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 001-39539

PMV PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**46-3218129**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1 Research Way Princeton, NJ	**08536**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (609) 642-6670

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 $0.00001	PMVP	The 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 voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market on June 30, 2022 (the last business day of the Registrant's most recently completed second fiscal quarter), was $543,361,107. Shares of the Registrant's common stock held by each executive officer, director and holder of 10% or more of the outstanding common stock have been excluded because such persons may be deemed affiliates. This calculation does not reflect a determination that certain persons are affiliates of the Registrant for any other purpose.

The number of shares of Registrant's Common Stock outstanding as of February 28, 2023 was 45,773,361.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive Proxy Statement relating to the 2023 Annual Meeting of Stockholders are incorporated herein by reference in 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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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, development plans, planned preclinical studies and clinical trials, future results of clinical trials, expected research and development costs, regulatory strategy, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may", "will", "should", "would", "expect", "plans", "anticipate", "could", "intend", "target", "project", "contemplate", "believe", "estimate", "predict", "potential" or "continue" or the negative of these terms or other similar expressions. Forward-looking statements contained in this Annual Report include, but are not limited to, statements about:

- our financial performance;
- the sufficiency of our existing cash, cash equivalents and short-term marketable securities to fund our future operating expenses and capital expenditure requirements;
- our need to raise additional funding before we can expect to generate any revenues from product sales;
- our ability to obtain additional funding for our operations, when needed, including funding necessary to complete further development and commercialization of our product candidates, if approved;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the implementation of our strategic plans for our business and product candidates;
- the size of the market opportunity for our product candidates and our ability to maximize those opportunities;
- the initiation, timing, progress and results of our research and development programs, preclinical studies, clinical trials and investigational new drug applications, or IND, and other regulatory submissions;
- the beneficial characteristics, safety, efficacy and therapeutic effects of our product candidates;
- our estimates of the number of patients for each of our programs including patients expected to have certain p53 mutations and the number of patients that will enroll in our clinical trials;
- the ability of our clinical trials to demonstrate safety and efficacy of our product candidates, and other favorable results;
- our plans relating to the clinical development of our product candidates, including the disease areas to be evaluated;
- the timing, progress and focus of our clinical trials, and the reporting of data from those trials;
- our ability to obtain and maintain regulatory approval of our product candidates;
- our plans relating to commercializing our product candidates, if approved;
- the expected benefits of potential future strategic collaborations with third parties and our ability to attract collaborators with development, regulatory and commercialization expertise;
- the success of competing therapies that are or may become available;
- the timing or likelihood of regulatory filings and approvals, including our expectation to seek accelerated reviews or special designations, such as breakthrough therapy and orphan drug designation, for our product candidates;
- our plans relating to the further development and manufacturing of our product candidates, including for additional indications that we may pursue;

- existing regulations and regulatory developments in the United States and other jurisdictions;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available;
- our plans to rely on third parties to conduct and support preclinical and clinical development;
- our ability to retain the continued service of our key personnel and to identify, hire and then retain additional qualified personnel; and
- the impact of the ongoing coronavirus disease 2019, or COVID-19, pandemic, geopolitical tensions such as the Ukraine-Russia war, macroeconomic events such as global supply chain challenges, elevated inflation and interest rates and monetary policy changes, or other related disruptions on our business

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions described in the section titled "Item 1A. Risk Factors" and elsewhere in this Annual Report. 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. 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.

In addition, statements that "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, and while 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 an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely upon these statements.

PART I

Item 1. Business.

We are a precision oncology company pioneering the discovery and development of small molecule, tumor-agnostic therapies targeting p53. p53 is a well-defined tumor suppressor protein known as the "guardian of the genome," and normal, or wild-type, p53 has the ability to eliminate cancer cells. However, mutant p53 proteins can be misfolded and lose their wild-type tumor suppressing function. These p53 mutations are found in approximately half of all cancers. The field of p53 biology was established by our co-founder Dr. Arnold Levine when he discovered the p53 protein in 1979. We have leveraged more than four decades of research experience and developed unique insights into p53 to create a precision oncology platform designed to generate selective, small molecule, tumor-agnostic therapies that structurally correct specific mutant p53 proteins to restore their wild-type function. We are deploying our precision oncology platform to target the top ten most frequent, or hotspot, p53 mutations that are collectively associated with approximately 10-15% of all cancers. In addition, we continue to utilize our platform to target other p53-related cancers.

Our lead product candidate, PC14586, is an orally available small molecule designed to potently and selectively correct p53 misfolding caused by a specific p53 mutation, Y220C, while sparing wild-type p53. The Y220C mutation is associated with 1.0-1.5% of all cancers, including breast, non-small cell lung cancer, or NSCLC, colorectal, pancreatic and ovarian cancers. PC14586 is designed to restore the wild-type conformation by occupying the crevice created by the tyrosine to cysteine mutation in amino acid position 220. While we are in the early stages of discovery and development of our product candidates and our novel approach is unproven, we are initially pursuing a tumor-agnostic development strategy and initiated a Phase 1/2 clinical trial in October 2020. Our strategy is to seek approval under an accelerated pathway, and we believe our Phase 1/2 clinical trial has the potential to serve as a pivotal study. In October 2020, we were granted U.S. Food and Drug Administration, or FDA, Fast Track designation of PC14586 for the treatment of patients with locally advanced or metastatic solid tumors that have a p53 Y220C mutation. We presented our preliminary Phase 1 clinical data in June 2022 and we continue to enroll patients in this trial. In December 2022, we opened a separate arm within the existing Phase 1/2 clinical trial combining PC14586 with KEYTRUDA® (pembrolizumab) in collaboration with Merck and Co. In addition, we are leveraging our precision oncology platform to develop a pipeline of oral small molecule product candidates that structurally correct other p53 hotspot mutations to restore their wild-type function and product candidates that target other p53-related cancers.

A better understanding of mutations that drive cancers have facilitated the development of precise, gene- and protein-specific drugs known as targeted therapies. Targeted therapies have the potential to transform treatment of some cancers by providing robust clinical benefit to patients. In many cases, clinical responses can be dramatic enough to support expedited regulatory approval of these therapies. Further, recent advancements in next-generation-sequencing, or genomic NGS, have accelerated the development of targeted therapies. A recent study found that 75% of oncologists in the United States employ genetic sequencing. We believe p53 mutations are particularly well-suited for the evolving precision oncology paradigm, as a single mutation can cause p53 malfunction, and p53 is one of the genes commonly sequenced, to our knowledge, in NGS panels. We believe that our precision oncology platform offers a substantial opportunity to expand the number of patients who will benefit from targeted therapies.

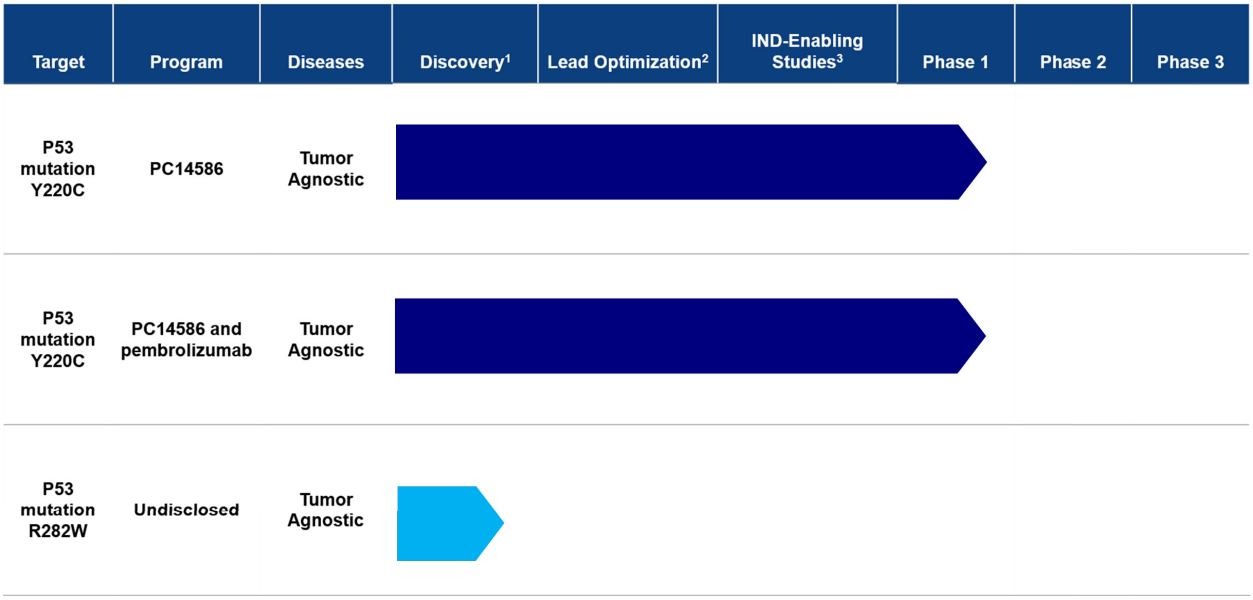
Our innovation engine consists of three complementary drivers:

- deep understanding of, and leadership in, p53 biology that enable unique insights into drugging individual mutations as well as targeting other p53-related cancers;
- ability to design on a structural basis selective, oral small molecule product candidates; and
- assays, screens, preclinical model systems and biomarkers that enable us to assess and optimize orally available selective small molecule drug product candidates for specific p53 mutants, and for inhibitors of wild-type p53 function

PC14586 and Pipeline

We are leveraging our precision oncology platform to develop a pipeline of orally available, potent and highly selective small molecule product candidates that are designed to structurally correct specific mutant p53 proteins to restore their wild-type function. In addition, we are expanding the utilization of our platform to target other p53-related cancers.

An overview of our development pipeline is shown in the table below.



(1) In Discovery, we screen compounds against biological assays to identify lead compounds.

(2) In Lead Optimization, we modify the lead compound to improve potency, selectivity, pharmacokinetic and toxicity parameters and physical chemical properties important for clinical development.

(3) In IND-Enabling Studies, we conduct preclinical studies, in accordance with Good Laboratory Practice, or GLP, required for an IND submission to the FDA.

Our lead product candidate, PC14586, is designed to be an orally available small molecule that structurally corrects the mutant p53 protein with the Y220C mutation. The Y220C mutation results from tyrosine being substituted by a cysteine at amino acid position 220 and is associated with 1.0-1.5% of all cancers, including breast, NSCLC, colorectal, pancreatic and ovarian cancers. There are currently no products approved by the FDA, and we are not aware of any other products in clinical development, that selectively target the p53 Y220C mutation.

PC14586 is designed to bind to the mutation site and structurally correct the misfolded p53 protein, while sparing wild-type p53. Our approach has yielded a highly selective product candidate, which we believe can maximize the potential therapeutic potency and minimize risk to normal functioning cells. In preclinical studies, PC14586 has shown selective on-target activity (*i.e.*, primarily functions in cells with the p53 Y220C mutation) and exhibited robust anti-tumor activity evidenced by potent tumor growth inhibition, or TGI, and strong tumor regression as a single agent. Further, preclinical studies have demonstrated significant synergistic effects in combination with anti-PD-1 therapy.

We initiated a Phase 1/2 clinical trial for PC14586 in October 2020. In addition, we were granted FDA Fast Track designation of PC14586 for the treatment of patients with locally advanced or metastatic solid tumors that have a p53 Y220C mutation in October 2020. We dosed our first patient in this clinical trial in the fourth quarter of 2020. The Phase 1 portion of the trial is designed to evaluate escalating doses of PC14586 to determine the maximum tolerated dose, or MTD, and recommended Phase 2 dose of PC14586 when administered orally to patients. Safety, tolerability and effects on biomarkers such as macrophage inhibitory cytokine-1, or MIC-1, will also be assessed. The Phase 1 portion is also designed to assess preliminary anti-tumor efficacy in patients with advanced solid tumors that have the p53 Y220C mutation. In June 2022, we presented initial Phase 1 data, as of a May 10, 2022 efficacy data cutoff date, from our Phase 1/2 clinical trial at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting: PC14586 was generally well-tolerated and the MTD was determined to be 1500mg BID. A total of 41 patients with the p53 Y220C mutation were enrolled, including 25 patients with measurable disease who were treated in the efficacious dose range, which was defined as a dose from 1150mg QD to 1500mg BID. In the efficacious dose range, partial responses were observed by investigator review (RECIST v1.1) in 32% (six confirmed partial responses and two partial responses pending confirmation as of May 10, 2022) across six different tumor types.

We believe the mechanism of action employed by PC14586 to structurally correct a specific p53 mutant and restore wild-type p53 activity could provide benefit to patients and offer a unique value proposition in oncology, and is a strategy that can be pursued broadly across other p53 mutations. To that point, we are developing a pipeline of candidates targeting other p53 hotspot mutations. We have other preclinical programs that have demonstrated biochemical validation, for which we are leveraging knowledge from our PC14586 Y220C program. We believe we can scale our discovery and development principles across all p53 hotspot mutations to streamline the process of further developing our pipeline.

In addition to targeting p53 hotspot mutants, we believe that our expertise and platform can also be applied to target other p53-related cancers. We are deploying our deep understanding of structure-based small molecule design, assays, screens, preclinical model systems and biomarkers to create a pipeline of therapeutics in this field. We believe that we can continue to scale our platform to develop novel therapeutics that structurally correct mutant p53 or other p53-related cancers.

Our Strategy

Our vision is to become a leading precision oncology company by designing, developing and commercializing novel precision medicines for every patient with a p53-driven tumor. We believe we are well positioned to leverage our deep experience in p53 biology, precision oncology platform and foundational knowledge acquired through our lead program to bring these therapies to patients. The critical components of our strategy include:

- **Advancing our lead product candidate, PC14586, as a tumor-agnostic, oral small molecule therapy for cancer patients**. We have designed PC14586 to be an orally available, tumor-agnostic therapeutic and, if approved, we believe it could become the first agent to address the p53 Y220C mutation-defined patient population. In October 2020, we initiated a Phase 1/2 clinical trial for PC14586 in multiple solid tumors with the p53 Y220C mutation. We plan to conduct our clinical trials in this genetically-defined patient population and leverage learnings from recently approved tumor-agnostic drugs to inform the clinical and regulatory pathways for PC14586. In June 2022, we presented our initial Phase 1 clinical data for PC14586 and observed partial responses across six different tumor types. In December 2022, we opened a separate arm within the existing Phase 1/2 clinical trial, to evaluate the combination of PC14586 with Merck's KEYTRUDA (pembrolizumab), in patients with advanced solid tumors harboring a p53 Y220C mutation.

- **Harnessing the power of our precision oncology platform to discover and develop additional differentiated product candidates that are designed to precisely target p53 mutant protein and inhibitors of wild-type p53 in cancer**. We believe that the general principles for our PC14586 Y220C program can be applied to other p53 hotspot mutations. Using our extensive in-house expertise, deep understanding of chemistry and decades of experience researching the p53 protein, we believe that we will be able to leverage and apply foundational knowledge from the advancement of PC14586 to the discovery and development of small molecules targeting other p53 mutations. We are advancing several early-stage programs focused on targeting the p53 hotspot mutations and other p53-related cancers. In an ongoing effort to bring forward new product candidates, we plan to continue to invest in our precision oncology platform, including our high-throughput screens that allow for quantitative visualization of the conversion from mutant to wild-type p53 in a dose-dependent manner.
- **Leveraging the advantages of precision medicine and our expertise in p53 biology to pursue accelerated approval of our product candidates**. For our lead product candidate, PC14586, we are actively working with physicians and leading academic centers to enroll patients with the p53 Y220C mutation identified through NGS in our Phase 1/2 clinical trial. In order to rapidly confirm mechanistic and clinical proof of concept, we utilize assays to measure target engagement and biomarkers, as well as assess clinical responses in patients. We expect this strategy, which we also plan to replicate for our other future product candidates, will enable a rapid determination of target engagement and has potential to serve as a predictive marker of efficacy, thereby providing clear decision points for clinical development and efficient advancement of our product candidates towards approval. If we obtain early and encouraging clinical results, we may seek breakthrough therapy designation from the FDA, which, if granted, is intended to expedite clinical development and regulatory review. We intend to maximize the benefit of our product candidates by pursuing a tumor-agnostic approach.
- **Identifying and exploring combination therapy approaches for our product candidates**. Though PC14586 has demonstrated clear and robust tumor regression as a single agent in preclinical animal models, we believe that the mechanism of correcting the structure of mutant p53 can be complementary to other oncology therapies. Leveraging our expertise in p53 biology, chemistry and cancer pharmacology, we plan to identify and explore combination strategies with multiple cancer therapies. For example, chemotherapy and radiation therapy, approaches that result in deoxyribonucleic acid, or DNA, damage and upregulate p53 are natural candidates for combining with our product candidates. In addition, we believe that p53 plays a role in influencing the tumor microenvironment. Therefore, immune checkpoint inhibitors, such as anti-PD-1 and anti-CTLA-4 agents, could also be considered as potential combination agents for use with our product candidates. We believe that our unique expertise will enable us to prioritize therapeutic strategies and optimize outcomes for clinical studies.

Background on Targeted Therapies

Cancer is a genetic disease that results from changes in a person's DNA that causes cells to grow and divide uncontrollably. Genes are the distinct segments in a cell's DNA that can encode proteins with structural or functional roles in the body. Alterations in some genes can lead to the expression of mutant proteins with impaired or abnormal functions that can cause cancer. Cancer has historically been both diagnosed and treated based on a tumor's organ site, such as the breast, lung, ovary, brain, pancreas, skin, bone or blood.

Recent advances in genetic sequencing and a better understanding of the genetic alterations that drive tumor development and growth have facilitated precise, gene and protein-specific drug development, known as targeted therapies. Targeted therapies have the potential to transform treatment of some cancers by providing robust clinical benefit to patients. In notable cases, the clinical outcomes have been dramatic enough to support expedited regulatory approval of these therapies. For example, Retevmo in RET-altered NSCLC and thyroid cancers (Lilly/Loxo); Ayvakit, in platelet-derived growth factor receptor alpha exon 18 mutated advanced gastrointestinal stromal tumor, or GIST (Blueprint); Rozlytrek, in solid tumors with a neurotrophic tropomyosin receptor kinase, or NTRK, gene fusion (Roche); Vitrakvi, in solid tumors with an NTRK gene fusion (Loxo/Bayer); Zykadia, in anaplastic lymphoma kinase-positive, or ALK+, advanced NSCLC (Novartis); Zelboraf, in advanced melanoma with a BRAF V600E mutation (Roche Genentech); Xalkori, in ALK+ advanced NSCLC (Pfizer); Tagrisso, in epidermal growth factor receptor mutation-positive, or EGFR+, advanced NSCLC (AstraZeneca); Qinlock, in GIST (Deciphera), and Krazati and Lumakras in KRAS G12C mutated NSCLC (Mirati and Amgen) all received approvals within five years of first dosing in humans. This time period is significantly reduced compared to conventional drug development timelines. Despite this progress, a recent analysis found that only 8% of patients with metastatic cancer have tumors with genetic profiles eligible for treatment with an approved targeted agent, which leaves a large opportunity for precision oncology.

There is an emerging change in the development of targeted therapies, in that cancer is increasingly being targeted through a tumor-agnostic approach with a focus on selectively targeting a genetic or protein mutation irrespective of tumor type. For example, there are now multiple tumor-agnostic product approvals that are based on a genetic mutation that defines the disease, as opposed to the tumor type. These include the aforementioned Vitrakvi and Rozlytrek approvals as well as KEYTRUDA and Jemperli, respectively, approval in metastatic microsatellite instability-high, or MSI-high, or deficient mismatch repair, or dMMR, solid tumors. KEYTRUDA is also approved in tumor mutational burden-high-(TMB-H) solid tumors. In addition, the combination of Taflinar and Mekinist was approved for BRAF V600E mutation positive unresectable or metastatic solid tumors (with the exception of colorectal cancer). We believe that these approvals represent a fundamental shift in the development of targeted therapies and will increasingly lead to cancer being characterized for treatment in a genetic, rather than in a tumor-specific, manner, based on a biological rationale.

The widespread recognition that cancer is a genetic disease, as much as it is a disease defined by histology or anatomical location, has driven the increased use of genetic sequencing, which is now employed by approximately 75% of oncologists in the United States. As DNA sequencing technology advances, the availability of well-defined genetic sequencing tests increases. With the increasing number of approved targeted therapies, we believe that physicians will seek a better understanding of the underlying genetic and protein abnormalities associated with a specific type of cancer in order to determine the optimal course of treatment. Advances in genetic sequencing are leading to transformations in the discovery and development of new targeted oncology drugs.

