inc., dated September 29, 2021.	S-1/A	333-259627	10.15	October 1, 2021	
10.16+	Employment Agreement between Pyxis Oncology, Inc. and Pamela Connealy.	S-1/A	333-259627	10.16	October 4, 2021	
10.17+	Employment Agreement between Pyxis Oncology, Inc. and Jay Feingold, M.D.	S-1/A	333-259627	10.17	October 4, 2021	
10.18†	License Agreement, dated March 28, 2022 between the registrant and Biosion USA, Inc.	10-Q	001-40881	10.1	May 13, 2022	
10.19†	Amended and Restated License Agreement by and between Pyxis Oncology, Inc. and Pfizer Inc., dated October 6, 2022	10-Q	001-40881	10.1	November 1, 2022	
10.20†	Letter Agreement by and between Pyxis Oncology, Inc. and Pfizer Inc., dated October 14, 2022	10-Q	001-40881	10.2	November 1, 2022	

10.21+	Amended Employment Agreement between Pyxis Oncology, Inc. and Lara Sullivan, M.D.	X
10.22+	Amended Employment Agreement between Pyxis Oncology, Inc. and Pamela Connealy	X
10.23+	Amended Employment Agreement between Pyxis Oncology, Inc. and Jitu Wadhane	X
10.24	Amendment No. 1 dated March 16, 2023 to Amended and Restated License Agreement by and between Pyxis Oncology, Inc. and Pfizer Inc., dated October 14, 2022	X
10.25†	Amendment No. 1 to License Agreement, dated March 28, 2022 between the registrant and Biosion USA, Inc.	X
10.26†	Amendment No. 2 to License Agreement, dated March 28, 2022 between the registrant and Biosion USA, Inc.	X
10.27†	Amendment No. 3 to License Agreement, dated March 28, 2022 between the registrant and Biosion USA, Inc.	X
21.1	List of Subsidiaries	X
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm.	X
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K)	X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

* The certifications furnished in Exhibits 32.1 and 32.2 hereto are deemed to accompany this Annual Report on Form 10-K and are not deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act, irrespective of any general incorporation language contained in such filing.

+ Indicates management contract or compensatory plan.

† Certain confidential information contained in this exhibit, marked by [***], has been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

Pyxis Oncology, Inc.

Date: March 22, 2023

By: /s/ Lara Sullivan
Lara Sullivan, M.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Lara Sullivan, M.D. and Pamela Connealy and each of them, as such person's true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for such person and in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or such person's substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Lara Sullivan **Lara Sullivan, M.D.**	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 22, 2023
/s/ Pamela Connealy **Pamela Connealy**	Chief Financial Officer and Chief Operating Officer *(Principal Financial Officer)*	March 22, 2023
/s/ Jitendra Wadhane **Jitendra Wadhane**	Chief Accounting Officer *(Principal Accounting Officer)*	March 22, 2023
/s/ John Flavin **John Flavin**	Chairman of the Board of Directors	March 22, 2023
/s/ Thomas Civik **Thomas Civik**	Director	March 22, 2023
/s/ Darren Cline **Darren Cline**	Director	March 22, 2023
/s/ Freda Lewis-Hall, M.D. **Freda Lewis-Hall, M.D.**	Director	March 22, 2023
/s/ Rachel Humphrey, M.D. **Rachel Humphrey, M.D.**	Director	March 22, 2023

PYXIS ONCOLOGY, INC.
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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Pyxis Oncology, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Pyxis Oncology, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for the years then ended, 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, 2022 and 2021, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

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 2021.

Boston, Massachusetts
March 22, 2023

PYXIS ONCOLOGY, INC.

Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31,	
	2022	**2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 179,293	$ 274,735
Restricted cash	1,472	1,472
Prepaid expenses and other current assets	5,847	2,466
Total current assets	186,612	278,673
Property and equipment, net	11,165	1,007
Operating lease right-of-use assets	13,602	232
Other assets, noncurrent	—	109
Total assets	**$ 211,379**	**$ 280,021**
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 7,097	$ 11,951
Accrued expenses and other current liabilities	24,537	6,592
Operating lease liabilities, current portion	—	165
Total current liabilities	31,634	18,708
Operating lease liabilities, net of current portion	18,921	—
Total liabilities	50,555	18,708
Commitments and contingencies (Note 16)		
Stockholders' equity:		
Preferred stock, par value $0.001 per share, 10,000,000 shares authorized; zero shares issued and outstanding	—	—
Common stock, $0.001 par value per share; 190,000,000 shares; 35,110,016 and 32,792,867 shares issued as of December 31, 2022 and 2021, respectively, and 34,958,730 and 32,222,881 shares outstanding as of December 31, 2022 and 2021, respectively	34	32
Additional paid-in capital	373,225	352,999
Accumulated deficit	(212,435)	(91,718)
Total stockholders' equity	160,824	261,313
Total liabilities and stockholders' equity	**$ 211,379**	**$ 280,021**

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

PYXIS ONCOLOGY, INC.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2022	**2021**
Operating expenses:		
Research and development	$ 86,129	$ 51,054
General and administrative	37,352	18,663
Total operating expenses	123,481	69,717
Loss from operations	(123,481)	(69,717)
Other income (expense):		
Interest income	2,764	23
Service fee income from related party	—	181
Change in fair value of derivative liability	—	(6,231)
Total other income (expense)	2,764	(6,027)
Loss from equity method investment in joint venture	—	(231)
Net loss and comprehensive loss	**$ (120,717)**	**$ (75,975)**
Net loss per common share - basic and diluted	$ (3.65)	$ (8.95)
Weighted average shares of common stock outstanding - basic and diluted	33,033,081	8,493,273

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

PYXIS ONCOL OGY, INC.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2020	**22,724,925**	**$ 21,942**	**1,289,342**	**$ 1**	**$ 97**	**$ (15,743)**	**$ (15,645)**
Issuance of Series B convertible preferred stock to Pfizer Inc. (Refer to Note 3)	12,152,145	20,000	—	—	—	—	—
Issuance of Series B convertible preferred stock, net of issuance costs of $419	92,660,103	152,081	—	—	—	—	—
Issuance of shares of common stock through initial public offering, net of underwriting commission and issuance costs of $15,704	—	—	10,500,000	11	152,285	—	152,296
Conversion of Series A and Series B convertible preferred stock into shares of common stock	(127,537,173)	(194,023)	20,056,145	20	194,003	—	194,023
Stock options exercised	—	—	70,396	—	170	—	170
Vesting of restricted common stock	—	—	306,998	—	3	—	3
Stock-based compensation	—	—	—	—	6,441	—	6,441
Net loss	—	—	—	—	—	(75,975)	(75,975)
Balance at December 31, 2021	**—**	**$ —**	**32,222,881**	**$ 32**	**$ 352,999**	**$ (91,718)**	**$ 261,313**
Issuance of common stock to Pfizer Inc. (Refer to Note 3)	—	—	2,229,654	2	4,279	—	4,281
Stock options exercised	—	—	73,841	—	183	—	183
Vesting of restricted common stock	—	—	432,354	—	—	—	—
Stock-based compensation	—	—	—	—	15,764	—	15,764
Net loss	—	—	—	—	—	(120,717)	(120,717)
Balance at December 31, 2022	**—**	**$ —**	**34,958,730**	**$ 34**	**$ 373,225**	**$ (212,435)**	**$ 160,824**