We believe p53 mutations are prime targets for precision oncology, as more than 50% of all human cancers contain a p53 mutation. Identifying the specific p53 gene mutation and structurally correcting the corresponding mutant p53 protein can potentially serve as a basis of treatment for these cancers. Diagnostic tests are currently used by physicians in their practice to identify patients with p53 mutations. Given the high prevalence of p53 mutations in cancers, we believe that an effective way to address p53-driven cancers is by targeting individual p53 mutations using a precision oncology approach and significantly expanding the scope of patients who can benefit from targeted therapies. In addition, we believe that our platform can also be leveraged to expand our pipeline by identifying targets that modulate wild-type p53. Given our deep understanding of and expertise in p53 biology, we believe that pursuing product candidates that target inhibitors of wild-type p53 can also expand the scope of patients who can benefit from targeted therapies.

Background on p53, the Most Frequently Mutated Gene in Human Cancer

The p53 gene provides instructions for the production of tumor suppression protein p53 and is the most widely mutated gene in human cancers. Since its discovery in 1979 by our co-founder Dr. Arnold Levine, p53 has been extensively studied by researchers and the pharmaceutical industry due to its central role in preventing the initiation and proliferation of liquid and solid tumors. p53 has long been referred to as the “guardian of the genome” because it regulates expression of a number of genes that comprise the body’s first line of cellular defense against cancers. Among its multiple biologic functions, p53 regulates a variety of tumor suppressive responses including cell cycle arrest, DNA repair, senescence and apoptosis.

p53 is a transcriptional factor, which binds to the promoters of its target genes in a sequence-specific manner and regulates their expression, thereby controlling cell cycle and cell death. p53 is activated when DNA damage is detected and when oxidative or other cellular stresses exceed thresholds for normal cellular function. p53 activation facilitates the repair of the cell's damaged DNA or triggers the killing of the damaged cell through a process known as programmed cell death, or apoptosis, before the cell can become cancerous and proliferate.

Under normal cellular conditions, p53 is kept at low levels by expression of murine double minute 2, or MDM2, a ubiquitin ligase that promotes the degradation of p53. Upon p53 activation by damaged DNA, and other types of stresses, p53 is upregulated and blocks the proliferation of pre-malignant and malignant cells or eliminates them by inducing apoptosis. Mutant p53 loses the ability to eliminate the proliferation of pre-malignant and malignant cells. Given that the mutational status of p53 in a tumor has a strong impact on sensitivity to commonly used anti-cancer drugs and radiotherapy, p53 is important both as a biomarker and as a novel therapeutic target.

A key challenge in the development of p53-targeted therapies is the vast number of p53 mutants that lose tumor suppression activity. To date, more than 25,000 unique p53 mutations have been discovered. The p53 hotspot mutations occur as a result of site-specific substitution of one amino acid for another and lead to loss of tumor suppression function for the p53 protein. Strategies that attempt to restore wild-type p53 activity in a non-selective manner (*i.e.*, regardless of which p53 mutation the tumor is harboring) are likely to face significant challenges, as a "one size fits all" drug is unlikely to address all p53 mutants and could have the potential for off-target toxicities. We are focusing on targeting the p53 hotspot mutations and other p53-related cancers.

Our Focus: Top Ten Most Frequent p53 Mutations

p53 Hotspot Mutation	Frequency Among p53 Mutations
R175H	**5.6%**
R248Q	**4.4%**
R273H	**4.0%**
R248W	**3.5%**
R273C	**3.3%**
R282W	**2.8%**
G245S	**2.1%**
R249S	**2.0%**
Y220C	**1.8%**
V157F	**1.0%**

Our Approach to Targeting p53

Our goal is to bring precision oncology therapies to a greater number of patients. Decades of p53 research has unveiled its potential as a precision oncology target, but prior drug development efforts have been unsuccessful. Mutant p53 historically has been classified as "undruggable" due to the difficulty of restoring wild-type p53 function. Mutations in p53 can give rise to mutant p53 proteins with different conformational structures. As a result, we are designing oral small molecule therapies that selectively target a specific p53 mutation while not binding to wild-type p53. We believe our novel approach designed to reactivate p53 function through the structural correction of mutant p53 protein to wild-type p53 represents a novel therapeutic strategy to target p53.

Our drug development efforts leverage our understanding that:

- mutations throughout the p53 protein can drive tumor formation and growth;
- a mutant p53 protein resulting from a specific mutation can potentially be structurally corrected by a selective small molecule, thereby reactivating wild-type p53 activity;
- the p53 hotspot mutations comprise approximately 30% of all p53 mutations and each p53 hotspot mutation represents an individual therapeutic target for drug discovery and development; and
- in addition to p53 mutant cancers, certain cancers result when wild-type p53 function is inhibited.

We believe we can address certain key limitations of current-generation precision oncology therapies by applying our platform to identify and generate therapies that address functional deficiencies associated with specific p53 mutations and other p53-related cancers. We believe this will allow us to design and develop potential therapies for patients with a high unmet medical need for whom there are currently no targeted treatment options.

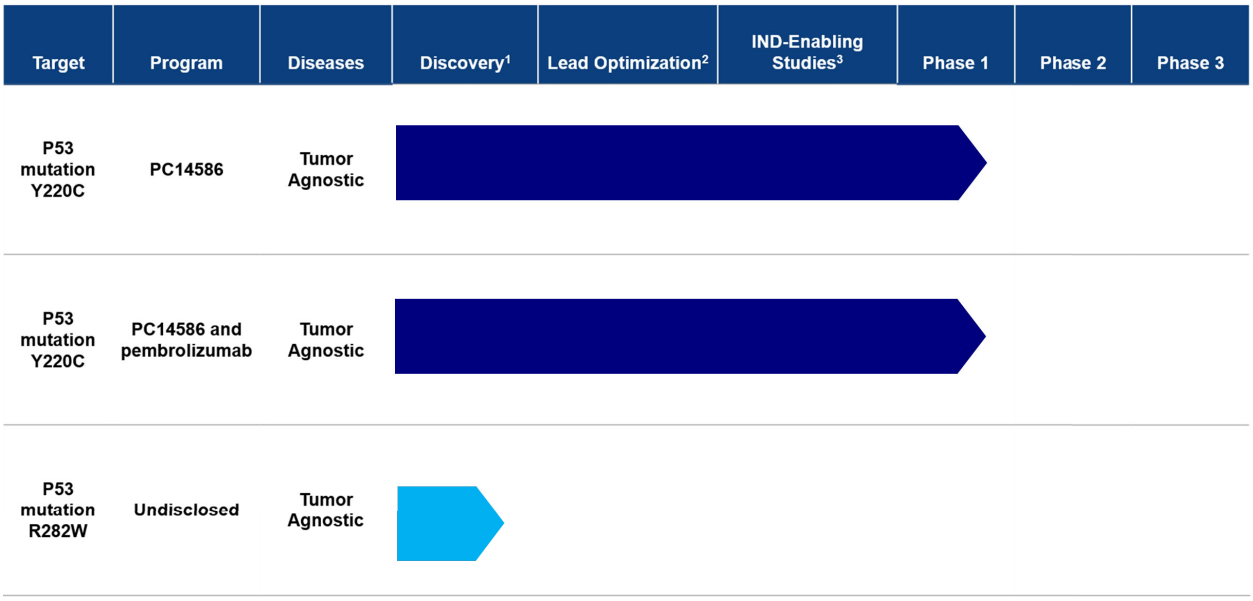
Our Innovation Engine

We have built an innovation engine that allows us to discover and develop potential targeted therapies for mutant p53-driven cancers and other p53-related cancers. This engine consists of three complementary drivers:

- **Deep understanding of, and leadership in, p53 biology that enable unique insights into targeting individual mutations and targeting other p53-related cancers.** We have leveraged more than four decades of research experience and developed unique insights into p53 biology, a field that was discovered and established by our co-founder Dr. Arnold Levine. Additionally, our SAB consists of some of the most prominent thought leaders in p53 biology. p53 is a highly complex gene, and thousands of distinct p53 mutations have been identified. A blanket approach to targeting mutant p53 has significant challenges, as a "one size fits all" drug is unlikely to address all p53 mutants. Based on our experience and expertise, we are developing oral small molecules that each selectively structurally correct a specific p53 hotspot mutation.
- **Ability to design structure-based oral small molecule product candidates that selectively target and correct specific p53 mutants and inhibitors of wild-type p53.** Designing molecules for p53 mutants requires an intricate understanding of the p53 protein structure and the associated biology. We leverage structure-based technologies to give our oral small molecule product candidates access to challenging binding sites that are generally not accessible using conventional small molecule drug discovery approaches. For each target, we take detailed data from structural and functional studies of mutated p53 proteins to design development candidates against the challenging binding sites. Our design techniques help us to identify potential product candidates that can selectively target a single p53 mutant, while sparing wild-type p53.
- **Assays, screens, preclinical model systems and biomarkers that enable us to assess and optimize selective small molecule product candidates.** We test our product candidates across a diverse set of human cancer cells based on research and understanding of bioinformatics and functional genomics. We also identify and monitor pharmacodynamic biomarkers and surrogates of clinical activity to help measure target engagement, including MIC-1, a serum-based biomarker. The biological insights we generate help us to better target various p53 mutants based on their structure and biology. In addition, we have built assays, screens and preclinical model systems and biomarkers that help assess and optimize our product candidates that target other p53-related cancers. We develop innovative preclinical *in vitro* and *in vivo* models to advance potential therapeutic programs for translation to the clinic.

Our Product Candidate and Development Programs

We are leveraging our precision oncology platform to develop a pipeline of oral small molecule product candidates that structurally correct other p53 hotspot mutations to restore their wild-type function and product candidates that target other p53-related cancers. We own worldwide commercial rights to all of our programs. An overview of our development pipeline is shown in the table below.



(1) In Discovery, we screen compounds against biological assays to identify lead compounds.

(2) In Lead Optimization, we modify the lead compound to improve potency, selectivity, pharmacokinetic and toxicity parameters and physical chemical properties important for clinical development.

(3) In IND-Enabling Studies, we conduct preclinical studies, in accordance with GLP required for an IND submission to the FDA.

We expect to initially seek approval of our product candidates in most instances, including with PC14586, at least as a second line therapy or for patients with no satisfactory alternative treatments or where the cancer has progressed following other treatment. Subsequently, depending on the nature of the clinical data and experience with any approved products or product candidates, if any, we may pursue approval as an earlier line therapy and potentially as a first line therapy. Cancer therapies are sometimes characterized as first line, second line or third line, and the FDA customarily approves new therapies for a second line or later lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapies, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery or a combination of these, proves unsuccessful, second line therapies may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies.

PC14586: A Selective Structural Corrector of p53 Y220C Mutations

p53 is the most widely mutated gene in human cancers. The vast majority of these mutations occur as a result of missense mutations that are found in the DNA binding domain. p53 Y220C mutations are found in approximately 1.0-1.5% of all cancers. This particular mutation is expressed in a large variety of solid tumors, including breast, NSCLC, colorectal, pancreatic and ovarian cancers. Our lead product candidate, PC14586, is designed to be an orally available small molecule that structurally corrects a p53 protein containing the Y220C mutation and restores wild-type p53 function.

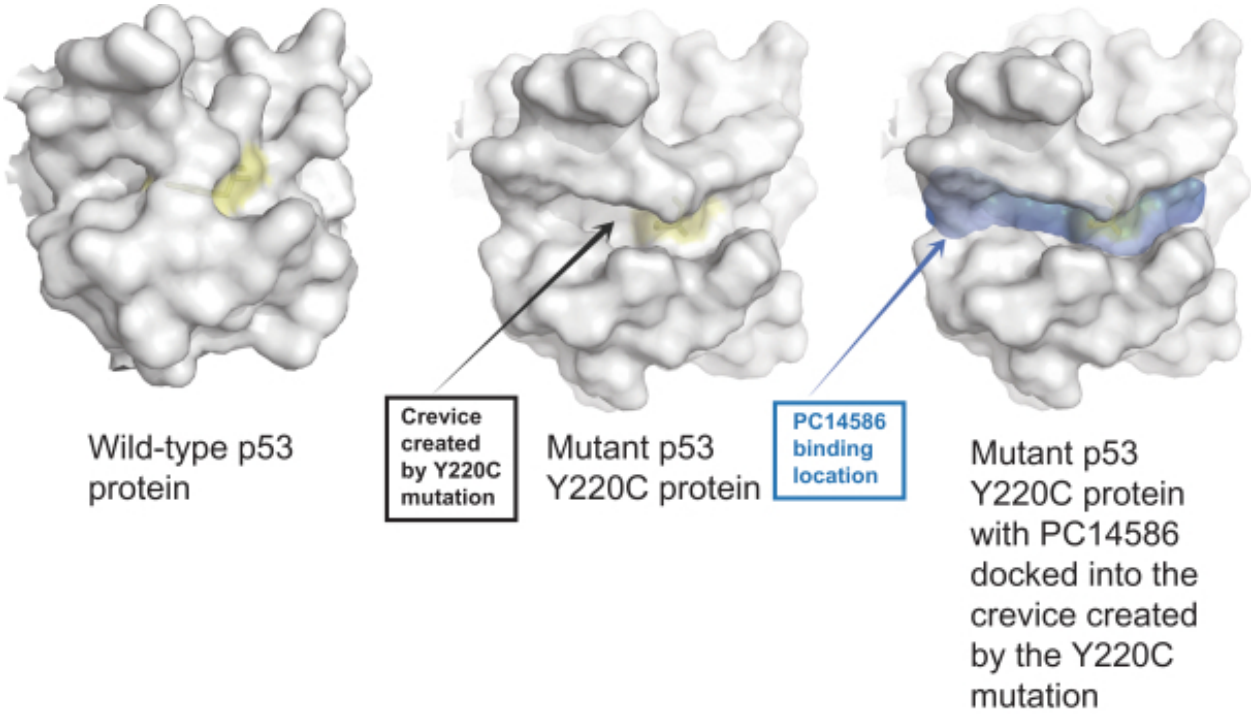
Wild-type p53 in a normal cell is at low to undetectable levels, but an external insult such as UV radiation or exposure to a carcinogen results in activation and upregulation of the protein. In these instances, wild-type p53 pauses the cell-cycle to survey the integrity of the genome, and if the damage to the genome cannot be repaired, wild-type p53 induces a potent program of cell suicide or programed cell death. Given wild-type p53's profound ability to induce cell death, it is tightly regulated in normal biology by an auto-regulatory loop with MDM2, a downstream induced target of wild-type p53 transcriptional activation. MDM2 production results in degradation of the wild-type p53 protein and re-sets the cell to normal function.

In the case of a mutant p53, there is a loss of p53 wild-type tumor suppression function due to a loss of downstream wild-type p53 transcriptional activation, including MDM2 induction. A consequence of this dysregulation is the inability of the cancer cell to degrade mutant forms of p53, resulting in a profound accumulation of mutant p53 protein in the cancer cell.

While treatment options such as surgery, chemotherapy, radiotherapy and immuno-therapy are available for breast, NSCLC, colorectal, pancreatic and ovarian cancer, there are no approved precision oncology therapies for the subset of patients with the p53 Y220C mutation. The availability of an oral small molecule selective for the p53 Y220C mutation may offer a novel precision therapy for this population, which we believe could potentially change the treatment paradigm for such patients.

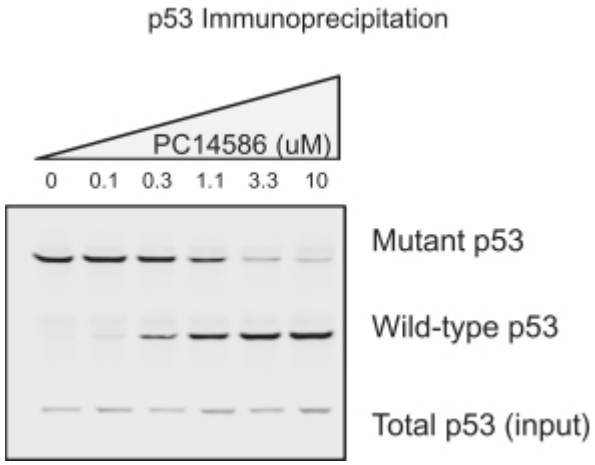
Mechanism of Action

PC14586 is an orally available small molecule candidate that is designed to selectively bind to the crevice created by the p53 Y220C mutation, and thereby restore the wild-type p53 protein structure and tumor suppressing function. In the diagram below, wild-type p53 protein is compared with a mutant p53 Y220C protein and a mutant p53 Y220C protein with PC14586 bound in the crevice created by the Y220C mutation. By docking into the crevice created by the Y220C mutation, PC14586 is designed to restore the wild-type p53 conformation and function.



In preclinical studies, we have demonstrated that PC14586 rapidly converts the large protein pool of mutant p53 Y220C protein to wild-type structure. As seen in the graphic below, in an *in vitro* study, PC14586 induced conversion of p53 protein from mutant to wild-type conformation in a dose-dependent manner as evidenced by a decrease in mutant p53 and an increase in wild-type p53, while total p53 remains relatively unchanged.

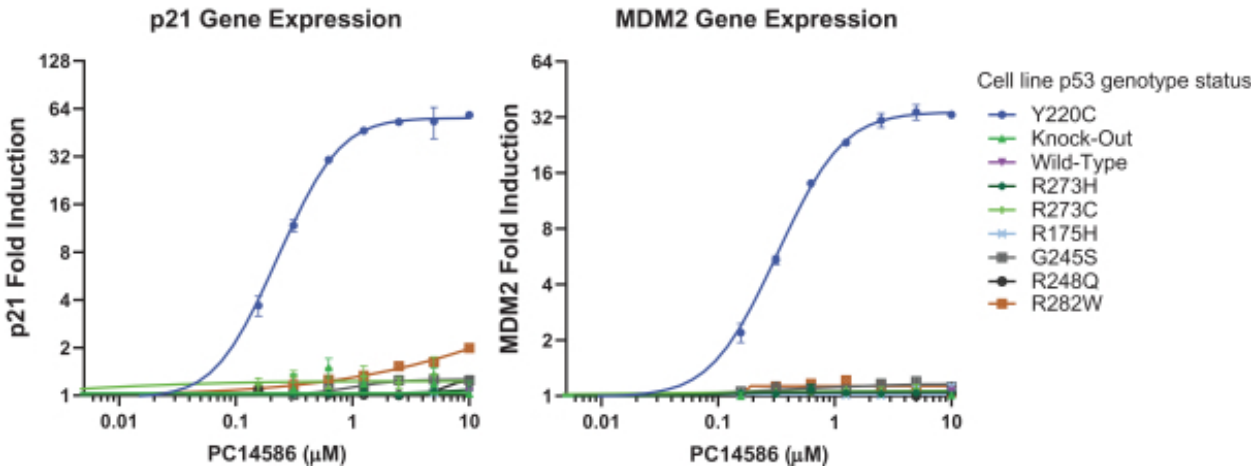
PC14586 Demonstrated Structural Conversion from Mutant p53 to Wild-type p53 *in vitro*



PC14586 selectively binds to the crevice created by the Y220C mutation as this molecule does not bind to wild-type p53 or other p53 mutations, including R273H, R273C, R175H, G245S, R248Q and R282W, as demonstrated by the lack of activity (as measured by p21 and MDM2 gene expression seen in the below diagrams). PC14586 only binds to the crevice created by the Y220C mutation, and none of the other tested p53 hotspot mutations, as illustrated by gene expression changes in the Y220C cell line when PC14586 is added in increasing concentrations.

Additionally, structural correction from a mutant p53 Y220C conformation to a wild-type p53 conformation by PC14586 restored p53-dependent transcription of downstream targets, which is indicative of wild-type p53 biological activity. For example, as shown in the figures below, p21 and MDM2, two of the downstream targets of p53, were selectively upregulated by PC14586 in a dose-dependent manner in cells where the p53 Y220C mutation was present. Since PC14586 is highly selective for the p53 Y220C mutation, it did not affect expression levels of p21 and MDM2 in tumor cell lines containing wild-type p53, p53 knock-out or other p53 hotspot mutations as noted in the figures below.