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

PYXIS ONCOLOGY, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2022	**2021**
Operating activities		
Net loss	$ (120,717)	$ (75,975)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	709	647
Stock-based compensation	15,764	6,441
Non-cash research and development expenses	9,281	20,000
Non-cash lease expense	1,127	604
Non-cash loss from equity method investment in joint venture	—	50
Changes in fair value of derivative liability	—	6,231
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(3,381)	(2,444)
Accounts payable	(8,328)	4,643
Accrued expenses and other current liabilities	11,951	5,092
Operating lease liabilities	4,259	(615)
Net cash used in operating activities	**(89,335)**	**(35,326)**
Investing activities		
Purchase of property and equipment	(6,399)	(540)
Investment in joint venture	—	(50)
Net cash used in investing activities	**(6,399)**	**(590)**
Financing activities		
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	—	151,581
Proceeds from issuance of common stock in initial public offering, net of issuance costs	—	152,296
Proceeds from the exercise of stock options	183	167
Net cash provided by financing activities	**183**	**304,044**
Net (decrease) increase in cash, cash equivalents, and restricted cash	(95,551)	268,128
Cash, cash equivalents and restricted cash at beginning of year	276,316	8,188
Cash, cash equivalents and restricted cash at end of period	**$ 180,765**	**$ 276,316**
Supplemental cash flow information:		
Cash received for interest	$ 2,166	$ —
Cash paid for taxes	$ 17	$ —
Noncash investing and financing activities:		
Property and equipment in accounts payable and accrued expenses	$ 4,479	$ 11
Operating lease right-of-use asset obtained in exchange for operating lease liabilities	$ 14,497	$ —
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 179,293	$ 274,735
Restricted cash	1,472	1,581
Total cash, cash equivalents and restricted cash shown in the statement of cash flows	**$ 180,765**	**$ 276,316**

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

1. Description of Business

Nature of Business

Pyxis Oncology, Inc. (the "Company"), a Delaware corporation, was founded in June 2018 and launched its operations in July 2019. The Company is a clinical stage company focused on defeating difficult-to-treat cancers. The company is efficiently building next-generation therapeutics that hold the potential for mono and combination therapies. The Company's therapeutic candidates are designed to directly kill tumor cells and to address the underlying pathologies created by cancer that enable its uncontrollable proliferation and immune evasion. The Company's antibody-drug conjugates ("ADCs") and immuno-oncology ("IO") programs employ novel and emerging strategies to target a broad range of solid tumors resistant to current standards of care.

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of assessing performance and allocating resources.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The Company's fiscal year ends on December 31 and its first three quarters end on March 31, June 30 and September 30. The accompanying consolidated financial statements are prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). 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 ("ASU") of the Financial Accounting Standards Board ("FASB"). The consolidated financial statements include the Company and its wholly owned subsidiary. All intercompany balances and transactions have been eliminated upon consolidation.

The Company is an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"). 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 irrevocably elected not to avail itself of this extended transition period, and, as a result, the Company will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Liquidity

As of December 31, 2022, the Company had an accumulated deficit of $212.4 million. The Company has incurred losses and negative cash flows from operations since inception, including net losses of $120.7 million and $76.0 million for the years ended December 31, 2022 and 2021, respectively.

The Company has not generated any revenue to date and does not anticipate generating any revenues unless and until it successfully completes development and obtains regulatory approval for its current or any future product candidates. The Company expects that its operating losses and negative cash flows will continue for the foreseeable future as the Company continues to expand its research and development programs and develop its product candidates.

The Company currently expects that its existing cash and cash equivalents of $179.3 million as of December 31, 2022 will fund its operating expenses and capital requirements at least twelve months from the date these audited consolidated financial statements are issued. Additional funding may be necessary to fund future clinical and preclinical activities.

The Company plans to continue to fund its losses from operations and capital funding needs through public or private equity, convertible or debt financing or other sources. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations and future prospects.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, expense, and related disclosures. The Company regularly evaluates estimates and assumptions related to assets, liabilities, stock-based compensation, operating leases, assessment of the useful lives of property and equipment, valuation of deferred tax assets and liabilities, impairment of investment in joint venture, and research and development costs. The Company bases its estimates and assumptions on historical experience and on various other factors that it believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources.

Actual results could differ from those estimates and there may be changes to management's estimates in future periods.

Risks and Uncertainties

The Company is subject to risks common to early-stage companies in the biopharmaceutical industry including, but not limited to, uncertainties related to commercialization of products, regulatory approvals, dependence on key suppliers for active ingredients and third-party service providers such as contract research and manufacturing organizations, protection of intellectual property rights and the ability to make milestone, royalty or other payments due under any license, collaboration or supply agreements.

Concentration of Credit Risks

Financial instruments that subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company's cash and cash equivalents are held at an accredited financial institution and the Company has not experienced any losses in such accounts. The Company maintains its cash in bank deposit accounts, which at times may exceed federally insured limits. The Company's cash equivalents consist primarily of short-term money market funds held in accredited financial institutions. The Company believes it is not exposed to any significant risk in cash and cash equivalents.

Cash and Cash Equivalents

The Company considers all short term, highly liquid investments with original maturities of 90 days or less to be cash equivalents. Cash equivalents consist primarily of money market funds as of December 31, 2022 and 2021.

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 principle 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, the first two are considered observable and the last is considered unobservable:

***Level* 1**—Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;

***Level* 2**—Quoted prices in markets that are not considered to be active or financial instrument valuations for which all significant inputs are observable, either directly or indirectly; and

***Level* 3**—Prices or valuations that require inputs that are both significant to the fair value measurement and unobservable.

To the extent that 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.

Property and Equipment, net

Property and equipment are recorded at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the estimated useful lives of the related assets as follows:

	Estimated Useful Life (Years)
Laboratory equipment	3
Furniture and office equipment	3
Leasehold improvements	Shorter of remaining life of lease or useful life
Construction in process	N/A

Depreciation and amortization expense is included in research and development and general and administrative expenses. Major additions and upgrades are capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are expensed as incurred. Upon retirement or sale, the cost of assets disposed of, and the related accumulated depreciation and amortization are removed from the respective accounts and any resulting gain or loss is included in income (loss) from operations.

Impairment of Long-Lived Assets

The Company evaluates the long-lived assets, which consist of property and equipment and operating lease right-of-use assets, for impairment at least annually and whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. Management then determines whether the remaining useful life continues to be appropriate, or whether there has been an impairment of long-lived assets based primarily upon whether expected future undiscounted cash flows are sufficient to support the assets' recovery. Recoverability of these assets is measured by comparison of the carrying amount of the asset to the future undiscounted cash flows the asset is expected to generate. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. The Company recognized no impairment losses for the years ended December 31, 2022 and 2021.

Leases

Operating lease right-of-use ("ROU") assets represent the Company's right to use an underlying asset during the lease term, and operating lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and lease liabilities are initially recognized and measured based on the present value of the future fixed lease payments over the expected lease term at the commencement date calculated using the Company's incremental borrowing rate applicable to the lease asset, unless the implicit rate is readily determinable. The Company determines the lease term as the non-cancelable period of the lease and may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Operating lease ROU assets also include any initial direct costs incurred and any lease payments made on or before the lease commencement date, less lease incentives received. Operating lease ROU assets are subsequently measured throughout the lease term at the carrying amount of the lease liability, plus initial direct costs, plus (minus) any prepaid (accrued) lease payments, less the unamortized balance of lease incentives received. Leases with a term of 12 months or less are not recognized on the consolidated balance sheets. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. Variable lease costs such as common area costs and other operating costs are expensed as incurred. The Company accounts for lease and non-lease components as a single lease component for all its facilities leases. The Company had no finance leases as of December 31, 2022 and 2021.

Investment in Joint Venture

Investment in the Company's joint venture is accounted for using the equity method of accounting. The Company applies the equity method of accounting to investments when the Company has significant influence, but not controlling interest in the investee. Judgment regarding the level of influence over equity method investment includes considering key factors such as ownership interest, representation on the board of directors, participation in policy-making decisions and material intercompany transactions. Under the equity method, investments are initially recorded at cost and are adjusted for dividends, distributed and undistributed earnings and losses, and additional investments. In the event the Company's share of a joint venture's cumulative losses exceeds the Company's investment balance, the balance is reported at zero value until proportionate income exceeds the losses. The Company assesses investments for impairment whenever events or changes in circumstances indicate that the carrying value of an investment may not be recoverable.

Contingencies

The Company, from time to time, may be a party to various disputes and claims arising from normal business activities. The Company continually assesses disputes and claims including resulting litigation to determine if an unfavorable outcome would lead to a probable loss or reasonably possible loss which could be estimated. The Company accrues for all contingencies at the earliest date at which the Company deems it probable that a liability has been incurred and the amount of such liability can be reasonably estimated. If the estimate of a probable loss is a range and no amount within the range is more likely than another, the Company accrues the minimum of the range. In the cases where the Company believes that a reasonably possible loss exists, the Company discloses the facts and circumstances of the contingencies, including an estimable range, if possible.

Research and Development Expenses

The Company expenses research and development costs as incurred. The Company's research and development expenses consist primarily of license fees to acquire intellectual property which does not meet the definition of intangible assets and costs incurred in performing research and development activities, including personnel-related expenses such as salaries, stock-based compensation and benefits, facilities costs, depreciation as well as external costs from third parties who conduct research and development activities (including manufacturing) on behalf of the Company. The Company accrues expenses related to development activities performed by third parties based on an evaluation of services received and efforts expended pursuant to the terms of the contractual arrangements. Payments under some of these contracts depend on preclinical and/or clinical trial milestones. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of expenses. In accruing service fees, the Company estimates 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 the estimate, the Company adjusts the accrual or prepaid expense accordingly.

Stock-Based Compensation

The Company maintains an equity incentive plan as a long-term incentive for employees, consultants, and directors. The Company accounts for all stock-based awards granted to employees and non-employees based on their fair value on the date of the grant and recognizes compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. The grant date fair value of the stock-based awards with graded vesting is recognized on a straight-line basis over the requisite service period. The Company recognizes forfeitures related to stock-based compensation awards as they occur and reverses any previously recognized compensation cost associated with forfeited awards in the period the forfeiture occurs. The Company classifies stock-based compensation expense in the statement of operations in the same manner in which the award recipients' payroll costs are classified or in which the award recipients' service payments are classified.

The Company values its stock options with service conditions using the Black-Scholes option-pricing model. The Company uses certain assumptions to determine fair value of the stock options pursuant to the Black-Scholes option-pricing model, including the expected life of the award, volatility of the underlying shares, the risk-free interest rate, expected dividend yield and the fair value of the Company's common stock. Since the Company lacks sufficient historical option exercise data to provide a reasonable basis upon which to estimate the expected term, the Company uses the simplified method described in the SEC's Staff Accounting Bulletin No. 107, *Share-Based Payment* ("SAB 107"), to determine the expected life of the option grants. The Company lacks sufficient company-specific historical and implied volatility information. Therefore, the Company estimates the expected stock volatility based on the historical volatility of a publicly traded set of peer companies. The risk-free interest rate is based on the rates paid on securities issued by the U.S. Treasury with a term approximating the expected life of the equity award. As the Company has never paid and does not anticipate paying cash dividends on its common stock, the expected dividend yield is considered as zero.

Prior to the completion of the Company's initial public offering ("IPO") of common stock, the fair value of the Company's common stock which is one of the key inputs in Black-Scholes option-pricing model, was determined by the board of directors with input from management and based on certain assumptions including probability weighting of events, business and market conditions, volatility, time to liquidation, a risk-free interest rate and an assumption for a discount for lack of marketability. The Company used 409A valuations to determine the fair value of the shares of common stock. The 409A valuations were performed using methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants *Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. After completion of the IPO on October 8, 2021, the Company uses the fair value of its publicly traded common stock to determine grant date fair value.

Income Taxes

The Company accounts for income taxes in accordance with FASB ASC 740, *Income Taxes* (“ASC 740”), which requires the use of the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between amounts in the consolidated financial statements and the tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income tax (benefit) expense in the consolidated statements of operations and comprehensive loss in the period that includes the enactment date.

The Company recognizes deferred tax assets to the extent that it believes these assets are more likely than not to be realized. In making such a determination, the Company considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies and results of recent operations. If the Company determines that it would be able to realize its deferred tax assets in the future in excess of its net recorded amount, the Company would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs.

When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances.

Net Loss per Share

Basic net income (loss) per share attributable to common stockholders is computed by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the diluted weighted average number of common shares outstanding for the period, including potential dilutive common shares.

In periods in which the Company reports a net loss, all common stock equivalents are deemed anti-dilutive such that basic net loss per common share and diluted net loss per common share are equivalent. Potentially dilutive common stock has been excluded from the diluted net loss per common share computations in all periods presented because such securities have an anti-dilutive effect on net loss per common share due to the Company’s net loss. There are no reconciling items used to calculate the weighted-average number of total common stock outstanding for basic and diluted net loss per common share data.

Recently Issued Accounting Pronouncements

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (“ASU 2016-13”), which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss model that requires the use of forward-looking information to calculate credit loss estimates. It also eliminates the concept of other-than-temporary impairment and requires credit losses on available-for-sale debt securities to be recorded through an allowance for credit losses instead of as a reduction in the amortized cost basis of the securities. For "emerging growth companies", ASU 2016-13 is effective for fiscal years beginning after December 15, 2022, and interim periods within those fiscal years. The Company is currently evaluating the new standard and expects it to have no material impact on the Company's consolidated financial statements and related disclosures.