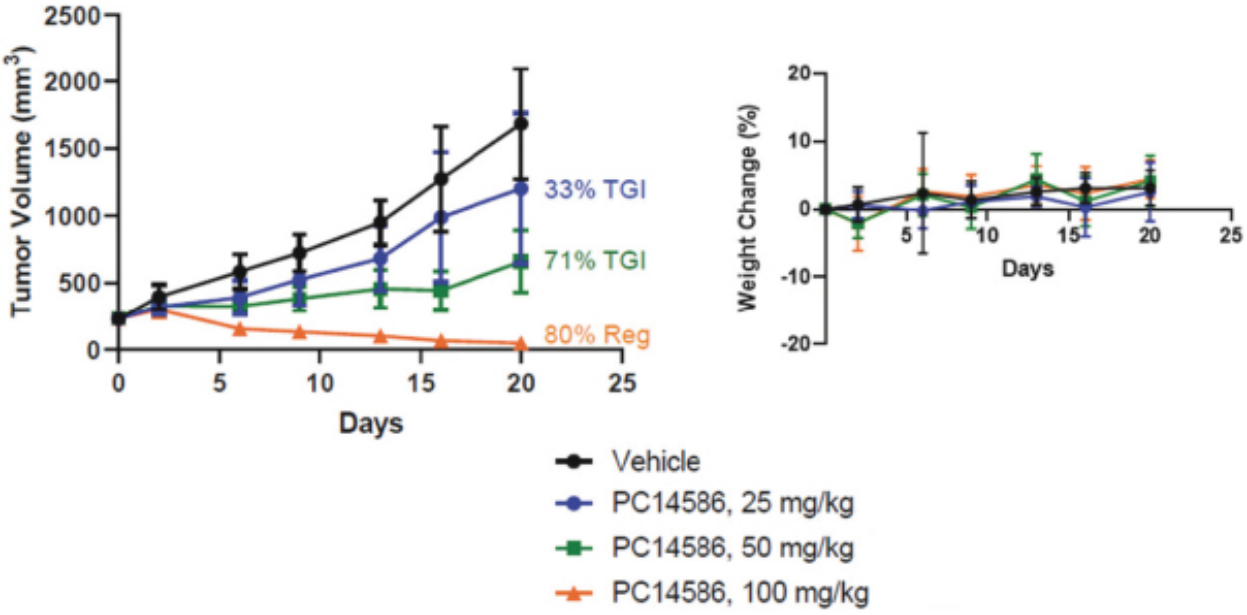
PC14586 Induced Transcription of p21 and MDM2 Only in Cell Lines with the p53 Y220C Mutation



Preclinical In Vivo Data

PC14586 exhibited single-agent anti-tumor activity in a dose-dependent manner against mutant p53 Y220C tumors, evidenced by both potent TGI and tumor regression. Oral once-daily dosing over 21 days of PC14586 was well tolerated in nude mice (ten mice per dosing group) bearing p53 Y220C NUGC3 xenograft tumors up to 100 mg/kg, as evidenced by the lack of body weight loss, which is the generally accepted surrogate for toxicity in mice. PC14586 demonstrated dose-dependent TGI at daily doses ranging from 25 mg/kg to 50 mg/kg and robust tumor regression at 100 mg/kg daily.

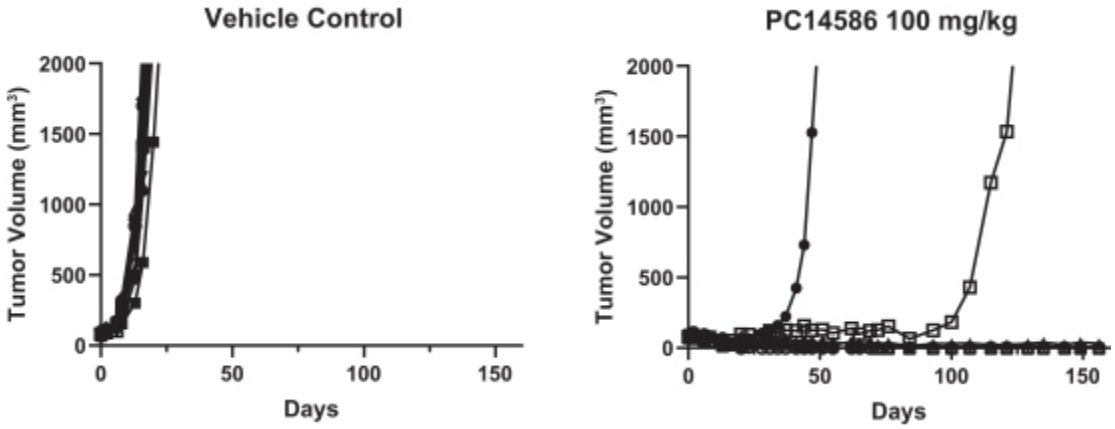
PC14586 Single-Agent Administration in NUGC3 Xenograft Model Resulted in Tumor Regression and was Well Tolerated



We also created a human p53 knock-in, or HUPKI, mouse that expresses a p53 protein with the human p53 DNA binding domain and the p53 Y220C mutation. The HUPKI mouse presents spontaneously with sarcomas at six to eight months of age, which we can harvest and re-implant in a wild-type mouse to create a mouse tumor model that has an intact immune system harboring a human p53 Y220C mutation. We believe this syngeneic mouse model better represents the patient population that we expect to see in the clinic, as compared to mouse xenograft models that incorporate human tumors in mice with no immune system. While some patients with cancer may have weakened immune systems, we believe that few patients have severely or fully dysfunctional immunocompromised systems, and therefore a syngeneic model may better represent the patient population than an immunocompromised mouse model. In addition, with an intact immune system, this model allows us to test anti-tumor activity of PC14586 in combination with immune checkpoint inhibitors.

As illustrated by the table below, PC14586, administered as a single-agent at a daily oral dose of 100 mg/kg for 70 days, demonstrated regression in tumors that express the p53 Y220C mutation in the syngeneic mouse model. The durability of the response was measured by median survival, where median survival for a 100 mg/kg dose of PC14586 exceeded 156 days, even though drug treatment was discontinued on day 70. This compared with median survival of only 17 days for the vehicle.

PC14586 Tumor Regression and Durable Responses in Syngeneic Mouse Model



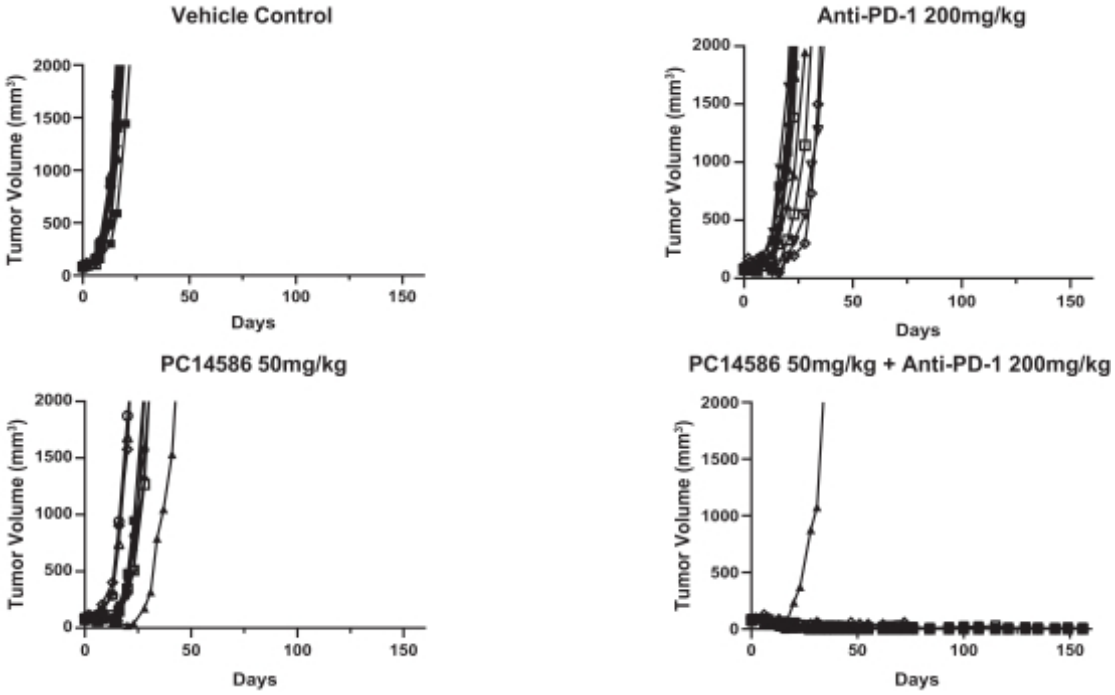
Note: Each line represents each mouse where each group has 10 mice

Group	Median Survival Time (Days)
Vehicle	17
PC14586 100 mg/kg	>156

Note: Dosing ceased on day 70 in the PC14586 arm.

PC14586 also exhibited anti-tumor activity in combination with anti-PD-1 therapy in syngeneic mouse models with the human p53 Y220C mutation. The scientific rationale for such a combination comes from the emerging literature suggesting an interplay between p53 and the immune system, which is the key mechanism of action of cancer immunotherapies such as anti-PD-1 antibodies. When PC14586 was administered at a sub-therapeutic daily oral dose of 50 mg/kg for 70 days in combination with a therapeutic dose of a PD-1 antibody, regression of tumors that express the p53 Y220C mutation was observed. As illustrated by the table below, median survival for a sub-therapeutic dose of PC14586 combined with anti-PD-1 treatment exceeded 156 days, even though drug treatment was discontinued on day 70, compared with median survival of only 24 days for anti-PD-1 treatment alone.

PC14586 + Anti-PD-1 Combination Showed Regression of Tumor Growth in Syngeneic Mouse Model



Note: Each line represents each mouse where each group has 10 mice

Group	Median Survival Time (Days)
Vehicle	17
Anti-PD-1 200 mg/kg	24
PC14586 50 mg/kg	28
PC14586 50 mg/kg + Anti-PD-1 200 mg/kg	>156

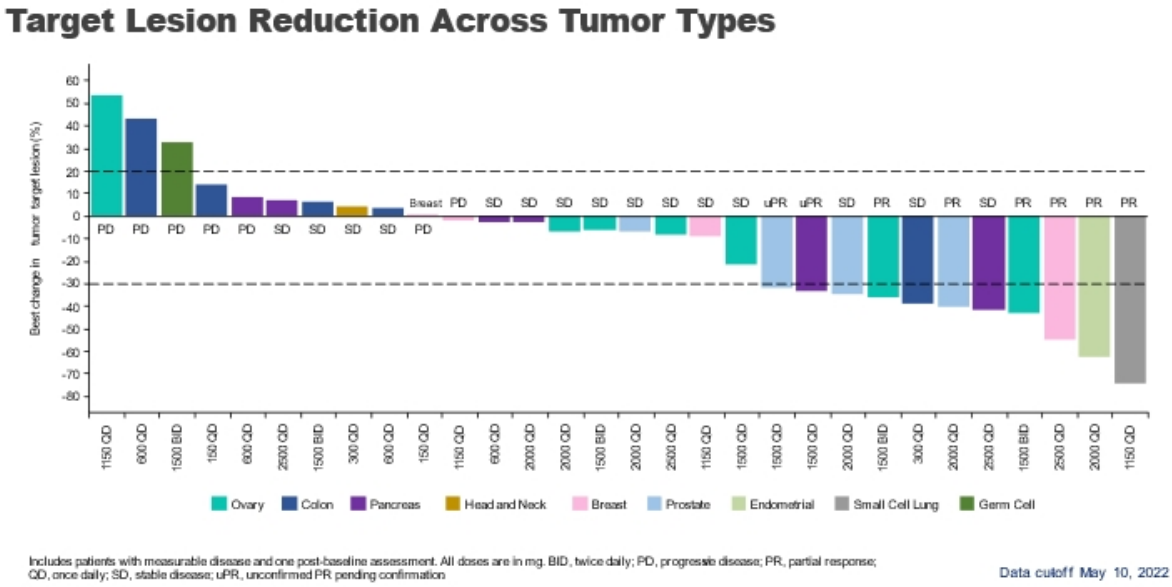
Note: Dosing ceased on day 70 in the PC14586 + Anti-PD-1 arm.

Clinical Development Plan of PC14586

We initiated a Phase 1/2 clinical trial, PYNNACLE, for PC14586 in October 2020. In addition, we were granted FDA Fast Track designation of PC14586 for the treatment of patients with locally advanced or metastatic solid tumors with a p53 Y220C mutation in October 2020. We dosed our first patient in this clinical trial in the fourth quarter of 2020.

In June 2022, we provided an update on the Phase 1/2 trial at the 2022 American Society for Clinical Oncology (ASCO) Annual Meeting. The interim data, as of a May 10, 2022 efficacy data cutoff date, included enrollment of 41 patients with the p53 Y220C mutation, 33 of whom had measurable disease and were included in the primary analysis. Patients in the study had a median age of 62 (range of 32-74 years of age) with a range of tumor types and were heavily pretreated with a median of three prior lines of therapy. Of these patients, 25 patients with measurable disease were treated in the efficacious dose range, which was defined as a dose from 1150mg QD to 1500mg BID. In the efficacious dose range, partial responses were observed by investigator review (RECIST v1.1) in 32% (six confirmed partial responses and two partial responses pending confirmation as of the cutoff date) across six different tumor types. Best response of stable disease (SD) or PR was observed in 19 of the 25 patients (76%) in the efficacious dose range.

In the ongoing monotherapy dose escalation phase of our trial, we continue to enroll patients to evaluate the preliminary safety, efficacy, and pharmacokinetics of PC14586 to establish the recommended dose for Phase 2.



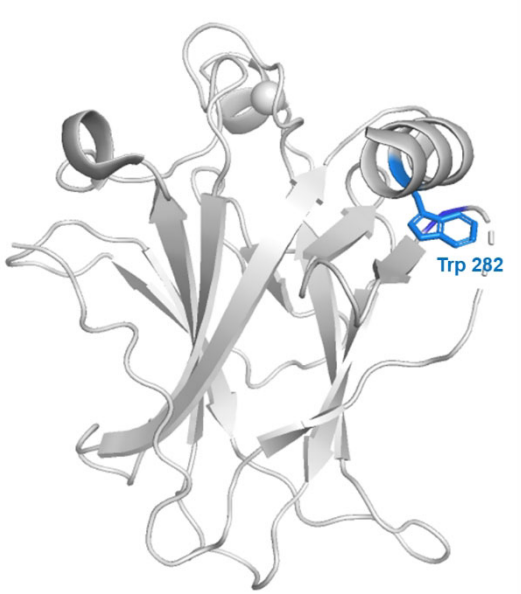
PC14586 was observed to be generally well-tolerated (across 41 patients treated with PC14586 monotherapy as of May 10, 2022). The majority of adverse events were mild or moderate (Grade 1 or 2) in severity with the most frequent adverse events being nausea, vomiting, aspartate transaminase (AST)/alanine transaminase (ALT) increase, anemia, blood creatine increase and fatigue.

PC14586 in a Clinical Collaboration with Merck

As a result of the preclinical combination data with PC14586 and an anti-PD1 antibody, we are evaluating this combination in patients. In July 2022, we announced a clinical collaboration agreement with Merck to evaluate the combination of PC14586 and Merck's anti-PD1 antibody, KEYTRUDA (pembrolizumab), in patients with advanced solid tumors in patients with a p53 Y220C mutation. This study is being conducted as a separate arm of our ongoing Phase 1/2 PYNNACLE trial in patients with advanced solid tumors. Approximately 36 patients are expected to be enrolled in the combination arm of the trial. This combination arm will assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PC14586 in combination with KEYTRUDA in patients with advanced solid tumors harboring a p53 Y220C mutation. Under the terms of the agreement, we will sponsor the trial and Merck will supply KEYTRUDA. In December 2022, we initiated enrollment in the PC14586 + pembrolizumab arm of the PYNNACLE study.

R282W: Our Second Mutant p53 Program

R282W is the sixth most frequent p53 mutation and accounts for approximately 2.8% of all TP53 mutations. The R282W mutation results from arginine being substituted by a tryptophan at amino acid position 282 and is considered a structural mutation. This structural mutation is thermodynamically unstable and cause the protein to lose shape and therefore its wild-type DNA binding activity at physiological temperature. This results in a lack of p53 transcription and pathway activation.



We are generating molecules designed to structurally correct the R282W p53 protein to restore its binding to the DNA. Our R282W program continues to progress towards lead optimization.

Other Pipeline Programs

In addition to our PC14586 Y220C and R282W programs, we are focused on developing a pipeline of product candidates targeting other p53 hotspot mutations and targeting inhibitors of wild-type p53. These programs have been developed internally using our precision oncology platform and expertise.

We are able to utilize the same general principles and similar drug discovery methods developed from our PC14586 Y220C program across other p53 hotspot mutations to facilitate the discovery of additional new product candidates. We study the structural and functional properties of the target. We use assays, screens, preclinical model systems and biomarkers to assess and optimize selective small molecules for specific p53 mutants. Specifically, many of the efficiencies from assays and model systems developed for our PC14586 Y220C program are being applied to other p53 hotspot mutations. In addition, the key insights gained from the medicinal chemistry campaigns are being leveraged across other p53 hotspot mutations. By leveraging our team's depth of expertise around p53, we are positioned to accelerate our efforts to expand the pipeline of therapies that selectively target p53 hotspot mutations and other p53-related cancers.

Competition

Our industry is intensely competitive and subject to rapid and significant technological change, as well as strong defense of intellectual property. While we believe that our knowledge, experience and scientific resources provide us with competitive advantages, we face substantial competition from major pharmaceutical companies and biotechnology companies worldwide. Many of our competitors have significantly greater financial, technical and human resources. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

We are a precision oncology company pioneering the discovery and development of small molecule therapies targeting p53 mutations and other p53-related cancers. We are aware of other product candidates that are in clinical development as potential treatments of various cancers through the modulation of p53. There are many product candidates that may affect the p53 pathway, such as through MDM2 inhibition. We are aware of molecules in development that also are being explored for p53 upregulation/activation in various stages of preclinical or clinical development being tested by Aprea Therapeutics and Jacobio Pharmaceuticals, among others. We are also aware of selective small molecule inhibitors that are designed to target wild-type p53 containing tumors through the p53-MDM2 interaction, which are in various stages of clinical development being tested by Aileron Therapeutics, Ascentage Pharma, Boehringer Ingelheim, Daiichi Sankyo (out-licensed worldwide rights to Rain Therapeutics), Kartos Therapeutics, Kymera Therapeutics, Otsuka Pharmaceutical, Novartis and Roche, including testing MDM2 inhibitors in combination with a variety of other anti-cancer agents.

We face competition with respect to our current product candidates and will face competition with respect to future product candidates, from segments of the pharmaceutical, biotechnology and other related markets that pursue targeted therapies for patients with genetically-defined cancers. If PC14586 or our future product candidates do not offer sustainable advantages over competing products, we may otherwise not be able to successfully compete against current and future competitors.

Our competitors may obtain regulatory approval of their products more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products.

In addition, we will likely need to develop our product candidates in collaboration with companion diagnostic companies, and we will face competition from other companies in establishing these collaborations. Our competitors will also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Furthermore, we also face competition more broadly across the market for cost-effective and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy or a combination of such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic, including branded generic, products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market will pose challenges. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

Manufacturing

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates undergoing preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval.

All of our product candidates are small molecules and are manufactured in synthetic processes from available starting materials. The chemistry appears amenable to scale up and does not currently require unusual equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

We generally expect to rely on third parties for the manufacture of companion diagnostics for our products, which are assays or tests to identify an appropriate patient population. Depending on the technology solutions we choose, we may rely on multiple third parties to manufacture and sell a single test.

Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with current Good Manufacturing Practice, or cGMP, requirements which impose certain production, manufacturing, procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP requirements and other aspects of regulatory compliance.

Commercialization

Subject to receiving marketing approvals, we expect to commence commercialization activities by building a focused sales and marketing organization to sell our products. We believe that such an organization will be able to address the community of oncologists who are the key specialists in treating the patient populations for which our product candidates are being developed.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine.

Intellectual Property

We strive to protect the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights. We also rely on know-how relating to our proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain our proprietary position. We also plan to rely on data exclusivity, market exclusivity and patent term extensions when available. Our commercial success will depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions and improvements; to defend and enforce our proprietary rights, including any patents that we may own in the future; and to operate without infringing the valid and enforceable patents and other proprietary rights of third parties. Intellectual property rights may not address all potential threats to our competitive advantage.

With respect to our existing and future product candidates and processes we intend to develop and commercialize in the normal course of business, we intend to pursue further patent protection covering, when possible, compositions, methods of use, dosing and formulations. We also may pursue patent protection with respect to manufacturing and drug development processes and technologies. Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies. We may not be able to obtain patent protections for our compositions, methods of use, dosing and formulations, manufacturing and drug development processes and technologies throughout the world. Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the United States can provide exclusionary rights for 20 years from the earliest effective filing date. In addition, in certain instances, the term of an issued U.S. patent that is directed to or claims an FDA-approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. This process is called "patent term extension." The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the United States varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of biopharmaceuticals has emerged in the United States. The relevant patent laws and their interpretation outside of the United States are also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have, or may obtain, blocking patents of which we are currently unaware that could be used to prevent us from developing or commercializing our product candidates and practicing our proprietary technology. Further, defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties or redesign our products. Doing so may be impossible or require substantial time and monetary expenditure. We may also elect to enter into a license agreement to settle litigation or to resolve disputes prior to litigation. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. Should a license to a third party patent become necessary, we cannot predict whether we would be able to obtain a license, or if a license were available, whether it would be available on commercially reasonable terms. If such a license is necessary and a license under the applicable patent is unavailable on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed. This scenario could materially adversely affect our business. Even if we obtain a license to third party intellectual property, we may later decide, or it may later become necessary, to terminate the license. If we do so, we may no longer be free to use the technology protected by the patents no longer under license. Also, if a competitor developed the technology protected by the patents no longer under license, we would not be able to block the competitor's progress. If the competitor's product was competitive with ours, then we may suffer economic harm from the competitive product.