In August 2020, the FASB issued ASU 2020-06, *Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity’s Own Equity (Subtopic 815-40)* (“ASU 2020-06”). ASU 2020-06 revises the guidance on calculating earnings per share, requiring use of the if-converted method for all convertible instruments and rescinding an entity’s ability to rebut the presumption of share settlement for instruments that may be settled in cash or other assets. As an "emerging growth company", ASU 2020-06 will become effective for the Company for fiscal years beginning after December 15, 2023, and early adoption is permitted. The Company is currently evaluating the new standard and expects it to have no material impact on the Company's consolidated financial statements and related disclosures.

Recent authoritative guidance issued by the FASB (including technical corrections to the ASC), the American Institute of Certified Public Accountants, and the SEC did not, or are not expected to, have a material impact on the Company’s audited consolidated financial statements and related disclosures.

3. Licensing Agreements

The University of Chicago Agreement

In April 2020, the Company entered into a license agreement (the "University License Agreement"), as well as a sponsored research agreement, with the University of Chicago (the "University"). Under the terms of the license, the Company has the global right to develop and commercialize products that are covered by a valid claim of a licensed patent, incorporate or use the licensed know-how and materials or are known to assess, modulate or utilize the activity of certain specified biological targets. In partial consideration for the license from the University, the Company issued to the University 48,919 shares of its common stock in 2020.

Pursuant to the University License Agreement, the Company is obligated to pay potential development and commercial milestones of up to $7.7 million as well as running royalties on net sales of licensed products at varying rates ranging from less than a percent to the low single digits, subject to a minimum annual royalty of up to $3.0 million during certain years following the effective date. The Company is also obligated to pay the University a percentage of certain sublicensing revenue ranging from low- to mid-teens based on the date of entering into the applicable sublicense.

The Company assessed the milestone and royalty events under University License Agreement as of December 31, 2022 and 2021, and determined that no such amounts were required.

Pfizer Inc. Agreement

In December 2020, the Company entered into a license agreement (as amended, the "Pfizer License Agreement") with Pfizer Inc. ("Pfizer") for worldwide development and commercialization rights to ADC product candidates directed to certain licensed targets, including PYX-201 and PYX-203, and products containing the ADC product candidates. The Company's rights are exclusive with respect to certain patents owned or controlled by Pfizer covering the licensed ADCs. Pfizer has also granted the Company a non-exclusive license to use Pfizer's ADC technology ("FACT") platform. The initial licensed targets include CD123 and extra domain B (EDB of fibronectin) and the Company has the option to expand the scope of its license to add additional licensed targets that have not been licensed to a third party or are not the subject of a Pfizer ADC development program. The Pfizer License Agreement became effective in March 2021 and the Company paid a combined $25.0 million for the license fee, consisting of an upfront cash payment of $5.0 million and issued 12,152,145 shares of Series B convertible preferred stock, which was converted into 1,911,015 shares of its common stock upon the IPO in October 2021, with a value of $20.0 million to Pfizer.

On October 6, 2022, the Company entered into an amended and restated license agreement (the "A&R License Agreement") with Pfizer, which amends and restates the Pfizer License Agreement. Pursuant to the A&R License Agreement, Pfizer granted to the Company exclusive worldwide rights under Pfizer's FACT Platform technology to develop and commercialize ADC product candidates directed to certain licensed targets, including PYX-201 and PYX-203, and products containing the ADC product candidates. Additional ADC targets may be licensed for a nominal upfront payment and milestones. Further, the Company granted the right of first negotiation to Pfizer, on an exclusive basis, to purchase or to develop, manufacture and commercialize licensed ADCs and licensed products in one or more countries directed to EDB and CD123. In accordance with the terms of the A&R License Agreement, the Company agreed to pay $8.0 million to Pfizer (which was paid in January 2023) and issued 2,229,654 shares of its common stock. Additionally, the Company will issue such number of shares of common stock 180 days following the effective date (the "Issuance Date"), equivalent to $5.0 million at a per share price equal to the closing price of the Company's common stock on the business day prior to the Issuance Date, such that Pfizer's ownership interest in the Company shall not exceed nineteen and a half percent (19.5%) with any difference in value between the value of shares and $5.0 million being payable in cash. The Company recorded $17.3 million as research and development expenses for the A&R License Agreement during fourth quarter of the calendar year 2022.

The Company is also obligated to pay future contingent payments including development, regulatory and commercial milestones up to an aggregate of $665 million for the first four licensed ADCs. In addition, the Company is required to pay future contingent payments including development, regulatory and commercial milestones for ADCs to each additional licensed target beyond the first four licensed ADC targets developed and commercialized via the FACT Platform. Additionally, if ADC licensed products are launched, the Company will pay Pfizer tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to mid-teens. The Company's royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. The Company is also obligated to pay Pfizer a percentage of certain sublicensing revenue ranging from twenty percent to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

The Company assessed the milestone and royalty events under A&R License Agreement as of December 31, 2022 and 2021, and determined that no such amounts were required.

LegoChem Biosciences, Inc. Agreements

In December 2020, the Company entered into a license agreement (the "LegoChem License Agreement") and an opt-in, investment and additional consideration agreement (the "Opt-In Agreement") with LegoChem Biosciences, Inc. ("LegoChem"). Pursuant to the LegoChem License Agreement, the Company obtained worldwide (other than Korea) license for development and commercialization rights for LCB67, an ADC product candidate targeting DLK-1, and products containing the licensed compound. The Company paid $9.0 million in March 2021 to LegoChem, which was recorded as research and development expenses. Additionally, the Company may purchase certain initial quantities of licensed products from LegoChem for an estimated cost of $7.0 million.

The Company is obligated to make future contingent payments including development, regulatory and commercial milestones as well as running royalties on net sales of licensed products at varying rates. During the year ended December 31, 2022, the Company stopped the continued development of LCB67, based on review and analysis of data from the toxicity studies, and anticipated clinical use and commercial prospects of anti-DLK1 ADC. Due to stoppage of clinical development of LCB67, no amounts were due and payable related to the manufacturing of the initial quantities of licensed product as well as the milestones and royalties related to LCB67 ADC of December 31, 2022.

In addition, as part of the Opt-in Agreement, LegoChem had an option to pay $8.0 million to the Company, in exchange for the right to receive a milestone payment (the "Extra Milestone Payment") of $9.6 million upon the earliest to occur of certain events, including the date of pricing or offer of the first public offering of its common stock or if the Company is the subject of a change in control transaction. The Company determined that the Extra Milestone Payment met the definition and recognition condition of derivative under ASC 815, *"Derivatives and Hedging"* for which there was a binding contract and firm commitment in January 2021. An initial derivative liability was recognized for $3.4 million with an offset to research and development expenses in January 2021. The derivative liability was re-measured at each reporting date, and as a result, $6.2 million was recorded in "Other income (expense)" in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2021. The liability was realized upon the IPO of the Company and Extra Milestone Payment of $9.6 million was paid to LegoChem in January 2022. The Company has no further obligations under the Opt-In Agreement as of December 31, 2022.

License Agreement with Biosion USA, Inc.

On March 28, 2022, the Company entered into a license agreement (the "Biosion License Agreement") with Biosion USA, Inc. ("Biosion"), pursuant to which the Company obtained an exclusive, worldwide (other than Greater China (mainland China, Hong Kong, Macau and Taiwan)) license for development, manufacture and commercialization rights for BSI-060T, a Siglec-15 targeting antibody, an IO product candidate (now referred to as PYX-106), and products containing the licensed compound. Under the terms of the Biosion License Agreement, each party granted to the other party a right of first offer to obtain an exclusive license in the other party's territory (Greater China for Biosion, and the rest of the world for Pyxis) to develop, manufacture and commercialize any bi-specific or multi-specific antibody any antibody-drug conjugate controlled by a party or its affiliate that inhibits, modulates or binds to Siglec-15 as an intended mechanism of action.

Pursuant to the Biosion License Agreement, the Company paid an upfront license fee of $10.0 million, which was recorded as research and development expenses. The Company is also obligated to pay future contingent payments including development, regulatory and commercial milestones up to an aggregate of $217.5 million in case of normal approval and $222.5 million in case of accelerated approval. Additionally, if products are launched, the Company will pay Biosion tiered royalties on net sales of licensed products in varying royalty rates ranging from low single digits to low teens. The Company's royalty obligations apply on a licensed product-by-licensed product and country-by-country basis from first commercial sale until the latest to occur of: (1) 12 years from first commercial sale; (2) the expiration of all regulatory or data exclusivity; and (3) the expiration of the last valid claim of a licensed patent covering the licensed product in a country. The Company is also obligated to pay Biosion a percentage of certain sublicensing revenue ranging from mid-double to low-double digits based on the stage of development of the licensed product at the time of entering into the applicable sublicense.

The Company assessed the milestone and royalty events involving Biosion as of December 31, 2022 and determined that no such amounts were required.

4. Joint Venture

In March 2021, the Company entered into definitive transaction agreements with Alloy Therapeutics, Inc. ("Alloy") and Voxall Therapeutics, LLC ("Voxall"), to finance and operate Voxall, a joint venture company formed in collaboration with Alloy to leverage the Company's technology and Alloy's ATX-Gx™ platform and antibody discovery services. Voxall granted to the Company and Alloy, 50% of the voting membership units of Voxall in exchange for certain initial contributions.

The Company accounted for investment in Voxall under the equity method of accounting. Voxall has incurred losses since inception and the Company's share in the losses of Voxall aggregated to $0.5 million and $1.2 million for the years ended December 31, 2022 and 2021, respectively. The Company recognized its share of losses of Voxall only to the extent of the carrying value of its

investment in Voxall and the promissory note issued by Voxall, which aggregated to $0.2 million for the year ended December 31, 2021. The remaining unabsorbed loss will be offset against future income, if any. As the Company has no commitment to fund the losses of the equity method investment, the carrying value of the equity method investment has not been reduced below zero.

5. Fair Value Measurements

The following tables present the financial instruments carried at fair value on a recurring basis as of December 31, 2022 and 2021, respectively, in accordance with the FASB ASC 820 hierarchy (in thousands):

	Fair Value Measurements at December 31, 2022			
	Level 1	Level 2	Level 3	Total
Assets				
Money market funds	$ 177,279	$ —	$ —	$ 177,279

	Fair Value Measurements at December 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets				
Money market funds	$ 272,210	$ —	$ —	$ 272,210

The Company's cash equivalents represent deposits in a short-term United States Treasury money market fund quoted in an active market and classified as a Level 1 asset. There were no assets or liabilities measured at fair value on a nonrecurring basis at December 31, 2022 and 2021. There were no transfers between Level 1 and Level 2 of the fair value hierarchy during the years ended December 31, 2022 and 2021.

The Company recorded the derivative liability of $3.4 million in January 2021 for Extra Milestone Payment due under the Opt-in Agreement with LegoChem. The fair value of the derivative liability was initially determined using a probability-weighted income approach and revalued at each reporting date. Changes in the fair value of the derivative liability of $6.2 million were recorded as expense within other (expense) income in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2021. The significant unobservable inputs used in the fair value measurement of the derivative liability include probability of payment factors and the discount rate. The liability was realized upon the IPO of the Company and Extra Milestone Payment of $9.6 million was paid to LegoChem in January 2022. Refer to Note 3, *Licensing Agreements*, for additional information on the derivative liability.

There were no Level 3 assets or liabilities as of December 31, 2022 and 2021.

6. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2022	2021
Research and development	$ 3,560	$ 619
Insurance	1,308	1,763
Accrued interest receivable	598	—
Other	381	84
Total prepaid expenses and other current assets	**$ 5,847**	**$ 2,466**

7. Property and Equipment, Net

Property and equipment, net, consisted of the following (in thousands):

	December 31,	
	2022	2021
Laboratory equipment	$ 2,247	$ 1,804
Furniture and office equipment	1,036	94
Leasehold improvements	530	225
Construction in process	9,177	—
	12,990	2,123
Less: accumulated depreciation and amortization	(1,825)	(1,116)
Total property and equipment, net	**$ 11,165**	**$ 1,007**

Depreciation and amortization expense for the years ended December 31, 2022 and 2021 was $0.7 million and $0.6 million, respectively.

8. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2022	2021
Research and development expenses	$ 17,414	$ 2,381
Employee compensation and benefits	4,238	2,963
Legal and professional fees	1,794	982
Other	1,091	266
Total accrued expenses and other current liabilities	**$ 24,537**	**$ 6,592**

9. Operating Leases

In September 2021, the Company entered into an operating lease agreement, with a lease term commencement date of April 1, 2022, the date the Company took control of the property, for an office and laboratory space in Boston, Massachusetts. The lease payments began on December 21, 2022 and will continue through December 31, 2032 and with scheduled rent increases each year of 3%. In addition to the rent, the Company bears the costs of certain insurance, property taxes and maintenance, which represent the Company's proportionate share of the actual expenses incurred by the landlord. There is an additional five-year option to extend the lease beyond December 31, 2032.

At the lease commencement date, the operating lease ROU assets of $15.3 million and lease liabilities of $15.3 million were recognized based on the present value of remaining fixed lease payments over the expected lease term using an incremental borrowing rate of 9.4%. As the Company's operating lease does not provide an implicit rate, an estimated incremental borrowing rate based on the information available at the time of lease commencement date was used in determining the present value of lease payments. Under the lease agreement the landlord provided for a tenant improvement allowance of $6.4 million to be applied to the costs of the construction of the leasehold improvements, of which $3.0 million was received by the Company during the year ended December 31, 2022. The tenant improvement allowance is recognized as a reduction in operating lease ROU assets and lease liabilities on the lease commencement date.