The issuance of a patent is not conclusive as to its scope, validity or enforceability and our issued patents may be challenged, invalidated, deemed unenforceable or circumvented. These scenarios could limit our ability to stop competitors from marketing-related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. 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. Moreover, any efforts to enforce our intellectual property rights are likely to be costly and may divert the efforts of our scientific and management personnel. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may also be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. 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, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to our product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent directed to such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

We generally file a provisional patent application with the U.S. Patent and Trademark Office, or USPTO, first and then subsequently file a corresponding non-provisional patent application. This process enables us to establish an earlier effective filing date in the subsequently filed non-provisional patent application. To benefit from the earlier effective filing date, we must file a corresponding non-provisional patent application, such as a utility application in the United States or an international application under the Patent Cooperation Treaty, or PCT, within 12 months of the date of the provisional patent application filing. Based on a PCT filing, we may file national and regional patent applications in the United States or foreign jurisdictions, such as the European Union, China, Japan and possibly others. To date, we have not filed for patent protection in all national and regional jurisdictions where such protection may be available, and we may decide to abandon national and regional patent applications before a patent is granted. In addition, the patent grant proceeding for each national or regional patent application that we file is an independent proceeding. As a result, it is possible for a patent application to be granted in one jurisdiction and denied in another jurisdiction, and depending on the jurisdiction, the scope of patent protection may vary. As of January 31, 2023, we owned three issued US patents and five granted foreign patents relating to methods of use and composition of matter of PMV compounds, including PC14586, at least 20 pending US patent applications, and at least 40 pending foreign patent applications, each of which relates to methods of use and composition of matter of PMV compounds. The three issued US patents are expected to expire in 2037, without taking into account any possible patent term adjustment or extensions.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, preclinical and clinical testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. Generally, before a new drug can be marketed, considerable data must be generated, which demonstrates the drug's quality, safety and efficacy. Such data must then be organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Food, Drug and Cosmetic Act, or FDCA, and its implementing regulations. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with FDA's good laboratory practice requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA after completion of all pivotal trials;
- determination by the FDA within 60 days of its receipt of an NDA to accept the filing for substantive review;
- 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 drug is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, and of selected clinical investigation sites to assess compliance with GCP requirements; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB or ethics committee for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, such as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, FDA may require, or sponsors may voluntarily pursue, post-approval trials, sometimes referred to as Phase 4 studies, that are conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, such as with accelerated approval drugs, the FDA may mandate the performance of post-approval clinical trials as a condition of approval of an NDA.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. In addition, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 1 and Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the meetings at the end of the Phase 2 trial to discuss Phase 2 clinical results and present plans for the pivotal Phase 3 clinical trials that they believe will support approval of the new drug.

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

While the IND is active and before approval, progress reports summarizing the results of the clinical trials and nonclinical studies performed since the last progress report must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans and any clinically important increased incidence of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure.

To the extent our clinical trial plans and future planned clinical trials may be adversely affected, delayed or interrupted by the ongoing COVID-19 pandemic, we may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects participating in clinical trials during the COVID-19 pandemic. For example, since March 2020, the FDA has issued various COVID-19 related guidance documents for trial sponsors and manufacturers, including guidance on conducting clinical trials during the pandemic, cGMP requirements, remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities, and drug product manufacturing and supply chain inspections, among others. The extent to which the COVID-19 pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence. Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of the termination of the public health emergencies on FDA and other regulatory policies and operations are unclear.

NDA Review and Approval Process

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing complies with cGMP requirements to assure and preserve the product's identity, strength, quality and purity. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

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

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP requirements. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA to address all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the NDA with a REMS to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Expedited Development and Review Programs

The FDA has various programs, including Fast Track designation, breakthrough therapy designation, accelerated approval and priority review, that are intended to expedite the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions. For example, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life- threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. The sponsor of a Fast Track product has opportunities for frequent interactions with the review team during product development and, once a NDA is submitted, the product may be eligible for priority review. With regard to a Fast Track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a Fast Track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review, accelerated approval and breakthrough therapy designation. A product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval 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. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product. On December 29, 2022, the Consolidated Appropriations Act, 2023, including the Food and Drug Omnibus Reform Act (FDORA), was signed into law. FDORA made several changes to the FDA's authorities and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements.

The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as "breakthrough therapies" that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a product candidate as a "breakthrough therapy" if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.

Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Post-approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual program fees for any marketed products. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements, which impose certain production, manufacturing, procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- 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 the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy that are approved by the FDA and in accordance with the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. 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, in their independent professional medical judgment, 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. 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. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and 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 pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation, or ODD, to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with either a patient population of fewer than 200,000 individuals in the United States, or a patient population greater of than 200,000 individuals in the United States when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States of that drug or biologic. ODD must be requested before submitting an NDA. After the FDA grants ODD, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

If a product that has received ODD and subsequently receives the first FDA approval 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 a full NDA, to market the same biologic for the same indication for seven years from the approval of the NDA, 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 drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of ODD are tax credits for certain research and a waiver of the NDA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received ODD. In addition, orphan drug 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.

In *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in *Catalyst*, FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the *Catalyst*order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

Marketing Exclusivity

Market exclusivity provisions authorized under the FDCA can delay the submission and approval of certain marketing applications for products containing the same active ingredient. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application, or ANDA, or an NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from accepting ANDAs or 505(b)(2) NDAs for drugs referencing the approved application for review. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to any preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the United States. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials. In addition, orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

Other Healthcare Laws

Pharmaceutical manufacturers are subject to additional healthcare fraud and abuse laws, regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, U.S. federal anti-kickback, false claims, civil monetary penalty, consumer fraud, pricing reporting, data privacy and security and physician payment transparency laws and regulations as well as similar foreign laws in the jurisdictions outside the U.S. Similar state and local laws and regulations may also restrict business practices in the pharmaceutical industry, such as state anti-kickback and false claims laws, which may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers or by patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information; state and local laws which require tracking gifts and other remuneration and transfer of value provided to physicians, other healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives; and state and local laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by the Health Insurance Portability and Accountability Act of 1996, thus complicating compliance efforts.

The risk of being found in violation of these or other laws and regulations is increased by the fact that many have not been fully interpreted by the regulatory authorities or the courts and their provisions are open to various interpretations. These laws and regulations are subject to change, which can increase the resources needed for compliance and delay drug approval or commercialization. Any action brought against us for violations of these laws or regulations, even successfully defended, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Also, we may be subject to private "qui tam" actions brought by individual whistleblowers on behalf of the federal or state governments. Violation of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in government healthcare programs and imprisonment.

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. Significant uncertainty exists as to the coverage and reimbursement status of any newly approved product. Decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. One third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product. As a result, the coverage determination process can require manufacturers to provide scientific, cost-effectiveness and clinical support for the use of a product to each payor separately and can be a time-consuming process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. 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 or the treatment or procedure in which the product is used may not be available, which may impact physician utilization. In addition, companion diagnostic tests that are used with applicable pharmaceutical products require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical products, will apply to companion diagnostics.

Moreover, third-party payors are increasingly reducing coverage and reimbursement for pharmaceutical products and related services. The U.S. government and state legislatures have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical products, in addition to questioning their safety and efficacy. 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 product. Furthermore, there is no assurance that a product will be considered medically reasonable and necessary for a specific indication, will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be established even if coverage is available or that the third-party payors' reimbursement policies will not adversely affect the ability for manufacturers to sell products profitably. Decreases in third-party reimbursement for any product or a decision by a third-party payor not to cover a product could reduce physician usage and patient demand for the product.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Pharmaceutical products may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products and may also compete with imported foreign products.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. In March 2010, the Affordable Care Act, or ACA, was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers in the United States. By way of example, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15.1% to 23.1%; required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; creates a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year, effective April 1, 2013, which will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments can vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. Specifically, there have been several recent U.S. Presidential executive orders, Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of approved products, which could have a material impact on our business. In August 2022, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The impact of these and future reform measures on us and the pharmaceutical industry as a whole is unclear.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs.

FDA Approval and Regulation of Companion Diagnostics

We expect that our product candidates may require use of a diagnostic to identify appropriate patient populations for our products. These diagnostics, often referred to as companion diagnostics, are medical devices, often in vitro devices, which provide information that is essential for the safe and effective use of a corresponding drug. 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 two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval. We expect that any companion diagnostic developed for our product candidates will utilize the PMA pathway.

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. 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. 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.

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, 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 at the same time. The review of *in vitro* companion diagnostics in conjunction with the review of our therapeutic treatments for cancer will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics. The guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND alone, or both an IND and an IDE. 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. 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 United States.

Employees and Human Capital Resources

As of February 28, 2023, we had 62 full-time employees, including 22 employees with Ph.D., M.D. or Pharm.D. degrees. Of these full-time employees, 45 employees are engaged in research and development activities.

None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good. Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing, and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel though the granting of stock-based and cash-based compensation awards, to increase stockholder value and our success by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Environmental, Social and Governance (ESG) Initiatives

As an early clinical-stage precision oncology company, we are rooted in our mission to fundamentally disrupt the course of cancer for patients with p53 gene mutations and other p53-related cancers. We believe integrating responsible environmental, social, and governance principles into our corporate strategy will drive sustainable value creation for our shareholders, employees, patients, and caregivers over the long term. We have formed an internal ESG Working Group with cross-functional senior leadership, and oversight by the nominating and corporate governance committee of our board of directors to oversee our sustainability efforts and have documented our initiatives in our inaugural 2022 ESG Highlights Report, which is available on our website at ir.pmvpharma.com. The content provided in our 2022 ESG Highlights Report or accessible through our website is not incorporated by reference as part of this Annual Report on Form 10-K.

Corporate Information

We were incorporated in Delaware in March 2013 under the name "PJ Pharmaceuticals, Inc." In July 2013, we changed our name to "PMV Pharmaceuticals, Inc." Our principal executive offices are located at 1 Research Way, Princeton, New Jersey 08536. Our telephone number is (609) 642-6670. Our website address is www.pmvpharma.com. Information contained on, or that can be accessible through, our website is not a part of this Annual Report on Form 10-K and the inclusion of our website address in this Annual Report on Form 10-K is an inactive textual reference only.

We use the name "PMV Pharma," the "PMV Pharma" logo and other marks as unregistered trademarks in the United States and other countries. This Annual Report on Form 10-K contains references to our trademarks and service marks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Annual Report, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate in any way that we or their owners will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable owner to these trademarks and trade names. We do not intend our use or display of other entities' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Available Information

Our Internet address is www.pmvpharma.com. We will file or furnish periodic reports and amendments thereto, including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K (and amendments to those reports), proxy and information statements and other information filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, with the Securities and Exchange Commission, or the SEC. The SEC maintains a website that contains reports, proxy and information statement, and other information regarding issuers that file electronically, which may be accessed through the SEC at http://www.sec.gov. Our reports, amendments thereto, proxy statements and other information are also made available, free of charge, on our investor relations website at ir.pmvpharma.com as soon as reasonably practicable after we electronically file or furnish such information with the SEC. The information contained on the websites referenced in this Annual Report on Form 10-K is not incorporated by reference into this filing. Further, our references to website URLs are intended to be inactive textual references only. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and in our other filings with the SEC, before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could materially adversely affect our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risk Factors Summary

Investing in our common stock involves a high degree of risk because our business is subject to numerous risks and uncertainties, as fully described below. The principal factors and uncertainties that make investing in our common stock risky include, among others:

- we have a limited operating history, have not completed any clinical trials, and have no products approved for commercial sale;
- we have incurred significant losses since our inception, and we expect to incur significant net losses for the foreseeable future and may not be able to achieve or sustain revenue or profitability in the future;
- we have not generated any revenue from our product candidates and may never generate revenue or be profitable and our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates;
- we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success;
- we will require substantial additional capital to finance our operations;
- our discovery and preclinical and clinical development is focused on the development of precision medicines for patients with genetically defined cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs targeting p53 hotspot mutations and other p53-related cancers is novel, may never lead to marketable products and may not ultimately represent a significant market;
- we are very early in our development efforts and are substantially dependent on our lead product candidate, PC14586. If we are unable to advance, obtain regulatory approval for and commercialize PC14586, our business, financial condition and results of operations will be materially adversely affected;
- interim "top-line" and preliminary data that we announce for our initial open-label Phase 1/2 clinical trial for PC14586 may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. If the interim, top-line or preliminary data that we report differ from actual results, our ability to obtain approval for our product candidates may be adversely affected, which could materially adversely affect our business, financial condition and results of operations;
- the subset of cancer patients that we are targeting are expected to have certain p53 mutations and we may not be able to identify a sufficient number of patients whom we can recruit and retain for our clinical trials to obtain approval for our current or future product candidates;
- the regulatory approval processes of the U.S. Food and Drug Administration, or FDA, and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approvals for our product candidates, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired;

- we currently rely, and plan to rely in the future, on third parties to conduct and support preclinical and clinical development, and these third parties may not meet expectations;
- if we are unable to obtain and maintain sufficient patent and other intellectual property protection for our product candidates and technology, our competitors could develop and commercialize products and technology similar or identical to ours;
- our success depends in part on our ability to protect our intellectual property; and
- our ability to develop companion diagnostics with third party collaborators, which must also separately be approved as medical devices by the FDA.

Risks Related to Our Limited Operating History, Business, Financial Condition, Results of Operations and Need for Additional Capital

We have a limited operating history, have not completed any clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and viability.

We are a clinical stage biotechnology company with a limited operating history. We commenced operations in March 2013, and our operations to date have been primarily limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, undertaking preclinical studies and, more recently, clinical studies, and establishing arrangements with third parties for the manufacture of initial quantities of product candidates. In September 2020, our lead product candidate, PC14586, received authorization to proceed under an investigational new drug application, or IND, with the FDA. Then, in October 2020, we received Fast Track designation for PC14586, from the FDA, and in the fourth quarter of 2020, we initiated patient dosing in our Phase 1/2 clinical trial of PC14586. We announced preliminary results from the Phase 1/2 clinical trial of PC14586 in June 2022, and have entered into a clinical trial collaboration with Merck to evaluate PC14586 in combination with Merck's anti-PD-1 therapy, KEYTRUDA, in patients with advanced solid tumors harboring a p53 Y220C mutation. We have not demonstrated an ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, 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.

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

We have incurred significant losses since inception, and we expect to incur significant losses for the foreseeable future and may not be able to achieve or sustain revenue or profitability in the future.

Investment in biopharmaceutical product development is a highly speculative undertaking and entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. We are still in the early stages of development of our product candidates. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. We have financed our operations primarily through private placements of our preferred stock and our initial public offering.

We have incurred significant net losses in each period since we commenced operations in March 2013. Our net losses were $73.3 million and $57.8 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $241.0 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Additionally, the net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indicator of our future performance.

We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase substantially if and as we:

- continue our research and development efforts and submit investigational new drug, or IND, applications for our product candidates;
- conduct preclinical studies and clinical trials;
- fail to demonstrate adequate efficacy or an acceptable safety profile in our clinical trials;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges;
- establish a sales, marketing and distribution infrastructure and scale-up manufacturing capabilities, whether alone or with third parties, to commercialize any product candidates for which we may obtain regulatory approval, if any;
- obtain, expand, maintain, enforce and protect our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel; and
- operate as a public company.

Because of the numerous risks and uncertainties associated with biopharmaceutical 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 succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development and other expenditures to develop, seek regulatory approval for and market additional product candidates. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We have not generated any revenue from our product candidates and may never generate revenue or be profitable. Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates.

Our ability to become profitable depends upon our ability to generate revenue. We have not received marketing approval for any product candidate, and we have not generated any revenue from any product sales. We do not expect to generate revenue unless or until we successfully complete preclinical and clinical development and obtain regulatory approval of, and then successfully commercialize, at least one product candidate. We announced preliminary results for our Phase 1/2 clinical trial of our lead product candidate, PC14586, in June 2022. We are continuing to transition from a company with a research focus to a company capable of supporting clinical development and commercial activities. We have not yet demonstrated our ability to successfully complete large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale product, or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. In addition, all of our other product candidates are still in preclinical development and have not been evaluated in humans. We face significant translational risk as our product candidates advance to the clinical stage, and promising results in preclinical studies may not be replicated in clinical trials. All of our current and future product candidates will require preclinical and clinical development, regulatory review and approval, substantial investment, access to sufficient commercial manufacturing capacity and significant marketing efforts before we can generate any revenue from product sales. Our ability to generate revenue depends on a number of factors, including, but not limited to:

- successful enrollment and timely completion of our clinical trials for our lead product candidate, PC14586, and timely initiation and completion of our preclinical studies for our future product candidates, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- establishing and maintaining relationships with contract research organizations, or CROs, and clinical sites for the clinical development of PC14586 and our future product candidates;
- our ability to complete IND-enabling studies and successfully submit and receive authorization to proceed under INDs or comparable applications;
- whether we are required by the FDA or other comparable foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- our ability to demonstrate to the satisfaction of the FDA and comparable foreign regulatory authorities the safety, efficacy, consistent manufacturing quality and acceptable risk-benefit profile of our small molecule product candidates or any future product candidates, and such regulatory authorities' acceptance of our tumor-agnostic development strategy;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future product candidates, if any;
- the timely receipt of necessary marketing approvals from the FDA and comparable foreign regulatory authorities;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of our product candidates or future product candidates over alternative or more conventional therapies, such as chemotherapy, to treat solid tumors;
- the actual and perceived availability, cost, risk profile and side effects and efficacy of our product candidates, if approved, relative to existing and future alternative cancer therapies and competitive product candidates and technologies;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities and develop, validate and maintain commercially viable manufacturing processes that are compliant with cGMP requirements;

- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the United States and internationally, if approved for marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- patient demand for our product candidates and any future product candidates, if approved;
- our ability to establish and enforce intellectual property rights in and to our product candidates or any future product candidates;
- obtaining coverage and adequate reimbursement by third-party payors for our product candidates;
- addressing any competing therapies and technological and market developments; and
- attracting, hiring and retaining qualified personnel.

Many of the factors listed above are beyond our control and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercializing our product candidates. Successful completion of preclinical studies and clinical trials does not mean that any of our current or future product candidates will receive regulatory approval. Even if regulatory approvals are obtained, we could experience significant delays or an inability to successfully commercialize our current and any future product candidates, which would materially harm our business. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the sale of our product candidates or any future product candidates, we may be unable to continue operations without continued funding.

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

Developing 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 conduct clinical trials of, and seek marketing approval for, PC14586, and advance our future product candidates. 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 or other regulatory agencies to perform preclinical studies or clinical trials 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 $243.5 million in cash, cash equivalents, and marketable securities. Although we believe that our available cash and cash equivalents will be sufficient to fund our planned operations at least through 2024, this belief 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.

Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing our current product candidates or any future product candidates we choose to pursue, and conducting preclinical studies and clinical trials, including our clinical trials of PC14586;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates or any future product candidates;

- the number and characteristics of any additional product candidates we develop or acquire;
- the timing and amount of any milestone, royalty and/or other payments we are required to make pursuant to any future license or collaboration agreements;
- the cost of manufacturing our product candidates or any future product candidates and any products we successfully commercialize;
- the cost of building a sales force in anticipation of product commercialization;
- the cost of commercialization activities of our product candidates, if approved for sale, including marketing, sales and distribution costs;
- our ability to establish future collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- any product liability or other lawsuits related to our products;
- the expenses needed to attract, hire and retain skilled personnel;
- the costs associated with being a public company;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing our intellectual property portfolio;
- the timing, receipt and amount of sales of any future approved products; and
- the impact of the COVID-19 pandemic, which may exacerbate the magnitude of the factors discussed above.

We do not have any committed external source of funds and adequate additional financing may not be available to us on acceptable terms, or at all. In addition, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions, inflation expectations, rising interest rates and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic and geopolitical tensions, such as the Ukraine-Russia war. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical trials or future commercialization efforts.

Risks Related to Product Development

Our discovery and product development is focused on the development of precision medicines for patients with genetically defined cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs targeting p53 is novel, may never lead to marketable products and may not ultimately represent a significant market.

The discovery and development of precision medicines for patients with genetically defined cancers is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. Further, despite decades of research on p53 as a target for precision medicines, prior product development efforts have been unsuccessful. Although we believe, based on our preclinical work and p53 research generally, that the top ten most frequent, or hotspot, p53 mutations have potential as precision oncology targets, clinical results may not confirm this hypothesis or may only confirm it for certain mutations or certain tumor types.

Further, even if our approach is successful in showing clinical benefit for tumors harboring the p53 mutation targeted by our lead product candidate, PC14586, we may never successfully identify additional product candidates for targeting p53 through our platform. Therefore, we do not know if our approach of treating patients with genetically defined cancers will be successful, and if our approach is unsuccessful, our business will be materially adversely affected.

In addition, because our approach targets genetically defined cancer patients and not specific tumors based on tumor or cancer types, we are initially pursuing a tumor-agnostic development strategy (*i.e.*, pursuing approval for a potential indication based on a specific genetic mutation rather than a specific type of tissue). There is currently a limited number of approved tumor-agnostic therapies and we may not receive approval for a broad tumor-agnostic indication or may be delayed in receiving broad tumor-agnostic approval. If our Phase 1/2 trial for PC14586 does not support a tumor-agnostic indication, but we observe clinical benefit in certain tumor or cancer types, we may decide to pursue a tumor- or cancer-specific indication which may require additional clinical trials. Further, even if our Phase 1/2 trial for PC14586 is successful, the FDA may not agree that such study can serve as a pivotal study, which would require us to conduct additional clinical trials prior to approval.

We are very early in our development efforts and are substantially dependent on our lead product candidate, PC14586. If we are unable to advance PC14586 or any of our future product candidates through clinical development, obtain regulatory approval and ultimately commercialize PC14586 or any of our future product candidates, or experience significant delays in doing so, our business, financial condition and results of operations will be materially adversely affected.

We are very early in our development efforts. We announced preliminary results for our Phase 1/2 clinical trial of our lead product candidate, PC14586, in June 2022. All of our other product candidates are still in preclinical development and have never been tested in human subjects. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization of PC14586 and one or more of our future product candidates. In addition, our product development programs contemplate the development with third party collaborators of companion diagnostics, which are assays or tests used to identify an appropriate patient population for our product candidates. Companion diagnostics are subject to regulation as medical devices and must themselves be approved for marketing by the FDA and comparable foreign regulatory agencies before we may commercialize such companion diagnostics with our product candidates. The success of our product candidates will depend on several factors, including the following:

- our ability to continue our business operations and product candidate research and development, and adapt to any changes in the regulatory approval process, manufacturing supply or clinical trial requirements and timing due to the ongoing COVID-19 pandemic and otherwise, including complying with new regulatory guidance or requirements on conducting clinical trials during the COVID-19 pandemic;

- timely and successful completion of preclinical studies and clinical trials;
- receipt of authorization to proceed under INDs for our planned clinical trials or future clinical trials;
- FDA acceptance of our tumor-agnostic development strategy;
- successful patient enrollment in and completion of clinical trials, which may be impacted by the COVID-19 pandemic;
- successful development with third party collaborators of companion diagnostics for use with our product candidates;
- safety, tolerability and efficacy profiles for our product candidates that are satisfactory to the FDA or any foreign regulatory authority for marketing approval;
- receipt of marketing approvals for our product candidates and any companion diagnostics from applicable regulatory authorities, which must be approved contemporaneously;
- completion of any required post-marketing approval commitments to applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of our product candidates, if any product candidates are approved;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other cancer therapies;
- obtaining and maintaining third-party coverage and adequate reimbursement; and
- maintaining a continued acceptable safety profile of our products following approval.

Many of these factors are beyond our control, and it is possible that we may never obtain regulatory approval for our product candidates even if we expend substantial time and resources seeking their development and approval. If we do not achieve regulatory approval in a timely manner or at all, we could experience significant delays or an inability to commercialize our current or future product candidates, which would materially adversely affect our business. If we do not receive regulatory approvals for our current or future product candidates, we will not be able to continue our operations.

The success of our business, including our ability to finance our company and generate revenue from products in the future, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and eventual commercialization of the product candidates we develop, which may never occur. Our current product candidates, and any future product candidates we develop, will require additional preclinical and clinical development, management of clinical, preclinical and manufacturing activities, marketing approval in the United States and other markets, demonstrating cost-effectiveness to pricing and reimbursement authorities, obtaining sufficient manufacturing supply for both clinical development and commercial production in accordance with cGMP, building of a commercial organization, and substantial investment and significant marketing efforts before we generate any revenue from product sales. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical trials or commercializing our product candidates on a timely or profitable basis, if at all. Changes in the manufacturing process or facilities will require further comparability analysis and approval by FDA before implementation, which could delay our clinical trials and product candidate development, and could require additional clinical trials, including bridging studies, to demonstrate consistent and continued safety and efficacy.

We have not previously submitted a NDA to the FDA or similar approval filings to a comparable foreign regulatory authority, for any product candidate. An NDA or other relevant regulatory filing must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe and effective for each desired indication. The NDA or other relevant regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product. We cannot be certain that our current or future product candidates will be successful in clinical trials or receive regulatory approval. Further, even if they are successful in clinical trials, our product candidates or any future product candidates may not receive regulatory approval. If we do not receive regulatory approvals for current or future product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market a product candidate, our revenue will depend, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights for each product candidate, as well as the availability of competitive products, whether there is sufficient third-party reimbursement and adoption by physicians.

The subset of cancer patients that we are targeting are expected to have certain p53 mutants and we may not be able to identify a sufficient number of patients whom we can recruit and retain for our clinical trials to obtain approval for our current or future product candidates.

The patient populations for our current product candidates are limited to those with specific p53 mutations, which represents a substantially smaller subset of the generally treated cancer patient population. We expect our future product candidates to be similarly limited. We will need to screen and identify patients with these targeted mutations. Further, even if we are successful in identifying patients, we cannot be certain that the resulting patient populations with each p53 hotspot mutation will be large enough to allow us to successfully conduct the requisite clinical trials necessary to obtain marketing approval for each mutation-specific product candidate before we can commercialize our products, if approved, and achieve profitability.

The results of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA or other comparable foreign regulatory authorities. Successful preclinical studies and clinical trials cannot provide assurance of successful commercialization.

We are required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective before we can seek marketing approvals for their commercial sale. Success in preclinical studies does not mean that future clinical trials will be successful. For instance, we do not know whether PC14586 will perform in its clinical trials as PC14586 has performed in preclinical studies, nor can we predict how our future product candidates will perform in future preclinical studies or clinical trials. Product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and other comparable foreign regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety, which could delay regulatory approval, limit the size of the patient population to which we may market our product candidates or prevent regulatory approval. In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our product candidates may also be undergoing surgical, radiation and chemotherapy treatments and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our product candidates. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes.

We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain approval to market any of our product candidates.

Even if we succeed in developing and commercializing our product candidates, we may never generate sufficient or sustainable revenue to enable us to be profitable.

We may need to use existing commercial diagnostic tests or develop or enter into a collaboration or partnership in the future to develop, novel companion diagnostics for some of our current or future product candidates. If we or our future partners are unable to successfully develop, validate and obtain approval for such companion diagnostics, or experience significant delays in doing so, we may not realize the full commercial potential of our future product candidates.

As one of the key elements of our product development strategy, we seek to identify cancer patient populations that may derive meaningful benefit from our current or future product candidates. Because specific genetic mutations will be used to identify the appropriate patients for our programs and our current or future product candidates, we believe that our success may depend, in part, on our ability to use existing diagnostic tests and genetic sequencing, or to develop novel companion diagnostics in collaboration with partners.

Such companion diagnostics would be used during our clinical trials as well as in connection with the commercialization of our product candidates. In our Phase 1/2 clinical trial, we are working with physicians and leading academic centers to enroll patients with the p53 Y220C mutation identified through next generation sequencing, or NGS. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges.

We have little experience as a company in the development of diagnostics. As such, we expect to rely on future partners for the design, development and manufacture of appropriate diagnostics to pair with our current or future product candidates. We have not yet begun discussions with any potential partners with respect to the development of companion diagnostics and may be unsuccessful in entering into collaborations for the development of companion diagnostics for our programs and our current or future product candidates. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these companion diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility or clinical validation of companion diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a companion diagnostic for a product candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the companion diagnostic.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities outside the United States as medical devices and require separate regulatory approval or clearance prior to commercialization. Moreover, the FDA generally requires the contemporaneous approval of companion diagnostics and the associated therapeutic.

We and our future collaborators may encounter difficulties in developing, obtaining regulatory approval for, manufacturing and commercializing companion diagnostics similar to those we face with respect to our product candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we, our partners, or any third parties that we engage to assist us, are unable to successfully develop and supply companion diagnostics for our current product candidates and any future product candidates, or experience delays in doing so:

- the development of our current product candidates and any future product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials; and
- we may not be able to obtain approval of our current product candidates and any future product candidates that require companion diagnostics on a timely basis or at all.

If any of these events were to occur, our business would be adversely impacted.

The COVID-19 pandemic could materially adversely impact our business, results of operations and financial condition, including our preclinical studies and clinical trials.

The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted, especially with respect to goods from China; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. While the extent of the impact of the COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID-19 pandemic could have a material adverse effect on our business, financial condition and results of operations. As a result of the COVID-19 pandemic, we may experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- delays or difficulties in enrolling and retaining patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- 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 of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as endoscopies that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- 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;
- interruptions in preclinical studies due to restricted or limited operations at our laboratory facility;
- 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 or delays to our sourced discovery and clinical activities; and
- changes in clinical site procedures and requirements as well as regulatory requirements for conducting clinical trials during the pandemic.

As a result of the COVID-19 pandemic, we continue to monitor changes in FDA policies and work with our clinical sites and investigators to mitigate potential risks to our ongoing clinical trials. The FDA, along with other global health authorities, has issued various guidance on COVID-19 related matters, including, among others, guidance for conducting clinical trials during the pandemic, manufacturing, supply chain, and drug and biological product inspections during the COVID-19 public health emergency; and GMP considerations for responding to COVID-19 infection in employees in biopharmaceutical manufacturing. If new guidance and policies are promulgated by the FDA that require changes in our clinical protocol or clinical development plans, our anticipated timelines and regulatory approval may be delayed or materially impacted. The extent to which the COVID-19 pandemic impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence.

The COVID-19 pandemic continues to evolve, with the status of operations and government restrictions evolving monthly. The extent to which the outbreak impacts our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the pandemic, travel restrictions and social distancing 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.

The trading prices for shares of other biopharmaceutical companies have been highly volatile partially as a result of the COVID-19 pandemic and the trading prices for shares of our common stock could also experience high volatility. In addition, broader markets have experienced significantly increased volatility due to, among other things, increases in inflation expectations, the corresponding increases in interest rate expectations and the Ukraine-Russia war. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of the COVID-19 could materially and adversely affect our business and the value of our common stock.

The ultimate impact of the COVID-19 pandemic on our business operations is highly uncertain and subject to change and will depend on future developments, which cannot be accurately predicted, including the duration of the pandemic, the ultimate geographic spread of the disease, additional or modified government actions, new information that will emerge concerning the severity and impact of COVID-19 and the actions taken to contain COVID-19 or address its impact in the short and long term, among others. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, our research programs, healthcare systems or the global economy. We will continue to monitor the situation closely.

If we experience delays or difficulties in the enrollment and/or retention of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials on a timely basis or at all for our product candidates if we are unable to recruit and enroll a sufficient number of eligible patients to participate in these trials through completion of such trials as required by the FDA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. For example, our enrollment for clinical trials of PC14586 will require patients to have the specific p53 Y220C mutation. If we are unable to locate a sufficient number of such patients, our clinical trial and development plans could be delayed.

Enrollment of patients in our clinical trials may be delayed or limited as our clinical trial sites limit their onsite staff or temporarily close as a result of the COVID-19 pandemic. In addition, patients may not be able to visit clinical trial sites for dosing or data collection purposes due to limitations on travel and physical distancing imposed or recommended by federal or state governments or patients' reluctance to visit the clinical trial sites during the pandemic. The drop-out rates in our clinical trials may be increased during the pandemic. Clinical trial patients who become infected with the COVID-19 virus may complicate the clinical trial data, procedures and analysis. These factors resulting from the COVID-19 pandemic could delay the anticipated readouts from our PC14586 clinical trials and our regulatory submissions, and increase the costs associated of the clinical trials.

Patient enrollment may also be affected if our competitors have ongoing clinical trials for programs that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' programs. Patient enrollment for our current or any future clinical trials may be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol;
- perceived risks and benefits of the product candidate under study;

- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or future product candidates being investigated for the indications we are investigating;
- clinicians' willingness to screen their patients for biomarkers to indicate which patients may be eligible for enrollment in our clinical trials;
- delays in or temporary suspension of the enrollment of patients in our clinical trials due to the COVID-19 pandemic;
- ability to obtain and maintain patient consents;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion, including as a result of contracting COVID-19 or other health conditions or being forced to quarantine, or, because they may be late-stage cancer patients, will not survive the full terms of the clinical trials.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods.

The market opportunities for our product candidates may be relatively small as it will be limited to those patients who are ineligible for or have failed prior treatments and our estimates of the prevalence of our target patient populations may be inaccurate.

Cancer therapies are sometimes characterized as first line, second line, or third line, and the FDA customarily approves new therapies only for a second line or later lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapies, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules or a combination of these. Third line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect to initially seek approval of our product candidates in most instances at least as a second line therapy. Subsequently, depending on the nature of the clinical data and experience with any approved products or product candidates, if any, we may pursue approval as an earlier line therapy and potentially as a first line therapy. But there is no guarantee that our product candidates, even if approved as a second or subsequent line of therapy, would be approved for an earlier line of therapy, and, prior to any such approvals, we may have to conduct additional clinical trials.

Our projections of both the number of people who have the p53 hotspot mutations we are targeting, who may have their tumors genetically sequenced, as well as the subset of people with these mutations in a position to receive a particular line of therapy and who have the potential to benefit from treatment with our product candidates, are based on our assumptions and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new therapies may change the estimated incidence or prevalence of the cancers that we are targeting. Consequently, even if our product candidates are approved for a second or third line of therapy, the number of patients that may be eligible for treatment with our product candidates may turn out to be much lower than expected. In addition, we have not yet conducted market research to determine how treating physicians would expect to prescribe a product that is approved for multiple tumor types if there are different lines of approved therapies for each such tumor type.

Our business may become subject to economic, political, regulatory, and other risks associated with international operations directly or indirectly. A variety of risks associated with marketing our product candidates, if approved, internationally may materially adversely affect our business.

Our business is subject to risks associated with business operations we conduct internationally, as well as indirect impacts from our relationships with collaborators, partners, or contractors who conduct business internationally. To the extent we seek regulatory approval of any of our product candidates outside of the United States, we expect that we will be subject to additional risks related to our operations in foreign countries. Accordingly, our future results could be harmed directly or indirectly by a variety of factors, including:

- differing regulatory requirements in foreign countries, changes in existing regulatory requirements, or implementation of new regulatory requirements or policies that impact our clinical development and business operations in foreign countries;
- foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials or our interpretation of data from preclinical studies or clinical trials;
- approval policies or regulations of foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- impact of the COVID-19 pandemic on our ability to produce our product candidates and conduct clinical trials in foreign countries;
- sociopolitical instability in particular foreign economies and markets;
- 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 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 of 1977 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;

- trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or non-U.S. governments; production or supply shortages resulting directly or indirectly from any events affecting raw material supply or manufacturing capabilities abroad, including, but not limited to, impacts due to the ongoing Ukraine-Russia war, addition of certain suppliers or companies to the Unverified List under the Export Administration Regulations, implementation of other export controls, restrictions or sanctions that can impact the supply chain, our business, or business operations of our suppliers, contractors or partners;
- business interruptions resulting directly or indirectly from geo-political actions, including the ongoing Ukraine-Russian war, other regional or geo-political conflicts, and terrorism; and supply and other disruptions resulting from the impact of public health epidemics, including the COVID-19 pandemic, on our strategic partners, third-party manufacturers, suppliers and other third parties upon which we rely.

These and other risks associated with international operations may materially adversely affect our business, financial condition, and results of operations.

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

Our industry is intensely competitive and subject to rapid and significant technological change as well as strong defense of intellectual property. While we believe that our knowledge, experience and scientific resources provide us with competitive advantages, we face substantial competition from major pharmaceutical companies and biotechnology companies worldwide. Many of our competitors have significantly greater financial, technical and human resources. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

In particular, we are aware of molecules in development that also are being explored for p53 upregulation/activation in various stages of preclinical or clinical development being tested by Aprea Therapeutics and Jacobio Pharmaceuticals, among others. We are also aware of selective small molecule inhibitors that are designed to target wild-type p53 containing tumors through the p53-murine double minute 2, or MDM2, interaction, which are in various stages of clinical development being tested by Aileron Therapeutics, Ascentage Pharma, Boehringer Ingelheim, Daiichi Sankyo (out-licensed worldwide rights to Rain Therapeutics), Kartos Therapeutics, Kymera Therapeutics, Otsuka Pharmaceutical, Novartis and Roche, including testing MDM2 inhibitors in combination with a variety of other anti-cancer agents.

We face competition with respect to our current product candidates and will face competition with respect to future product candidates, from segments of the pharmaceutical, biotechnology and other related markets that pursue targeted therapies for patients with genetically-defined cancers. If PC14586 or our future product candidates do not offer sustainable advantages over competing products, we may otherwise not be able to successfully compete against current and future competitors.

Our competitors may obtain regulatory approval of their products more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products.

In addition, we will likely need to develop our product candidates in collaboration with companion diagnostic companies, and we will face competition from other companies in establishing these future collaborations. Our competitors will also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Furthermore, we also face competition more broadly across the market for cost-effective and reimbursable cancer treatments. The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy or a combination of such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic, including branded generic, products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our product candidates that we successfully introduce to the market will pose challenges. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

Product candidates that we may successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Key product features that would affect our ability to effectively compete with other therapeutics include the efficacy, safety and convenience of our products.

Our long-term prospects depend in part upon discovering, developing and commercializing additional product candidates, which may fail in development or suffer delays that adversely affect their commercial viability.

Our future operating results are dependent on our ability to successfully discover, develop, obtain regulatory approval for and commercialize product candidates beyond our lead product candidate, PC14586, and those we currently have in preclinical development. A product candidate can unexpectedly fail at any stage of preclinical and clinical development. The historical failure rate for product candidates is high due to risks relating to safety, efficacy, clinical execution, changing standards of medical care and other unpredictable variables. The results from preclinical testing or early clinical trials of a product candidate may not be predictive of the results that will be obtained in later stage clinical trials of the product candidate.

The success of future product candidates we may develop will depend on many factors, including the following and the other factors relating to product development described elsewhere in this “Risk Factors” section:

- generating sufficient data to support the initiation or continuation of clinical trials;
- obtaining regulatory permission to initiate clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- successful enrollment of patients in, and the completion of, clinical trials on a timely basis;
- the timely manufacture of sufficient quantities of the product candidate for use in clinical trials; and
- adverse events in the clinical trials.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize additional product candidates, which would materially adversely affect our business, financial condition and results of operations.

Even if we successfully advance any future product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this “Risk Factors” section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, commercialize or generate significant revenue from our future product candidates.

Our product candidates may cause significant adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials when used alone or in combination with other approved products or investigational new drugs we may need to interrupt, delay or 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. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may adversely affect our business, financial condition and prospects significantly.

While our lead product candidate, PC14586, is still in early clinical development and although it has been generally well-tolerated per our preliminary data release, as is the case with all oncology drugs, it is likely that there may be significant side effects associated with its use. PC14586 or future product candidates may be used in populations for which safety concerns may be reviewed by regulatory agencies. In addition, we recently opened a separate arm within the existing Phase 1/2 clinical trial to evaluate the combination of PC14586 with Merck's anti-PD1 therapy, KEYTRUDA, and we may study PC14586 in combination with other additional therapies, which may exacerbate adverse events associated with the therapy. Further, our product candidates will be used in patients that have weakened immune systems, which may exacerbate any potential side effects associated with their use. Patients treated with PC14586 or any of our future product candidates may also be undergoing surgical, radiation and chemotherapy treatments, which can cause side effects or adverse events that are unrelated to our product candidate but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. For example, it is expected that some of the patients enrolled in our PC14586 clinical trials will die or experience major clinical events either during the course of our clinical trials or after participating in such trials. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects.

If further significant adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially adversely affect our business, financial condition and prospects. Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates previously not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early stage clinical trials.

We are currently developing PC14586 in a combination study, and expect to develop our current or future product candidates in combination with other therapies, which exposes us to additional risks.

We recently opened a separate arm within the existing Phase 1/2 clinical trial to evaluate the combination of PC14586 with Merck's anti-PD1 therapy, KEYTRUDA, in patients with advanced solid tumors harboring a p53 Y220C mutation. We also intend to develop our current or future product candidates in combination with one or more other approved cancer therapies or therapies in development. Patients may not be able to tolerate PC14586 or any of our future product candidates in combination with other therapies or dosing of PC14586 or any of our future product candidates in combination with other therapies may have unexpected consequences. Even if any of our current or future product candidates were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or other comparable foreign regulatory authorities could revoke approval of the therapy used in combination with any of our product candidates, or safety, efficacy, manufacturing or supply issues could arise with these existing therapies. In addition, it is possible that existing therapies with which our product candidates are approved for use could themselves fall out of favor or be relegated to later lines of treatment. This could result in the need to identify other combination therapies for our product candidates or our own products being removed from the market or being less successful commercially.