The components of lease expense were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Lease cost		
Operating lease cost	$ 1,978	$ 650
Short-term lease cost	1,681	5
Variable lease cost	121	75
Total lease cost	**$ 3,780**	**$ 730**
Other information		
Operating lease right-of-use asset obtained in exchange for new operating lease liabilities	$ 14,497	$ —
Cash paid for amounts included in the measurement of lease liabilities, included in operating cash flows	—	$ 663
Weighted-average remaining lease term (in years)	10.00	0.25
Weighted-average discount rate	9.40%	10.00%

Variable lease costs primarily relate to common area costs and other operating costs, which are assessed based on the Company's proportionate share of such costs for the leased premises. Total lease costs are included as operating expenses in the Company's consolidated statements of operations and comprehensive loss.

Maturities of lease liabilities as of December 31, 2022, were as follows (in thousands):

Years Ending December 31,	Operating Leases
2023	$ 2,557
2024	3,208
2025	3,302
2026	3,399
2027	3,499
Thereafter	18,750
Total undiscounted payments	34,715
Less: tenant improvement allowance	(3,026)
Less: present value adjustment	(12,768)
Present value of future payments	18,921
Less: current portion of operating lease liabilities	—
Operating lease liabilities, net of current portion	$ 18,921

10. Convertible Preferred Stock

Series A Convertible Preferred Stock

In June 2019, the Company entered into a securities purchase agreement (as amended, "Series A Agreement") with certain investors to sell shares of Series A convertible preferred stock ("Series A") at $0.9681 per share. In June and July 2019, the Company issued 22,724,925 shares of Series A to institutional investors at $0.9681 per share for gross cash proceeds of $22.0 million, less issuance costs of $0.1 million, resulting in net proceeds of $21.9 million. On October 1, 2021, the Company effected a 1-for-6.359 reverse stock split. Upon completion of the IPO, 22,724,925 shares of Series A were converted to 3,573,659 shares of common stock.

Series B Convertible Preferred Stock

On March 5, 2021, the Company entered into a securities purchase agreement (as amended, "Series B Agreement") with certain investors to sell shares of Series B convertible preferred stock ("Series B") at $1.6458 per share. In March 2021, the Company issued 92,356,299 shares of Series B to institutional investors at $1.6458 per share for gross cash proceeds of $152.0 million, less issuance costs of $0.4 million, resulting in net proceeds of $151.6 million. In addition, the Company granted 12,455,949 shares, or $20.5 million, of Series B convertible preferred stock through separate agreements with Pfizer and LegoChem. On October 1, 2021, the Company effected a 1-for-6.359 reverse stock split. Upon completion of the IPO, the entire outstanding shares of 104,812,248 of Series B were converted to 16,482,486 shares of common stock.

11. Stockholders' Equity

Preferred Stock

In connection with the closing of the IPO, the Company filed an Amended Certificate of Incorporation and authorized 10,000,000 shares of preferred stock, with a par value of $0.001 per share. The board of directors has the authority, without further action by the stockholders to issue such shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, and to fix the dividend, dividend rights, conversion rights, voting, redemption terms, liquidation preference and other rights, preferences and privileges of the shares. There were no issued and outstanding shares of preferred stock as of December 31, 2022 and 2021, respectively.

Common Stock

Initial Public Offering

On October 8, 2021, the Company completed an IPO in which the Company issued and sold 10,500,000 shares of its common stock at a public offering price of $16.00 per share, for aggregate gross proceeds of $168.0 million. The Company raised approximately $152.3 million in net proceeds after deducting underwriting discounts and commissions of $11.8 million and offering expenses of $3.9 million.

The Company was authorized to issue up to 190,000,000 shares of common stock as of December 31, 2022 and 2021, respectively, of which 35,110,016 and 32,792,867 shares were issued as of December 31, 2022 and 2021, respectively, 34,958,730 and 32,222,881 shares were outstanding at December 31, 2022 and 2021, respectively.

Voting, dividend and liquidation rights of the holders of the common stock are subject to and qualified by the rights, powers and preferences of the holders of the preferred stock.

Voting—Each holder of outstanding shares of common stock shall be entitled to one vote in respect of each share.

Reserved Shares— The Company reserved the following shares of common stock for issuance:

	December 31,	
	2022	**2021**
Stock options outstanding	5,720,415	5,926,969
Unvested restricted stock awards	3,015,387	618,494
Stock options available for issuance	1,697,166	1,289,259
Employee stock purchase plan	752,524	424,595
Total	**11,185,492**	**8,259,317**

12. Stock-Based Compensation

2022 Equity Inducement Plan

On July 1, 2022, the Company's board of directors approved the 2022 Equity Inducement Plan (the "2022 Plan"), which became effective on that date. The 2022 Plan allows the Company to make equity-based incentive awards to its officers and employees without stockholder approval pursuant to Rule 5635(c)(4) of the NASDAQ Listing Rules, or any successor rule relating to inducement awards. Unless earlier terminated by the Board, 2022 Plan will terminate on the tenth anniversary of the effective date. The Company has initially reserved 1,400,000 shares of its common stock for the issuance of awards under the 2022 Plan. As of December 31, 2022, options to purchase 400,692 shares of common stock and 320,550 restricted stock units were outstanding under the 2022 Plan and 678,758 shares remained available for future issuance under the 2022 Plan.

2021 Equity Incentive Plan

On September 27, 2021, the Company's board of directors and stockholders approved the 2021 Equity Incentive Plan (the "2021 Plan"), which became effective on October 7, 2021, when the Company's registration statement was declared effective by the SEC. The 2021 Plan allows the Company to make equity-based and cash-based incentive awards to its officers, employees, directors and consultants. The Company has initially reserved 3,852,807 shares of its common stock for the issuance of awards under the 2021 Plan. The number of shares of common stock reserved for issuance under the 2021 Plan will automatically increase annually on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2022, and continuing until (and including) the fiscal year ending December 31, 2031 by the lesser of (i) 5% of the total number of shares of common stock outstanding on December 31st of the immediately preceding fiscal year and (ii) the number of shares as may be determined by the board of directors. As a result of the evergreen provision of the 2021 Plan, the Company added an additional 1,639,643 shares of common stock to the 2021 Plan as of January 1, 2022. The maximum number of shares of common stock that may be issued pursuant to the exercise of incentive options under the 2021 Plan is 7,705,614. Unless earlier terminated by the Board, 2021 Plan will terminate on the tenth anniversary of the effective date. As of December 31, 2022, options to purchase 2,668,700 shares of common stock and 2,449,172 restricted stock units were outstanding under the 2021 plan and 360,924 shares remained available for future issuance under the 2021 plan.

2019 Equity Incentive Plan

In 2019, the Company established the 2019 Equity Incentive Plan (the "2019 Plan"), under which the Company is allowed to grant options and restricted stock to its employees and non-employees. The maximum number of shares of common stock reserved for issuance under the 2019 Plan is 4,042,408 shares. Options granted under the 2019 Plan include incentive stock options that can be granted only to the Company's employees and non-statutory stock options that can be granted to the Company's employees, consultants, advisors and directors. The 2019 Plan also permits the Company to issue restricted stock awards. Unless earlier terminated by the Board, the 2019 Plan will terminate on the tenth anniversary of the effective date.

Prior to the IPO, the exercise prices, vesting and other restrictions of the awards granted under the 2019 Plan were determined by the board of directors, except that no stock option may be issued with an exercise price less than the fair market value of the common stock at the date of the grant or have a term in excess of ten years. Options granted under the 2019 Plan are exercisable in whole or in part at any time subsequent to vesting. As of December 31, 2022, options to purchase 2,651,023 shares of common stock and 94,379 restricted stock units were outstanding under the 2019 Plan and 657,484 shares remained available for future issuance under the 2019 Plan.

2021 Employee Stock Purchase Plan

On September 27, 2021, the Company's board of directors and stockholders approved the 2021 Employee Stock Purchase Plan (the "2021 ESPP"), which became effective on October 7, 2021, when the Company's registration statement was declared effective by the SEC. The 2021 ESPP initially reserved and authorized the issuance of up to a total of 424,595 shares of common stock to participating employees. The number of shares of common stock reserved for issuance under the ESPP will automatically increase annually on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2022, and continuing until (and including) the fiscal year ending December 31, 2031 by the lesser of (1) 1% of the total number of shares of common stock outstanding on December 31st of the immediately preceding fiscal year and (ii) the number of shares as may be determined by the board of directors. As a result of the evergreen provision of the 2021 ESPP, the Company added an additional 327,929 shares of common stock to the 2021 ESPP as of January 1, 2022. No shares are issued under 2021 ESPP plan as of the date of issuance of these consolidated financial statements. As of December 31, 2022, the authorized number of shares and shares available for issuance under the 2021 ESPP is 752,524.

Stock Options

Stock options granted under the 2022 Plan, 2021 Plan and 2019 Plan (together, the "Plans") to employees generally vest over four years and expire after 10 years.

The following table summarizes stock option activity for the year ended December 31, 2022 (in thousands, except share and per share amounts):

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding at January 1, 2022	5,926,969	$ 10.03	9.5	$ 16,414
Granted	1,178,280	4.06		
Exercised	(73,841)	2.48		
Forfeited	(834,095)	7.24		
Expired	(476,898)	5.51		
Outstanding at December 31, 2022	**5,720,415**	**$ 9.68**	**8.8**	**$ 72**
Options exercisable at December 31, 2022	**2,037,934**	**$ 9.34**	**8.5**	**$ 59**

The weighted-average grant-date fair value of options granted during the years ended December 31, 2022 and 2021, was $3.06 and $7.57 per share, respectively. The aggregate intrinsic value is calculated as the difference between the exercise price of all outstanding and exercisable stock options and the fair value of the Company's common stock of $1.34 per share as of December 31, 2022. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2022 and 2021 was less than $0.1 million and $0.6 million, respectively.

The Company estimated the fair value of each option on the date of grant using the Black-Scholes option-pricing model applying the range of assumptions in the following table:

	Year Ended December 31,	
	2022	2021
Expected volatility	96.09% - 101.66%	72.88% - 103.41%
Risk-free interest rate	1.60% - 4.02%	0.81% - 1.36%
Expected dividend yield	0.00%	0.00%
Expected term (in years)	6.00 - 6.11	5.25 - 7.00

Stock-based compensation expense related to stock options recorded in the statements of operations is as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Research and development	$ 4,330	$ 2,396
General and administrative	7,617	3,976
Total	**$ 11,947**	**$ 6,372**

The Company has an aggregate $25.2 million of gross unrecognized stock-based compensation expense as of December 31, 2022, remaining to be amortized over a weighted average period of 2.29 years. The Company has not recognized and does not expect to recognize in the near future, any tax benefit related to employee stock-based compensation expense as a result of the full valuation allowance related to its net deferred tax assets.

Restricted Stock Awards

Under the 2019 Plan, 2021 Plan and 2022 Inducement Plan, the Company issued 3,174,656 restricted stock units ("RSU") to employees and non-employees. Compensation costs related to these RSUs were recorded based on the Company's stock price on the date of issuance and amortized over the service period.

Additionally, the Company issued certain shares of restricted common stock ("RSA") to the employee co-founders and certain non-employee consultants in 2019. The shares of restricted common stock were issued pursuant to standalone restricted stock purchase agreements that are independent of the 2019 Plan, 2021 Plan and 2022 Inducement Plan. The shares of restricted common stock pursuant to standalone restricted stock purchase agreements carried a purchase price equivalent of $0.01 per share. As of December 31, 2022, 151,286 RSAs were unvested and outstanding.

Under the terms of the restricted stock purchase agreements, the Company has a repurchase option whereby it has the right to repurchase any unvested shares upon termination at a price per share equal to the lesser of (i) the fair market value of the Company's common stock on the date of repurchase and (ii) the original purchase price. The shares of restricted common stock issued to the Company's co-founders and non-employee consultants vest based on a predefined number of shares.

The Company recognized an associated deposit liability for restricted stock awards issued pursuant to standalone restricted stock purchase agreements upon issuance based on the purchase price of the awards as the unvested shares are subject to repurchase upon termination. As the awards of restricted stock vest, the Company reclassifies the deposit liability to additional paid-in capital. The compensation cost was measured based on the fair value of the underlying common stock less the purchase price of the restricted common stock and the Company recognizes compensation costs over the requisite service period.

The following table summarizes restricted stock activity for the year ended December 31, 2022:

	Number of Shares	Weighted Average Grant Date Fair Value
Non-vested at December 31, 2021	618,494	$ 3.04
Granted	3,174,656	3.69
Vested and settled	(432,354)	0.55
Forfeited	(345,409)	3.74
Non-vested and unsettled at December 31, 2022	**3,015,387**	**$ 3.64**

The Company has recorded stock-based compensation expense related to the restricted stock of $3.8 million and $0.1 million for the years ended December 31, 2022, and 2021, respectively. The Company has an aggregate $7.4 million of gross unrecognized restricted stock-based compensation expense as of December 31, 2022, remaining to be amortized over a weighted average period of 2.26 years.

13. Income Taxes

During the years ended December 31, 2022 and 2021, the Company recorded no current or deferred income tax expenses or benefits as the Company has incurred losses since inception and has provided a full valuation allowance against its deferred tax assets.