We may also evaluate our current or future product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval.

If the FDA or other comparable foreign regulatory authorities do not approve or withdraw their approval of these other therapies, or if safety, efficacy, commercial adoption, manufacturing or supply issues arise with the therapies we choose to evaluate in combination with PC14586 or any future product candidate, we may be unable to obtain approval of or successfully market any one or all of the current or future product candidates we develop. Additionally, if the third-party providers of therapies or therapies in development used in combination with our current or future product candidates are unable to produce sufficient quantities for clinical trials or for commercialization of our current or future product candidates, or if the cost of combination therapies are prohibitive, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

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

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and 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 or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could materially adversely affect our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be adversely affected, which could materially adversely affect our business, financial condition and results of operations.

Even if we obtain regulatory approval of our product candidates, the products may not gain market acceptance among physicians, patients, hospitals, cancer treatment centers and others in the medical community.

The use of precision medicines as a potential cancer treatment is a recent development and may not become broadly accepted by physicians, patients, hospitals, cancer treatment centers and others in the medical community. Various factors will influence whether our product candidates are accepted in the market, including:

- the clinical indications for which our product candidates are approved;
- physicians, hospitals, cancer treatment centers and patients considering our product candidates as a safe and effective treatment;
- the potential and perceived advantages of our product candidates over alternative treatments;
- our ability to demonstrate the advantages of our product candidates over other cancer medicines;
- the prevalence and severity of any side effects;
- the prevalence and severity of any side effects for other precision medicines and public perception of other precision medicines;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- limitations or warnings contained in the labeling approved by the FDA;
- the timing of market introduction of our product candidates as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate coverage, reimbursement and pricing by third-party payors and government authorities;
- the willingness of patients to pay out-of-pocket in the absence of coverage by third-party payors and government authorities;
- relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and
- the effectiveness of our sales and marketing efforts.

If our product candidates receive regulatory approval but fail to achieve market acceptance among physicians, patients, hospitals, cancer treatment centers or others in the medical community, we will not be able to generate significant revenue.

In addition, although our product candidates differ in certain ways from other precision medicine approaches, serious adverse events or deaths in other clinical trials involving precision medicines, even if not ultimately attributable to our product or product candidates, could result in increased government regulation, unfavorable public perception and publicity, potential regulatory delays in the testing or licensing of our product candidates, stricter labeling requirements for those product candidates and a decrease in demand for any such product candidates.

Even if our products achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Our product candidates may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices, or healthcare reform initiatives, which would adversely affect our business. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may materially change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates we may develop obtain marketing approval.

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments such as gene therapy products. Sales of these or future product candidates that we may identify will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. 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. Reimbursement by a third-party payor may depend upon a number of factors, including, but not limited to, the third-party payor's determination that use of a product is:

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

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. No uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States and have not been approved for reimbursement in certain European countries. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products we may develop could have a material adverse effect on our business, financial condition and results of operations, our ability to raise capital needed to commercialize product candidates and our overall financial condition.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates third-party payors for any approved products that we develop could have a material adverse effect on our business, financial condition and results of operations, our ability to raise capital needed to commercialize products and our overall financial condition.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. In order to obtain reimbursement, physicians may need to show that patients have superior treatment outcomes with our products compared to standard of care drugs, including lower-priced generic versions of standard of care drugs. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

Additionally, we may develop companion diagnostic tests for use with our product candidates. We, or our collaborators, may be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. Even if we obtain regulatory approval or clearance for such companion diagnostics, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates. Medicare reimbursement methodologies, whether under Part A, Part B or clinical laboratory fee schedule may be amended from time to time, and we cannot predict what effect any change to these methodologies would have on any product candidate or companion diagnostic for which we receive approval. Our inability to promptly obtain coverage and adequate reimbursement from both third-party payors for the companion diagnostic tests that we develop and for which we obtain regulatory approval could have a material and adverse effect on our business, financial condition, results of operations and prospects.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants
- initiation of investigations by regulators;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize any product candidate; and
- a decline in our share price.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Although we have clinical trial insurance, our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage such inability could have an adverse effect on our business and financial condition.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an FDA or other comparable foreign regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs. FDA or other comparable foreign regulatory authority investigations could potentially lead to a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. 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 and substantial monetary awards to trial participants or patients. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our product candidates, if approved. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition.

We currently have no marketing and sales organization and have no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. We intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue arrangements with third-party sales, marketing and distribution collaborators regarding the sales and marketing of our products, if approved. However, there can be no assurance that we will be able to establish or maintain such arrangements on favorable terms or if at all, or if we are able to do so, that these third-party arrangements will provide effective sales forces or marketing and distribution capabilities. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

Risks Related to Regulatory Process and Other Legal Compliance Matters

The regulatory approval processes of the FDA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our product candidates, including our lead product candidate PC14586, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for each targeted indication.

Securing regulatory approval also requires the submission of information about the drug manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Further, our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval.

The process of obtaining regulatory approvals, both in the United States and abroad, is unpredictable, expensive and typically takes many years following commencement of clinical trials, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations or changes in regulatory review for each submitted IND, NDA or equivalent application types, may cause delays in the approval or rejection of an application. For example, FDA has issued various COVID-19 related guidance documents for trial sponsors and manufacturers, including guidance on conducting clinical trials during the pandemic, among others. Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of the termination of the public health emergencies on FDA and other regulatory policies and operations are unclear.

FDA's Oncology Center of Excellence initiated Project Optimus to reform the dose optimization and dose selection paradigm in oncology drug development and Project FrontRunner to help develop and implement strategies to support approvals in the early clinical setting, among other goals. How the FDA plans to implement these goals and their impact on specific clinical programs and the industry are unclear. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Our product candidates could be delayed in receiving, or fail to receive, regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials, including our Phase 1/2 clinical trial design for PC14586, or require us to modify the design of our clinical trials, including additional procedures and contingency measures in response to the COVID-19 pandemic or as required by clinical sites, IRBs, FDA or other regulatory authorities;
- the FDA or comparable foreign regulatory authorities may disagree with our tumor-agnostic development strategy;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a drug candidate is safe and effective for its proposed indication, or a related companion diagnostic is suitable to identify appropriate patient populations;
- the FDA or other comparable regulatory authorities may fail to approve companion diagnostic tests that may be required for our product candidates;

- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks, or that a product candidate has an acceptable benefit-risk ratio for its proposed indication;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures, specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;
- our third-party contractors may fail to comply with regulatory requirements or otherwise fail or be unable to adequately perform their obligations to allow for the conduct of our planned or future clinical studies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would materially adversely affect our business, results of operations and prospects.

The FDA or a comparable foreign regulatory authority may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request (including failing to approve the most commercially promising indications), may grant approval contingent on the performance of costly post-marketing clinical studies, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

We may not be able to obtain orphan drug designation or obtain or maintain the benefits associated with orphan drug designation, such as orphan drug exclusivity and, even if we do, that exclusivity may not prevent the FDA or other comparable foreign regulatory authorities, from approving competing products.

As part of our business strategy, we may seek orphan drug designation, or ODD, for any eligible product candidates we develop, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing and making available the drug will be recovered from sales in the United States. Our target indications may include diseases with large patient populations or may include orphan indications. However, there can be no assurances that we will be able to obtain orphan designations for our product candidates.

In the United States, ODD entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has ODD subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity or if FDA finds that the holder of the orphan exclusivity has not shown that it can ensure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the product was designated. The applicable exclusivity period is 10 years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for ODD or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain ODD for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained ODD for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process.

Further, in *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in *Catalyst*, FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the *Catalyst* order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

We may seek and fail to obtain or maintain breakthrough therapy or Fast Track designations for our current or future product candidates. Even if we are successful, such programs may not lead to a faster development or regulatory review process, and they do not guarantee we will receive approval for any product candidate. We may also seek to obtain accelerated approval for one or more of our product candidates but the FDA may disagree that we have met the requirements for such approval.

If a product is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address an unmet medical need for this condition, the product sponsor may apply for Fast Track designation. In October 2020, we received Fast Track designation for PC14586 from the FDA. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular future product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Further, even though we have received Fast Track designation for PC14586, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may rescind the Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

We may also seek breakthrough therapy designation for any product candidate that we develop. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Like Fast Track designation, breakthrough therapy designation is within the discretion of the FDA. Accordingly, even if we believe a product candidate we develop 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 breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if a product candidate we develop qualifies as a breakthrough therapy, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the designation.

Separately from Fast Track or breakthrough therapy designation, we may seek accelerated approval for one or more of our product candidates. A product candidate intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval if it is determined to have 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. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-approval clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires pre-approval of promotional materials for accelerated approval products, once approved. We cannot guarantee that the FDA will agree any of our product candidates has met the criteria to receive accelerated approval, which would require us to conduct additional clinical testing prior to seeking FDA approval. Even if any of our product candidates received approval through this pathway, the required post-approval confirmatory clinical trials may fail to verify the predicted clinical benefit of the product, and we may be required to remove the product from the market or amend the product label in a way that adversely impacts its marketing. In addition, on December 29, 2022, the Consolidated Appropriations Act, 2023, including the Food and Drug Omnibus Reform Act (FDORA), was signed into law. FDORA made several changes to the FDA's authorities and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements.

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

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

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential product candidates will be adversely affected.

Preclinical and clinical development involves a lengthy and expensive process with uncertain outcomes, and results of earlier studies and trials may not be predictive of future clinical trial results. We may encounter substantial delays in clinical trials, or may not be able to conduct or complete clinical trials on the expected timelines, if at all. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our product candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such product candidate.

Our lead product candidate, PC14586, is in early clinical development and all of our other product candidates are in discovery or preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any drug candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Our clinical trials may not be conducted as planned or completed on schedule, if at all, and a failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. Our preclinical studies and clinical trials may not be successful.

We cannot be certain that our preclinical study and clinical trial results will be sufficient to support regulatory approval of our product candidates, or that FDA or other comparable regulatory authorities will find our planned clinical strategy to be acceptable. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Human clinical trials are expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Failure or delay can occur at any time during the clinical trial process. In addition, the COVID-19 pandemic is still evolving as of this time and much of its impact remains unknown, and it is impossible to predict the impact the COVID-19 pandemic may have on the development of our product candidates, our preclinical studies and clinical trials and our business.

Additionally, our PC14586 Phase 1/2 clinical trial is, and other clinical trials we conduct in the future may be, open-label in study design and conducted at a limited number of clinical sites on a limited number of patients. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may 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. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new 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.

We may experience delays in obtaining the FDA's authorization to initiate clinical trials, completing ongoing clinical trials of PC14586 and preclinical studies of our other product candidates and initiating our planned preclinical studies and clinical trials. Additionally, we cannot be certain that preclinical studies or clinical trials for our product candidates will begin on time, not require redesign, enroll an adequate number of research subjects or patients on time, or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the availability of financial resources to commence and complete clinical trials;
- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- the FDA or comparable foreign regulatory authorities disagreeing with our tumor-agnostic development strategy;
- delays in obtaining regulatory approval or authorization to commence a clinical trial, including delays or issues relating to any future companion diagnostics which we may develop;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining IRB or ethics committee approval at each clinical trial site;
- recruiting an adequate number of suitable patients to participate in a clinical trial;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate;
- the cost of clinical trials of our product candidates may be greater than we anticipate, for example, if we experience delays or challenges in identifying patients with the mutations required for our clinical trials, we may have to reimburse sites for genetic sequencing costs in order to encourage sequencing of additional patients;
- having subjects complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from clinical trial protocol or dropping out of a clinical trial;
- having third-party contractors fail to complete their obligations in a timely manner or failing to comply with applicable regulatory requirements;
- addressing subject safety concerns that arise during the course of a clinical trial;
- adding a sufficient number of clinical trial sites; or
- obtaining sufficient product supply of product candidate for use in preclinical studies or clinical trials from third-party suppliers.

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 moderately positive or if there are safety concerns, our business and results of operations may be adversely affected and we may incur significant additional costs. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such clinical trials are being conducted, by the Data Safety Monitoring Board, if any, for such clinical trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from the product candidates, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

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

If we experience delays in the completion, or termination, of any preclinical study or clinical trial of our product candidates, the commercial prospects of our product candidates may be adversely affected, and our ability to generate revenue from any of these product candidates will be delayed or not realized at all. In addition, any delays in completing our preclinical studies or clinical trials may increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may materially adversely affect our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. If one or more of our product candidates generally prove to be ineffective, unsafe or commercially unviable, our entire pipeline and platform would have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects.

Changes in funding or 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, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, 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 and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of 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 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. Separately, in response to the COVID-19 public health emergency, since March 2020 when foreign and domestic inspections facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. While the FDA has largely caught up with domestic preapproval inspections, it continues to work through its backlog of foreign inspections. If a prolonged government shutdown or other disruption occurs, including delays or disruptions due to travel restrictions, foreign COVID-19-related policies, staffing shortages or public health reasons, or if global health or other concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities in a timely manner, 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, in our operations as a public company, future government shutdowns or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Even if we receive regulatory approval of our product candidates, we will be subject to extensive 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.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries.

Following potential approval of any of our current or future product candidates, the FDA or other comparable regulatory authorities may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time-consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the product. The FDA may also require a risk evaluation and mitigation strategy, or REMS, in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP requirements, GLP requirements and good clinical practice, or GCP, requirements, for any clinical trials that we conduct post-approval. 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, among other things:

- restrictions on the marketing or manufacturing of our product candidates, withdrawal of the product from the market or voluntary or mandatory product recalls;
- manufacturing delays and supply disruptions where regulatory inspections identify observations of noncompliance requiring remediation;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, which may include distribution or use restrictions;
- requirements to conduct additional post-market clinical trials to assess the safety of the product;
- fines, warning or untitled letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our 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. For example, certain policies and regulations promulgated during the Trump administration as well as those implemented by the Biden administration may impact our business and industry. To the extent any current or future executive or legislative actions impose significant changes in or burdens on, or otherwise materially delay, FDA's ability to engage in routine oversight activities, such as implementing regulations through rulemaking, issuance of guidance, and agency review and approval of marketing applications on a timely basis, our business and clinical development plans could be negatively impacted. It remains to be seen how the Biden administration and new leadership at the HHS and FDA will impact our business. If we, as well as our contractors, are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may be delayed in obtaining regulatory approval, lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates, if approved, and generate revenue.

Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Affordable Care Act, or ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (increased pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Other legislative changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments may vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, for example, under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at increasing competition for prescription drugs. In August 2022, Congress passed the Inflation Reduction Act of 2022, which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

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

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

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

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

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If any of our product candidates are approved and we are found to have improperly promoted off-label uses of those products, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, if approved. In particular, while the FDA permits the dissemination of truthful and non-misleading information about an approved product, a manufacturer may not promote a product for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees, corporate integrity agreements or permanent injunctions under which specified promotional conduct must be changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors acting for or on our behalf may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, research, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and material adversely affect to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our product candidates, if approved. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment and exclusion from government healthcare programs. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution;

- federal civil and criminal false claims laws, including the False Claims Act, or FCA, which can be enforced through civil "qui tam" or "whistleblower" actions, and civil monetary penalty laws, impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay money to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. 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. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil FCA, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the federal Physician Payment Sunshine Act, created under the ACA and its implementing regulations, which require applicable manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to HHS information related to payments or other transfers of value made to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other non-physician healthcare providers (such as physician assistants and nurse practitioners, among others), and teaching hospitals, as well as ownership and investment interests held by physicians, as defined by law, and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom are compensated in the form of stock or stock options for services provided to us and may be in the position to influence the ordering of or use of our product candidates, if approved, may not comply with current or future statutes, regulations, agency guidance 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 the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Data collection is governed by restrictive regulations governing the use, processing and cross-border transfer of personal information.

In connection with our clinical trials or enrollment of patients in any future clinical trials, we will be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR increased our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation and reputational harm in connection with our European activities. Further, the United Kingdom's vote in favor of exiting the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

In the United States, most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations. HIPAA impose requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. Even when HIPAA does not apply, according to the Federal Trade Commission, or FTC, failing to take appropriate steps to keep consumers' personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act, 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, certain states have enacted additional laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. By way of example, California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies' data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA went into effect on January 1, 2020, and the California Attorney General may bring enforcement actions for violations beginning July 1, 2020. The CCPA was amended on September 23, 2018. In November 2020, California passed the California Privacy Rights Act, or CPRA, which amends and expands the CCPA. Although the CCPA includes exemptions for certain clinical trial data, the law may increase our compliance costs and potential liability with respect to other personal information. The CCPA and CPRA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Compliance with U.S. and international data protection laws and regulations could require us to take on more onerous obligations in our contracts, restrict our ability to collect, use and disclose data, or in some cases, impact our ability to operate in certain jurisdictions. Failure to comply with U.S. and international data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation or adverse publicity and could materially adversely affect our business, financial condition and results of operations. Moreover, clinical trial subjects about whom we or our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could adversely affect our business.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material 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 operations may involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations may also 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. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations. We can face serious consequences for violations.

Among other matters, U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions and other trade laws and regulations, which are collectively referred to as Trade Laws, prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We also expect our non-U.S. activities to increase in time. We plan to engage third parties for clinical trials and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals and we can be held liable for the corrupt or other illegal activities of our personnel, agents or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

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

We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including our Chief Executive Officer and President, our Chief Operating Officer and Chief Financial Officer, our Chief Medical Officer and our Chief Regulatory and Quality Officer. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could materially adversely affect our business, financial condition and results of operations. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be adversely affected.

Additionally, we rely on our founders and other scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting relationships with our scientific founders or if they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be materially adversely affected.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of February 28, 2023, we had 62 full-time employees, including 45 employees engaged in research and development activities. In order to successfully implement our development and commercialization plans and strategies, and as we are a relatively new public company, we expect to need additional managerial, operational, sales, marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA and other comparable foreign regulatory agencies' review process for PC14586 and any future product candidates, while complying with any contractual obligations to contractors and other third parties we may have; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and, if approved, commercialize PC14586 and future product candidates will depend, in part, on our ability to effectively manage any future growth. Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of clinical development and manufacturing. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third-party service providers is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of PC14586 and any future product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third-party service providers, we may not be able to successfully implement the tasks necessary to further develop and commercialize PC14586 and future product candidates and, accordingly, may not achieve our research, development and commercialization goals.

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

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems, and those of our third-party CROs, other contractors (including sites performing our clinical trials) and consultants, these systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to the loss, destruction, alteration or dissemination of, or damage to, our data. For example, companies have experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic. To the extent that any disruption or security breach were to result in a loss, destruction, unavailability, alteration or dissemination of, or damage to, our data or applications, or for it to be believed or reported that any of these occurred, we could incur liability and reputational damage and the development and commercialization of our product candidates could be delayed. We cannot assure you that our data protection efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties, will prevent significant breakdowns or breaches in systems or other cyber incidents that cause loss, destruction, unavailability, alteration or dissemination of, or damage to, our data that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation and/or unauthorized access, use or disclosure of, or the prevention of access to, data (including trade secrets or other confidential information, intellectual property, proprietary business information and personal information), which could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business.

Notifications and follow-up actions related to a security incident 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 or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security breach. We 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 incident were to result in a loss, destruction or alteration 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 and/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 in or, failure or security breach of our systems or third-party systems where information important to our business operations or commercial development is stored. 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.

Business disruptions could materially adversely affect our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our CROs, CMOs and other contractors, consultants and third parties could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, pandemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously adversely affect our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce and process our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

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

As of December 31, 2022, we had federal and state net operating loss, or NOL, carryforwards of $174.7 million, and research and development credit carryforwards of approximately $9.7 million. Our federal NOLs generated in tax years ending on or prior to December 31, 2017 are only permitted to be carried forward for 20 taxable years, and therefore could expire unused. Under the Tax Cuts and Jobs Act, as amended by the CARES Act, our federal NOLs generated in tax years beginning after December 31, 2017 may be carried forward indefinitely, but for taxable years beginning after December 31, 2020, the deductibility of federal NOLs generated in tax years beginning after December 31, 2017 is limited to 80% of current year taxable income. Our federal NOL carryforwards will begin to expire in 2033, and our federal credit carryforwards will begin to expire in 2034, if not fully utilized. Some of our state NOL carryforwards and state credit carryforwards may also expire unused.

In addition, under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change" (generally defined as a cumulative change (by value) in the corporation's ownership by "5-percent shareholders" that exceeds 50 percentage points over a rolling three-year period), the corporation's ability to use its pre-change NOLs and certain other pre-change tax attributes to offset its post-change taxable income or tax liabilities may be limited. Similar rules may apply under state tax laws. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. We have not conducted any studies to determine whether we have experienced an ownership change or the annual limitations, if any, that could result from such an ownership change. Our ability to utilize our NOLs and certain other tax attributes could be limited by an ownership change as described above and consequently, we may not be able to utilize a material portion of our NOLs and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations. There is also a risk that due to federal or state regulatory changes, such as suspensions on the use of NOLs, our existing NOLs could expire or otherwise be unavailable to offset future income tax liabilities.

Changes in tax laws or regulations that are applied adversely to could have a material adverse effect on our business, financial condition and results of operations.

New income, sales, use or other tax laws or regulations could be enacted at any time, which could affect our tax profile and our business and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Cuts and Jobs Act of 2017 eliminates the option to deduct research and development expenditures currently and requires taxpayers to capitalize and amortize them over five or fifteen years pursuant to Section 174 of the Code, beginning in 2022. Further, the Inflation Reduction Act of 2022, among other changes, imposes a one-percent excise tax on stock repurchases made on or after January 1, 2023. Any further changes in tax laws or regulations that are applied adversely to us could have a material adverse effect on our business, financial condition and results of operations.

A portion of our chemistry-based product development and sourcing of certain manufacturing raw materials for our product candidates takes place in China through third-party manufacturers. A significant disruption in the operation of those manufacturers, a trade war or political unrest in China could materially adversely affect our business, financial condition and results of operations.

We currently contract certain product development and manufacturing operations to third parties outside the United States, including in China, and we expect to continue to use such third-party manufacturers for such product candidates. Any disruption in production or inability of our manufacturers in China to produce adequate quantities to meet our needs, whether as a result of a natural disaster or other causes, including COVID-19, 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 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 United States 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 adversely affect our business, financial condition 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. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third-party or clinical researcher interest and support of proposed trials. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currency in China. Future appreciation of the local currency could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in China.

Risks Related to Reliance on Third Parties

We currently rely, and plan to rely in the future, on third parties to conduct and support our preclinical studies and clinical trials. If these third parties do not properly and successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.

We have utilized and plan to continue to utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs, CMOs and strategic partners to conduct and support our preclinical studies and clinical trials under agreements with us. We are continuing to build our internal chemistry, manufacturing and controls, biology and preclinical development capabilities to supplement activities conducted by third parties on our behalf. As part of this personnel build out, we may incur additional costs or experience delays in engaging directly with other third-party CROs and CMOs.

We expect to have to negotiate budgets and contracts with CROs, trial sites and CMOs and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our preclinical studies and clinical trials, and we control only certain aspects of their activities. As a result, we will have less direct control over the conduct, timing and completion of these preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the GCP regulations. In addition, our clinical trials must be conducted with pharmaceutical product produced under cGMP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our product candidates. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be adversely affected, our costs could increase and our ability to generate revenue could be delayed.

Switching or adding third parties to conduct our preclinical studies and clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines.

We currently rely and expect to rely in the future on the use of manufacturing suites in third-party facilities or on third parties to manufacture our product candidates, and we may rely on third parties to produce and process our products, if approved. Our business could be adversely affected if we are unable to use third-party manufacturing suites or if the third-party manufacturers fail to provide us with sufficient quantities of our product candidates or fail to do so at acceptable quality levels or prices.

We do not currently own any facility that may be used as our clinical-scale manufacturing and processing facility and must currently rely on outside vendors to manufacture our product candidates. We have not yet caused our product candidates to be manufactured on a commercial scale and may not be able to do so for any of our product candidates. We will need to negotiate and maintain contractual arrangements with these outside vendors for the supply of our product candidates and we may not be able to do so on favorable terms. We have not yet caused any product candidates to be manufactured on a commercial scale and may not be able to do so for any of our product candidates, if approved.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other comparable foreign regulatory authorities following inspections that will be conducted after we submit an application to the FDA or other comparable foreign regulatory authorities. We may not control the manufacturing process of, and may be completely dependent on, our contract manufacturing partners for compliance with cGMP requirements and any other regulatory requirements of the FDA or other regulatory authorities for the manufacture of our product candidates. Beyond periodic audits, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any approval in the future, we may need to find alternative manufacturing facilities, which would require the incurrence of significant additional costs and materially adversely affect our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Similarly, if any third-party manufacturers on which we will rely fail to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability, our business, financial condition and prospects could be materially adversely affected.

Our anticipated reliance on a limited number of third-party manufacturers exposes us to a number of risks, including the following:

- we may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must inspect any manufacturers for cGMP compliance as part of our marketing application;
- a new manufacturer would have to be educated in, or develop substantially equivalent processes for, the production of our product candidates;
- our third-party manufacturers might be unable to timely manufacture our product candidates or produce the quantity and quality required to meet our clinical and commercial needs, if any;
- contract manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our future contract manufacturers may not perform as agreed, may not devote sufficient resources to our product candidates or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products, if any;
- manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards and we have no control over third-party manufacturers' compliance with these regulations and standards;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates;
- our third-party manufacturers could breach or terminate their agreements with us;

- raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects;
- our contract manufacturers and critical reagent suppliers may be subject to inclement weather, as well as natural or man-made disasters; and
- our contract manufacturers may have unacceptable or inconsistent product quality success rates and yields, and we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel.

Our business could be materially adversely affected by business disruptions to our third-party providers that could materially adversely affect our potential future revenue and financial condition and increase our costs and expenses. Each of these risks could delay or prevent the completion of our clinical trials or the approval of any of our product candidates by the FDA, result in higher costs or adversely impact commercialization of our product candidates. In addition, we will rely on third parties to perform certain specification tests on our product candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm and the FDA could place significant restrictions on our company until deficiencies are remedied.

We currently, and may in the future, depend on single-source suppliers for some of the ingredients, components and materials used in, and the manufacturing processes required to develop, our product candidates.

We currently, and may in the future, depend on single-source suppliers for some of the ingredients, components and materials used in, and manufacturing processes required to develop, our product candidates. There are, for certain of these components, relatively few alternative sources of supply and there is limited need for multiple suppliers at this stage of our business. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, ingredients, components, key processes and finished goods exposes us to several risks, including disruptions in supply, price increases or late deliveries. These suppliers may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single-source supplier or service provider could lead to supply delays or interruptions which would materially adversely affect our business, financial condition and results of operations.

If we have to switch to a replacement supplier, the manufacture and delivery of our product candidates may be interrupted for an extended period, which could materially adversely affect our business. Establishing additional or replacement suppliers for any of the components or processes used in or for our product candidates, if required, may not be accomplished quickly and would create increased cost. If we are able to find a replacement supplier, the replacement supplier would need to be qualified, would need to process our technology transfer and may require additional regulatory authority approval, which could result in further delay. While we seek to maintain adequate inventory of the single-source ingredients, components and materials used in our products, any interruption or delay in the supply of ingredients, components or materials or our inability to obtain ingredients, components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to meet the demand for our product candidates.

If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

Our manufacturing process needs to comply with FDA regulations relating to the quality and reliability of such processes. Any failure by us or our third-party manufacturers to comply with relevant regulations could result in delays in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals.

In order to commercially produce our products either at our own facility or at a third party's facility, we will need to comply with the FDA's cGMP regulations and guidelines. We may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We are subject to inspections by the FDA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, fill-finish, packaging or storage of our precision medicines as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our product candidates, including leading to significant delays in the availability of our precision medicines for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

We may, in the future, form or seek collaborations or strategic alliances or enter into licensing arrangements, and we may not realize the benefits of such collaborations, alliances or licensing arrangements.

We may, in the future, form or seek strategic alliances, create joint ventures or collaborations, or enter into 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 is time-consuming and complex. 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 and efficacy and obtain marketing approval.

Further, collaborations involving our product candidates are subject to numerous risks, which may include the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property.

As a result, if we enter into future collaboration agreements and strategic partnerships or license our product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into future 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.

If conflicts arise between us and our future collaborators or strategic partners, these parties may act in a manner adverse to us and could limit our ability to implement our strategies.

If conflicts arise between our future corporate or academic collaborators or strategic partners and us, the other party may act in a manner adverse to us and could limit our ability to implement our strategies. Future collaborators or strategic partners may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our current or future product candidates. Our current or future collaborators or strategic partners may preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could adversely affect our product development efforts.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and/or acquire intangible assets that could result in significant future amortization expense.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient patent and other intellectual property protection for our product candidates and technology, our competitors could develop and commercialize products and technology similar or identical to ours, and we may not be able to compete effectively in our market or successfully commercialize any product candidates we may develop.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. We will only be able to protect our product candidates, proprietary technologies and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or trade secret protections cover them. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

Composition-of-matter patents on the active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our products for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own may fail to result in issued patents in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability, inventorship or scope thereof. Such a challenge may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. This will require us to be cognizant of the time from invention to filing of a patent application.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. We may also rely on trade secret protection as temporary protection for concepts that may be included in a future patent filing. However, trade secret protection will not protect us from innovations that a competitor develops independently of our proprietary know how. If a competitor independently develops a technology that we protect as a trade secret and files a patent application on that technology, then we may not be able to patent that technology in the future, may require a license from the competitor to use our own know-how, and if the license is not available on commercially-viable terms, then we may not be able to launch our product. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, and this scenario could materially adversely affect our business, financial condition and results of operations.

Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to protect our intellectual property rights throughout the world.

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates. These candidates include PC14586 and others, their respective components, formulations, methods used to manufacture them and methods of treatment. Our commercial success will also depend on successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patenting 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. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our pending and future patent applications may not result in issued patents that protect our technology or products, in whole or in part. In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies.

If we delay in filing a patent application, and a competitor files a patent application on the same or a similar technology before we do, we may face a limited ability to secure patent rights. We may not be able to patent the technology at all. Even if we can patent the technology, we may be able to patent only a limited scope of the technology, and the limited scope may be inadequate to protect our products, or to block competitor products that are similar or adjacent to ours. Our earliest patent filings have been published. A competitor may review our published patents and arrive at the same or similar technology advances for our products as we developed. If the competitor files a patent application on such an advance before we do, then we may no longer be able to protect the technology, we may require a license from the competitor, and if the license is not available on commercially-viable terms, then we may not be able to launch our product.

In the future we may in-license intellectual property from licensors. We may rely on these licensors to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We may have limited control over these activities or any other intellectual property that may be in-licensed. For example, we cannot be certain that such activities by licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

The growth of our business may depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compounds and pre-existing pharmaceutical compounds. These pharmaceutical compounds may be covered by intellectual property rights held by others. We may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would adversely affect our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license under such intellectual property rights, any such license may be non-exclusive, and may allow our competitors access to the same technologies licensed to us.

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

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive for commercializing our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

During the course of business we have decided not to pursue certain products or processes and have terminated certain corresponding intellectual property license agreements, and we may do so again in the future. If it is later determined that our activities or product candidates infringe this intellectual property we may be liable for damages, enhanced damages or subjected to an injunction, any of which could have a material adverse effect on our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years, patent rights have been the subject of significant litigation. 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 in the United States or in other jurisdictions which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. 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 be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the U.S. Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. For example, we may become involved in opposition, interference, derivation, *inter partes* review or other proceedings challenging our patent rights, and the outcome of any proceedings are highly uncertain. Such challenges may result in the patent claims of our owned or in-licensed patents being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our collaborators and suppliers. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors or use such information to compete with us. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be adversely affected and this would have a material adverse effect on our business.

If any of our patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates. Likewise, our current patents covering our proprietary technologies and our product candidates are expected to expire through 2037, without taking into account any possible patent term adjustments or extensions. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and further, may infringe our patents in territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement or protection of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. We have contract research and manufacturing relationships with contract organizations that operate in certain countries that are at heightened risk of theft of technology, data and intellectual property through direct intrusion by private parties or foreign actors, including those affiliated with or controlled by state actors. Accordingly, our efforts to protect or enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated if we fail to comply with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Any issued patents we may own covering our product candidates could be narrowed or found invalid or unenforceable if challenged in court or before administrative bodies in the United States or abroad, including the USPTO.

Any of our intellectual property rights could be challenged or invalidated despite measures we take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary technology. For example, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the U.S. and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material information from the USPTO or the applicable foreign counterpart, or made a misleading statement, during prosecution. A litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such a challenge is unpredictable.

With respect to challenges to the validity of our patents, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. The cost of defending such a challenge, particularly in a foreign jurisdiction, and any resulting loss of patent protection could have a material adverse impact on one or more of our product candidates and our business. Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend, particularly in a foreign jurisdiction, and could require us to pay substantial damages, cease the sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially reasonable terms or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel.

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

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable.

If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. In addition, if the breadth or strength of protection provided by our patents and patent applications or those of our future licensors is threatened, it could dissuade other companies from collaborating with us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings.

We may be required to protect our patents through procedures created to attack the validity of a patent at the USPTO. The USPTO hears post-grant proceedings, including PGR, IPR and derivation proceedings. An adverse determination in any such submission or proceeding could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the possibility of post-grant proceedings could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours for a meaningful amount of time, or at all.

Depending upon the timing, duration and conditions of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union and certain other countries. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. Only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for the applicable product candidate will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be expected, and our competitive position, business, financial condition, results of operations and prospects could be materially adversely affected.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate. Any of the foregoing could adversely affect our competitive position, business, financial condition, results of operations and prospects.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us. United States Congress has in recent years considered legislation to reduce the term of certain drug patents in order to ease generic entry and increase competition. Evolving judicial interpretation of patent law could also adversely affect our business. For example, 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 decisions by the U.S. Congress, the U.S. federal courts, the USPTO or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

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

We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our product candidates. Also, former employees may become employed by competitors who develop similar technology, and could assist the competitor in designing around our patents. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or our ownership of our patents, trade secrets or other intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

We use and will continue to use registered and/or unregistered trademarks or trade names to brand and market ourselves and our products. Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain. Defending against such lawsuits will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields relating to our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our product candidates infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our issued patents or our pending applications, or that we were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our patent applications or patents, which could require us to obtain rights to issued patents covering such technologies.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights.

If a third party claims that we infringe its intellectual property rights, we may face a number of issues, including, but not limited to: infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business; substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees; a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third party licenses its product rights to us; however, the third party is not required to grant the license; if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our products; and redesigning our product candidates or processes so they do not infringe; redesign may not be possible or may require substantial monetary expenditures and time.

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

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

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information or alleged trade secrets of third parties or competitors or are in breach of non-competition or non-solicitation agreements with our competitors or their former employers.

As is common in the biotechnology and pharmaceutical industries, we employ individuals and engage the services of consultants who previously worked for other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that our consultants have used or disclosed trade secrets or other proprietary information of their former or current clients. 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 or other legal proceedings relating to intellectual property claims 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, and, 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. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. 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 substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We may in the future enter into license agreements with third parties under which we receive rights to intellectual property that are important to our business. These intellectual property license agreements may impose on us various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to bankruptcy-related proceedings, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

We may also in the future enter into license agreements with third parties under which we are a sublicensee. If our sublicensor fails to comply with its obligations under its upstream license agreement with its licensor, the licensor may have the right to terminate the upstream license, which may terminate our sublicense. If this were to occur, we would no longer have rights to the applicable intellectual property unless we are able to secure our own direct license with the owner of the relevant rights, which we may not be able to do on reasonable terms, or at all, which may impact our ability to continue to develop and commercialize our product candidates incorporating the relevant intellectual property.

We may need to obtain licenses in the future from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that there are no third-party patents which might be enforced against our product candidates in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we license in the future prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the affected product candidates, which would have a material adverse effect on our business.

In addition, certain of our future agreements with third parties may limit or delay our ability to consummate certain transactions, may impact the value of those transactions, or may limit our ability to pursue certain activities. For example, we may in the future enter into license agreements that are not assignable or transferable, or that require the licensor's express consent in order for an assignment or transfer to take place.

Risks Related to Ownership of Our Common Stock

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

The trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors include:

- the results of our ongoing, planned or any future preclinical studies, clinical trials or clinical development programs;
- the commencement, enrollment, or results of clinical trials of our product candidates or any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results or delays in preclinical studies and clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial, including due to the suspension of a clinical trial by the FDA or other regulatory authorities;
- any delay in our regulatory filings or any adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- changes in laws or regulations applicable to our products, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers or our manufacturing plans;
- our inability to obtain adequate product supply for any licensed product or inability to do so at acceptable prices;
- our inability to establish collaborations if needed;
- our failure to commercialize our product candidates;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- the size and growth of our initial cancer target markets;
- our ability to successfully treat additional types of cancers or at different stages;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or immunotherapy in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;

- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to intellectual property or proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including intellectual property or stockholder litigation;
- the impact of any natural disasters or public health emergencies, such as the COVID-19 pandemic;
- general economic, political, industry and market conditions, including the rising rate of inflation and the Ukraine-Russia war; and
- other events or factors, many of which are beyond our control.

The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In particular, the trading prices for pharmaceutical, biopharmaceutical and biotechnology companies have been highly volatile as a result of the COVID-19 pandemic. In addition, broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would materially adversely affect our business, financial condition and results of operation.

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

Prior to the closing of our initial public offering in September 2020, there was no public trading market for our common stock. Although our common stock is listed on the Nasdaq Global Select Market, the market for our shares has demonstrated varying levels of trading activity. Furthermore, an active trading market for our common stock may not be sustained in the future. The lack of an active market may impair investors' ability to sell their shares at the time they wish to sell them or at a price that they consider reasonable may reduce the market value of their shares and may impair our ability to raise capital.

If securities or industry analysts do not publish research or reports, or if they publish 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 will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. We do not have any control over these analysts. 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.

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

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and 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 may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships, alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms unfavorable to us.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

Certain holders of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Registration of these shares under the Securities Act would result in the shares becoming freely tradeable in the public market, subject to the restrictions of Rule 144 in the case of our affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market price for our common stock.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.

As of December 31, 2022, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 83% of our voting stock. As a result, this group of stockholders may be able to impact matters requiring stockholder approval. For example, they may be able to impact elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

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

We have never declared or paid any cash dividends on our capital stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which other terms prohibiting or limiting the amount of dividends that may be declared or paid on our capital stock. Any return to stockholders will therefore be limited to any appreciation in the value of their stock.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. These provisions, among other things:

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

In addition, Section 203 of the General Corporation Law of the State of Delaware, or DGCL, prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware) is the exclusive forum for the following (except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within 10 days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than such court or for which such court does not have subject matter jurisdiction):

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Securities Act of 1933, as amended, or Securities Act, the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction.

Our amended and restated bylaws further provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. We note that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

These exclusive forum provisions 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 lawsuits against us and our directors, officers and other employees. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. If a court were to find these types of provisions to be inapplicable or unenforceable, and if a court were to find the exclusive forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could materially adversely affect our business.

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

We are subject to Section 404 of the Sarbanes-Oxley Act and the related rules of the SEC and Nasdaq, which, among other things, require that we maintain effective internal control over financial reporting. In addition, Section 404 requires our management to report on the effectiveness of our internal control over financial reporting. We are also required to disclose changes made in our internal controls and procedures on a quarterly basis.

The requirements of these rules and regulations are difficult, time-consuming and costly, and place significant strain on our personnel, systems and resources. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. In order to maintain and improve the effectiveness of our disclosure controls and procedures and internal control over financial reporting, we have expended and anticipate we will continue to expend significant resources, including accounting-related costs, and provide significant management oversight. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on the Nasdaq Global Select Market.

Any testing by us conducted in connection with Section 404, or any subsequent testing, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. In addition, undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

If we are unable to assert that our internal control over financial reporting is effective, we could lose investor confidence in the accuracy and completeness of our financial reports, which would cause the price of our common stock to decline, and we may be subject to investigation or sanctions by the SEC.

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.

We are subject to increased risk of securities class action litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could materially adversely affect our business.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our board of directors, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our current product candidates and any future product candidates and research-stage programs, which will change from time to time;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the cost of manufacturing our current product candidates and any future product candidates, which may vary depending on FDA or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies or other assets;
- the timing and outcomes of clinical trials for our future product candidates, or competing product candidates;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- competition from existing and potential future products that compete with our product candidates and any of our future product candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval of our product candidates;
- the level of demand for our future product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future products that compete with our product candidates;
- our ability to commercialize our product candidates, if approved, inside and outside of the United States, either independently or working with third parties;
- our ability to establish and maintain future collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies; and
- the changing and volatile global economic and political environment.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located at 1 Research Way, Princeton, New Jersey 08540, where we lease a facility containing 50,581 square feet of office and laboratory space. The lease term extends through 2032, and has a five-year extension option.

The Company leases a facility at 8 Clarke Drive, Cranbury, New Jersey 08512, containing 18,446 square feet of office and laboratory space pursuant to a lease agreement that expires in June 2022 with an option to renew on a month-to-month basis for up to one year. We also lease 6,297 square feet of laboratory space at 3000 Eastpark, South Brunswick, New Jersey 08512 pursuant to a lease that expires in July 2022 with an option to renew on a month-to-month basis for up to one year. In January 2022, the Company signed lease extensions for both leases through June 2023 and July 2023, respectively, with the option to terminate upon 120 days of written notice, with an increase in base rent as per the lease extension.