A reconciliation of the expected income tax benefit computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	**2021**
Income tax computed at federal statutory rate %	21.0%	21.0%
State taxes, net of federal benefit	5.6	5.7
Change in valuation allowance	(26.6)	(27.7)
Research and development credit carryovers	1.7	1.9
Permanent differences	(1.7)	(0.9)
Effective income tax rate %	**0.0%**	**0.0%**

The Company's effective tax rate was 0% for the years ended December 31, 2022 and 2021, as a result of the valuation allowance that eliminates the company's net deferred tax assets.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's net deferred tax assets as of December 31, 2022 and 2021 are as follows (in thousands):

	Year Ended December 31,	
	2022	**2021**
Deferred tax assets:		
Net operating losses	$ 13,108	$ 12,918
Intangibles	69	75
Tax credit carryforwards	3,674	1,648
Derivative	1,455	1,577
Stock-based compensation	2,645	1,003
Reserves and accruals	1,105	804
Capitalized research expenditures	20,059	—
License fees	14,235	7,716
Operating lease liability	5,107	45
Other	29	25
Total deferred tax assets before valuation allowance	61,486	25,811
Less: valuation allowance	(57,812)	(25,748)
Total deferred tax assets	**$ 3,674**	**$ 63**
Deferred tax liabilities:		
Operating lease ROU assets	(3,674)	(63)
Net deferred tax asset	**$ —**	**$ —**

As of December 31, 2022, the Company's federal and state net operating losses ("NOL") in the United States were $10.1 million ($48.0 million before tax) and $3.0 million ($48.1 million before tax) respectively. The federal net operating loss carryforwards in the United States can be carried forward indefinitely but may be subject to annual usage limitations to the extent certain substantial changes in the entity's ownership occur. The state net operating loss carryforwards begin expiring in 2039. In addition, as of December 31, 2022, the Company had $2.5 million and $1.2 million of federal and state credit carryovers which begin to expire in 2039. These loss and credit carryforwards are subject to review and possible adjustment by the appropriate taxing authorities.

The Company assesses the realizability of the deferred tax assets at each balance sheet date based on the available positive and negative evidence in order to determine the amount which is more likely than not to be realized and records a valuation allowance as necessary. Due to the Company's cumulative loss position which provides significant negative evidence, which is difficult to overcome, the Company has recorded a valuation allowance of $57.8 million as of December 31, 2022, representing the portion of the deferred tax asset that is not more likely than not to be realized. For the years ended December 31, 2022 and 2021, the valuation allowance for deferred tax assets increased by $32.2 million and $21.4 million, respectively. The amount of the deferred tax asset considered realizable, could be adjusted for future factors that would impact the assessment of the objective and subjective evidence. The Company will continue to assess the realizability of deferred tax assets at each balance sheet date in order to determine the proper amount, if any, required for a valuation allowance.

The Tax Cuts and Jobs Act contained a provision which requires the capitalization of Section 174 costs incurred in the years beginning on or after January 1, 2022. Section 174 costs are expenditures which represent research and development costs that are incident to the development or improvement of a product, process, formula, invention, computer software or technique. This provision changes the treatment of Section 174 costs such that the expenditures are no longer allowed as an immediate deduction but rather must be capitalized and amortized. We have included the impact of this provision, which results in a deferred tax asset of approximately $20.1 million as of December 31, 2022.

The U.S. tax attributes may be subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986 (the “Code”), and similar state provisions if the Company experiences one or more ownership changes, which would limit the amount of the tax attributes that can be utilized to offset future taxable income. In general, an ownership change as defined by Section 382, results from the transactions increasing ownership of certain stockholders or public groups in the stock of the corporation of more than fifty percentage points over a three-year period. If a change in ownership occurs in the future, the net operating loss and research and development credit carryforwards could be eliminated or restricted. If eliminated, the related asset would be removed from the deferred tax asset schedule with a corresponding reduction in the valuation allowance. Due to the existence of the valuation allowance, limitations created by future ownership changes, if any, will not impact the Company’s effective tax rate.

The Company is subject to tax and will continue to file federal income tax returns in the United States as well as in certain state and local jurisdictions. The Company is subject to tax examinations for tax years ended December 31, 2019 and forward in all applicable income tax jurisdictions. Tax audits and examinations can involve complex issues, interpretations and judgements. The resolution of matters may span multiple years particularly if subject to litigation or negotiation. The Company believes that it has appropriately recorded its tax position using reasonable estimates and assumptions, however the potential tax benefits may impact the results of operations or cashflows in the period of resolution, settlement, or when the statutes of limitations expire. The Company does not currently have any reserves related to unrecognized tax benefits.

14. Net Loss per Share

Basic and diluted net loss per share was calculated as follows (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2022	**2021**
Numerator:		
Net loss	$ (120,717)	$ (75,975)
Denominator:		
Weighted-average common shares outstanding, basic and diluted	33,033,081	8,493,273
Net loss per share, basic and diluted	**$ (3.65)**	**$ (8.95)**

The Company's potentially dilutive securities, which include restricted stock, and stock options, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

The following potentially dilutive securities have been excluded from the calculation of diluted net loss per common share due to their anti-dilutive effect:

	December 31,	
	2022	**2021**
Stock options outstanding	5,720,415	5,929,969
Unvested restricted stock awards	3,015,387	618,494
Stock options available for issuance	1,697,166	1,289,259
Employee stock purchase plan	752,524	424,595
Total	**11,185,492**	**8,262,317**

15. Related Parties

The Company was founded out of Dr. Thomas Gajewski's laboratory at the University of Chicago. In 2020, the Company entered into the License Agreement with the University of Chicago, as well as a sponsored research agreement. The Company incurred $0.3 million and $0 for the years ended December 31, 2022 and 2021, respectively, with regards to the University License Agreement. Refer to Note 3 for additional discussion.

Pfizer owns more than 10% of the Company and is considered the principal owner of the Company. On October 6, 2022, the Company entered into the A&R License Agreement with Pfizer, which amends and restates the previously executed license agreement between Pfizer and the Company. During the year ended December 31, 2022, the Company incurred $17.3 million of research and development expenses for the A&R License Agreement. During the year ended December 31, 2021, the Company incurred $25.0 million of research and development expenses towards license fee. Refer to Note 3 for additional discussion.

The Company and Alloy formed a joint venture company, Voxall Therapeutics, LLC ("Voxall") to leverage the Company's technology and Alloy's ATX-Gx™ platform and antibody discovery services. The Company and Alloy contributed $50 thousand each to Voxall along with certain license in 2021. During the year ended December 31, 2022, the Company has not incurred expenses related to Voxall. During the year ended December 31, 2021, the Company provided services to Voxall for which it recognized service fee other income of $181 thousand. Refer to Note 4 for additional discussion.

16. Commitments and Contingencies

Legal Proceedings

From time to time, the Company may become involved in various legal proceedings that arise in the ordinary course of business. The Company is not currently a party to any material legal proceedings and is not aware of any pending or threatened legal proceeding against it that the Company believes could have an adverse effect on its business, operating results or financial condition.

Commitments

In the normal course of business, the Company enters into agreements with various third parties for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes, which are generally cancellable by the Company at any time, subject to payment of remaining obligations under binding purchase orders and, in certain cases, nominal early-termination fees. These commitments are not deemed significant.

17. Subsequent Event

Leases

On February 2, 2023, the Company entered into a sublease agreement for approximately 17,729 square feet of office and laboratory space in the building located at 321 Harrison Avenue, Boston, Massachusetts. The sublease is for the fixed period of 36 months and will expire on February 1, 2025. The Company will receive approximately $5.2 million in base rent payments over the sublease term. The subtenant will also be responsible for certain other costs under the sublease, such as operating expenses, taxes, insurance, property management fee and utilities.

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