Additionally, we lease 3,292 square feet of office space at 420 Bedford Drive, Lexington, Massachusetts 02420 pursuant to a lease that expires in August 2023, with an option to extend for an additional three years.

We believe that our current facilities are suitable and adequate for our current and near term conduct of our business operations and that suitable additional or substitute space at commercially reasonable terms will be available as needed to accommodate any future expansion of our operations.

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 February 28, 2023, we were not a party to any legal matters or claims that, in the opinion of management, are likely to have a material effect on our business. In the future, we may become party to legal matters and claims in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows. Regardless of outcome, litigation, or other legal proceedings can have an adverse impact on us because of legal fees and settlement costs, diversion of management resources, and other factors.

Item 4. Reserved.

PART II

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

Market Information

Our common stock has been listed on the Nasdaq Global Select Market under the symbol "PMVP" since September 25, 2020. Prior to that date there was no public trading market for our common stock.

Holders

As of February 28, 2023, there were approximately six holders of record of our common stock. We believe actual number of stockholders is greater than this number of record holders. The approximate number of holders includes holders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose share may be held in trust by other entities.

Dividend Policy

We have never declared or paid cash dividends on our common stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors might deem relevant.

Recent Sales of Unregistered Securities

There were no unregistered sales of our equity securities during the fiscal year ended December 31, 2022.

Use of Proceeds

On September 24, 2020, our registration statement on Form S-1 (File No. 333-248627) relating to our IPO of common stock was declared effective by the SEC. The IPO closed on September 25, 2020 at which time we issued 13,529,750 shares of common stock (including the exercise in full by the underwriters of their option to purchase an additional 1,764,750 shares of common stock) at a public offering price of $18.00 per share. We received net proceeds from the IPO of approximately $223.2 million, after deducting the underwriting discounts and commissions of approximately $17.0 million and estimated offering related expenses of approximately $3.3 million. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to our affiliates. Goldman Sachs & Co. LLC, BofA Securities, Cowen, and Evercore IS acted as joint book-running managers for the offering.

There has been no material change in the planned use of proceeds from the IPO from that described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on September 24, 2020.

On October 4, 2021, our shelf registration statement on Form S-3 (File No. 333-260012) was automatically declared effective by the SEC for our future follow-on offering. The potential gross proceeds from this future offering are approximately $150.0 million. The company has not issued any shares of common stock pursuant to the offering. There has been no material change in the planned use of proceeds from the follow-on offering as described in the Form S-3 Registration Statement. None of the expenses associated with the follow-on offering were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to our affiliates.

Purchases of Equity Securities by the Issuer and Affiliated Purchases

None.

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 the financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements based upon current expectations that involve risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those discussed in "Part I, Item 1A. Risk Factors" and in other parts of this Annual Report on Form 10-K.

A discussion of our financial performance for the year ended December 31, 2022 as compared to the year ended December 31, 2021 appears below under the captions "Results of Operations" and "Liquidity and Capital Resources." A discussion of our financial performance for the year ended December 31, 2021 compared to the year ended December 31, 2020 can be found in our Annual Report filed on Form 10-K, in the "Part II, Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations", under the same captions, filed with the SEC on March 1, 2022, which is available free of charge on the SEC's website at *www.sec.gov* and our Investor Relations website at *ir.pmvpharma.com/financial-information/sec-filings*. These website addresses are intended to be inactive, textual references only. None of the materials on, or accessible through, these websites are part of this report or are incorporated by reference herein.

Overview

We are a precision oncology company pioneering the discovery and development of small molecule, tumor-agnostic therapies targeting p53. p53 is a well-defined tumor suppressor protein known as the "guardian of the genome," and normal, or wild-type, p53 has the ability to eliminate cancer cells. However, mutant p53 proteins can be misfolded and lose their wild-type tumor suppressing function. These p53 mutations are found in approximately half of all cancers. The field of p53 biology was established by our co-founder Dr. Arnold Levine when he discovered the p53 protein in 1979. We have leveraged more than four decades of research experience and developed unique insights into p53 to create a precision oncology platform designed to generate selective, small molecule, tumor-agnostic therapies that structurally correct specific mutant p53 proteins to restore their wild-type function. We are deploying our precision oncology platform to target the top ten most frequent, or hotspot, p53 mutations that are collectively associated with approximately 10-15% of all cancers. In addition, we are expanding the utilization of our platform to target other p53-related cancers.

Since our formation in March 2013, we have devoted substantially all of our time and efforts to performing research and development activities and raising capital. We are not profitable and have incurred losses in each year since our inception. Our net losses were $73.3 million, $57.8 million, and $34.4 million for the years ended December 31, 2022, 2021, and 2020, respectively. As of December 31, 2022, we had an accumulated deficit of $241.0 million. We do not currently have any product candidates approved for sale, and we continue to incur significant research and development and general administrative expenses related to our operations. We initiated a Phase 1/2 clinical trial in October 2020 for our lead product candidate, PC14586. In October 2020, we were granted FDA Fast Track Designation of PC14586 for the treatment of patients with locally advanced or metastatic solid tumors that have a p53 Y220C mutation. We dosed our first patient in this clinical trial in the fourth quarter of 2020. In June 2022, we presented our initial Phase 1 clinical data for PC14586. We expect that our operating expenses will increase significantly as we advance our product candidates through preclinical and clinical development, seek regulatory approval, and prepare for and, if approved, proceed to commercialization; acquire, discover, validate, and develop additional product candidates; obtain, maintain, protect, and enforce our intellectual property portfolio; and hire additional personnel. Furthermore, we have incurred and will continue to incur additional costs associated with operating as a public company that we did not experience as a private company. We expect to continue to incur significant losses for the foreseeable future.

Our ability to generate product revenue will depend on the successful development, regulatory approval, and eventual commercialization of one or more of our product candidates. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through private or public equity or debt financings, collaborative, or other arrangements with corporate sources, or through other sources of financing. Adequate funding may not be available to us on acceptable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of our product candidates.

We plan to continue to use third-party service providers, including clinical research organizations, or CROs, and contract manufacturing organization, or CMOs, to carry out our preclinical and clinical development and to manufacture and supply the materials to be used during the development and commercialization of our product candidates. We do not currently have a sales force.

Revenue

To date, we have not generated any revenue from any sources, including from product sales, and we do not expect to generate any revenue from the sale of products in the foreseeable future. If our development efforts for our product candidates are successful and result in regulatory approval, or license agreements with third parties, we may generate revenue in the future from product sales. However, there can be no assurance as to when we will generate such revenue, if at all.

Operating Expenses

Research and Development Expenses

Our research and development expenses consist primarily of costs incurred to conduct research, such as the discovery and development of our product candidates as well as the development of future product candidates. Research and development expenses include personnel costs, including stock-based compensation expense, third-party contractor services, laboratory materials and supplies, and depreciation and maintenance of research equipment. We expense research and development costs as they are incurred.

As we are at a very early stage of development, we do not allocate our costs by product candidate or development program, as a significant amount of research and development expenses include compensation costs, materials, supplies, depreciation on and maintenance of research equipment, and the cost of services provided by outside contractors, which are not tracked by product candidate or development program. In particular, with respect to internal costs, several of our departments support multiple product candidate research and development programs, and therefore the costs cannot be allocated to a particular product candidate or development program. Substantially all of our research and development costs are associated with our lead product candidate, PC14586. We initiated a Phase 1/2 clinical trial in October 2020 for our lead product candidate, PC14586. In October 2020, we were granted FDA Fast Track Designation of PC14586 for the treatment of patients with locally advanced or metastatic solid tumors that have a p53 Y220C mutation. We dosed our first patient in this clinical trial in the fourth quarter of 2020. In June 2022, we presented our initial Phase 1 clinical data for PC14586 at the 2022 ASCO Annual Meeting.

We expect our research and development expenses to increase substantially in absolute dollars in the future as we advance our product candidates into and through clinical trials and pursue regulatory approval of our product candidates. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming. The actual probability of success for our product candidates may be affected by a variety of factors including: the safety and efficacy of our product candidates, early clinical data, investment in our clinical program, the ability of any future collaborators to successfully develop our licensed product candidates, competition, manufacturing capability, and commercial viability. We may never succeed in achieving regulatory approval for any of our product candidates. As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects.

General and Administrative Expenses

General and administrative expenses include personnel costs, expenses for outside professional services and other allocated expenses. Personnel costs consist of salaries, bonuses, benefits, and stock-based compensation. Outside professional services consist of legal, accounting and audit services and other consulting fees. Allocated expenses consist of rent expense related to our office and research and development facilities. We have incurred additional expenses as a public company, including expenses related to compliance with the rules and regulations of the SEC, and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administrative and professional services. We have increased our headcount significantly to support our operations as a public company. We also expect to increase our general and administrative expenses as we advance our product candidates through preclinical research and development, manufacturing, clinical development, and commercialization.

Interest Income, Net

Interest income, net primarily consists of interest income from our interest-bearing cash, cash equivalents and marketable securities and interest costs related to amortization of premiums and discounts on marketable securities.

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations (in thousands):

	Year Ended December 31,		
Statement of operations data:	**2022**	**2021**	**Change**
Operating expenses:			
Research and development	$ 51,988	$ 36,493	$ 15,495
General and administrative	25,052	21,800	3,252
Total operating expenses	77,040	58,293	18,747
Loss from operations	(77,040)	(58,293)	(18,747)
Other income (expense):			
Interest income, net	3,627	449	3,178
Other income (expense), net	87	21	66
Total other income (expense)	3,714	470	3,244
Loss before (benefit) provision for income taxes	(73,326)	(57,823)	(15,503)
(Benefit) provision for income taxes	(9)	23	(32)
Net loss	$ (73,317)	$ (57,846)	$ (15,471)

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the periods indicated (in thousands):

	Year Ended December 31,		
Statement of operations data:	**2022**	**2021**	**Change**
Research	$ 6,712	$ 8,296	$ (1,584)
Development	32,470	19,436	13,034
Personnel related	9,340	7,321	2,019
Stock-based compensation	3,466	1,440	2,026
Total	$ 51,988	$ 36,493	$ 15,495

Research and development expenses were $52.0 million for the year ended December 31, 2022, compared to $36.5 million for the year ended December 31, 2021. The increase of $15.5 million was primarily due to the following:

- $1.6 million decrease in research expenses, largely driven by decreased contractual research organization costs focused on discovery research;
- $13.0 million increase in development expenses, primarily associated with increased effort advancing our lead compound PC14586 through the Phase 1/2 clinical trial; and
- $4.0 million increase in expenses for personnel related costs and stock-based compensation, primarily driven by increased headcount.

General and Administrative Expenses

General and administrative expenses were $25.1 million for the year ended December 31, 2022, compared to $21.8 million for the year ended December 31, 2021. The increase of $3.3 million was primarily due to the following:

- $2.4 million increase in personnel related expenses due to increased headcount to build out general and administrative infrastructure; and
- $0.2 million decrease in finance and legal support, $0.3 million decrease for directors and officers insurance, and a $1.4 million increase due to facility and equipment related costs for our new headquarters in Princeton, New Jersey.

Interest Income, Net

Interest income, net primarily consists of interest income from our interest-bearing cash, cash equivalents and marketable securities and interest costs related to amortization of premiums and discounts on marketable securities. Interest income, net was $3.7 million for the year ended December 31, 2022, compared to $0.5 million for the year ended December 31, 2021. The increase of $3.2 million in 2022 is driven by increased interest rates from cash investments in marketable securities and U.S. treasuries and was partially offset by lower average balances in cash and investments in marketable securities.

Liquidity and Capital Resources

Our financial condition is summarized as follows:

	As of December 31,		
	2022	2021	Change
Financial assets:			
Cash and cash equivalents	$ 108,297	$ 172,467	$ (64,170)
Marketable securities – current	132,757	124,696	8,061
Marketable securities – noncurrent	2,495	16,911	(14,416)
Total financial assets	$ 243,549	$ 314,074	$ (70,525)
Working capital:			
Current assets	$ 247,006	$ 301,286	$ (54,280)
Current liabilities	10,832	12,219	(1,387)
Total working capital	$ 236,174	$ 289,067	$ (52,893)

Sources of Liquidity

Since our inception, we have not generated any revenue from any product sales or any other sources and have incurred significant operating losses and negative cash flows from our operations. We have not yet commercialized any of our product candidates and we do not expect to generate revenue from sales of any product candidates for several years, if at all. As of December 31, 2022, we had cash, cash equivalents, and marketable securities of $243.5 million and an accumulated deficit of $241.0 million. We have financed our operations primarily through issuances of our convertible preferred and common stock. In July 2020, we sold an aggregate of 5,321,864 shares of our Series D convertible preferred stock to accredited investors, generating gross proceeds of $70.0 million. In September 2020, we completed an IPO of 13,529,750 shares of our common stock, which includes the exercise in full by the underwriters of their option to purchase 1,764,750 additional shares of common stock, at a public offering price of $18.00 per share for aggregate gross proceeds of $243.5 million. We received $223.2 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us. In October 2021, we filed a shelf registration statement on Form S-3, which may result in aggregate gross process of up to $150.0 million. We did not sell any shares pursuant to the shelf registration statement and did not receive any gross proceeds in fiscal year 2022.

Contractual Obligations and Commitments

We enter into contracts in the normal course of business with CROs and other vendors to assist in the performance of our research and development activities and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

In January 2021, we signed a lease for 50,581 square feet of office and laboratory space at 1 Research Way in Princeton, New Jersey. That lease term extends through 2032, has a five-year extension option, and is intended to replace our two existing facilities. Payments under this lease will total $19.9 million through May 2032. Amounts related to future lease payments under the 1 Research Way lease as of December 31, 2022, totaled $19.4 million, with $2.3 million to be paid within the next 12 months.

Plan of Operation and Future Funding Requirements

We use our capital resources primarily to fund operating expenses, mainly research and development expenditures. We plan to increase our research and development expenses for the foreseeable future as we continue the preclinical and clinical development of our product candidates. At this time, due to the inherently unpredictable nature of preclinical and clinical development and given the early stage of our product candidates, we cannot reasonably estimate the costs we will incur and the timelines that will be required to complete development, obtain marketing approval and commercialize our current product candidates or any future product candidates, if at all. For the same reasons, we are also unable to predict when, if ever, we will generate revenue from product sales or whether, or when, if ever, we may achieve profitability. Clinical and preclinical development timelines, the probability of success, and development costs can differ materially from expectations. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

Due to our significant research and development expenditures, we have generated substantial operating losses in each period since inception. We have incurred an accumulated deficit of $241.0 million through December 31, 2022. We expect to incur substantial additional losses in the future as we expand our research and development activities.

Our cash operating expenditures were $63.8 million in 2022 and $46.6 million in 2021, and we expect to increase our investment in operations in 2023. Based on our research and development plans, we expect that our cash balances as of December 31, 2022 will be sufficient to fund our operations at least through 2024.

We have based this estimate on assumptions that may prove to be wrong, however, and we could use our capital resources sooner than we expect.

The timing and amount of our operating expenditures will depend largely on:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the timing and amount of milestone payments we may receive under any future collaboration agreements;
- our ability to maintain future licenses and research and development programs and to establish new collaboration and/or in-licensing arrangements;
- the costs involved in prosecuting and enforcing patent and other intellectual property claims;
- the cost and timing of regulatory approvals; and
- our efforts to build out our new office and laboratory headquarters, enhance operational systems and hire additional personnel, including personnel to support development of our product candidates and satisfy our obligations as a public company.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to fund our operations and capital funding needs through equity and/or debt financing. We may also consider entering into collaboration arrangements or selectively partnering for clinical development and commercialization. The sale of additional equity would result in additional dilution to our stockholders. The incurrence of debt financing would result in debt service obligations and the instruments governing such debt could provide for operating and financing covenants that would restrict our operations or our ability to incur additional indebtedness or pay dividends, among other items. If we raise additional funds through governmental funding, collaborations, strategic partnerships and 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 not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could materially and adversely affect our business, financial condition, results of operations and prospects.

Cash Flows

The following table summarizes our cash flows for the period indicated (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Cash used in operating activities	$ (63,760)	$ (46,571)	$ (32,739)
Cash (used in) provided by investing activities	(1,368)	(143,584)	27,911
Cash provided by financing activities	958	2,022	292,972
Net (decrease) increase in cash, cash equivalents, and restricted cash	$ (64,170)	$ (188,133)	$ 288,144

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022, was $63.8 million, which consisted primarily of net loss of $73.3 million decreased by non-cash charges of $10.1 million and a net change of $0.6 million in our net operating assets. The non-cash charges primarily consisted of stock-based compensation of $10.2 million, depreciation of $0.3 million, and non-cash lease expense of $0.3 million, partially offset by changes in premiums on marketable securities of $0.6 million. The change in our net operating assets and liabilities was primarily due to an increase in prepaid expenses and other assets, an decrease in accrued expenses, and a decrease in outstanding payables.

Net cash used in operating activities for the year ended December 31, 2021, was $46.6 million, which consisted primarily of net loss of $57.8 million decreased by non-cash charges of $7.2 million and a net change of $4.1 million in our net operating assets. The non-cash charges primarily consisted of stock-based compensation of $5.3 million, amortization of premiums on marketable securities and depreciation of $0.9 million, and non-cash lease expense of $1.0 million. The change in our net operating assets and liabilities was primarily due to a decrease in prepaid expenses and other assets, an increase in accrued expenses, and an increase in outstanding payables.

Investing Activities

Our investing activities used $1.4 million of cash during the year ended December 31, 2022, which consisted primarily of purchases of marketable securities of $229.2 million, along with purchase of property and equipment of $8.0 million, partially offset by maturities of marketable securities of $235.8 million.

Our investing activities used $143.6 million of cash during the year ended December 31, 2021, which consisted primarily of purchases of marketable securities of $256.8 million, along with purchase of property and equipment of $1.3 million partially offset by maturities of marketable securities of $114.6 million.

Financing Activities

Our financing activities provided $1.0 million of cash during the year ended December 31, 2022, which consisted primarily of common stock issued under the employee stock purchase plan and proceeds from the exercise of stock options.

Our financing activities provided $2.0 million of cash during the year ended December 31, 2021, which consisted primarily of common stock issued under the employee stock purchase plan and proceeds from the exercise of stock options.

Critical Accounting and Estimates

The preparation of our financial statements in conformity with accounting principles generally accepted in the United States requires us to make estimates and judgments that affect the amounts reported in those financial statements and accompanying notes. Although we believe that the estimates we use are reasonable, due to the inherent uncertainty involved in making those estimates, actual results reported in future periods could differ from those estimates.

We believe that the accounting policies described below involve a high degree of judgment and complexity. Accordingly, these are the policies we believe are the most critical to aid in fully understanding and evaluating our financial condition and results of our operations.

Research and Development Costs, Accrued Research and Development Costs and Related Prepaid Expenses

Research and development costs are expensed as incurred. Research and development expenses consist principally of personnel costs, including salaries, stock-based compensation and benefits for employees, third-party license fees and other operational costs related to our research and development activities, including sourcing of raw materials and manufacturing of our product candidates, allocated facility-related expenses and external costs of outside vendors, and other direct and indirect costs. Non-refundable research and development advance payments are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or services are performed.

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of 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 financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of the estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors, including research laboratories, in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical studies and clinical trials; and
- CMOs in connection with drug substance and drug product formulation of preclinical studies and clinical trial materials.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that supply, conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We measure all stock options and other stock-based awards granted to our employees, directors, consultants, and other non-employee service providers based on the fair value on the date of the grant. Compensation expense related to awards to employees and directors with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is typically the vesting term.

We classify stock-based compensation expense in our statement of operations in the same way the award recipient's payroll costs are classified or in which the award recipients' service payments are classified.

We use the Black-Scholes option pricing model to estimate the fair value of stock options on the date of grant. Using the Black-Scholes option pricing model requires management to make significant assumptions and judgments. We determined these assumptions for the Black-Scholes option-pricing model as discussed below.

- *Expected Term*—The expected term represents the period that the stock-based awards are expected to be outstanding. As we do not have sufficient historical experience for determining the expected term of the stock option awards granted, we based our expected term for awards issued to employees and non-employees using the simplified method which is presumed to be the midpoint between the vesting date and the end of the contracted term.
- *Risk-Free Interest Rate*—The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury constant maturity notes with terms approximately equal to the stock-based awards' expected term.

- *Expected Volatility*—Since we do not have adequate trading history of our common stock, the expected volatility was derived from the average historical stock volatilities of the common stock of several public companies within the industry that we consider to be comparable to our business over a period equivalent to the expected term of the stock-based awards.
- *Dividend Rate*—The expected dividend rate is zero as we have not paid and do not anticipate paying any dividends in the foreseeable future.
- *Fair Value of Common Stock*—Since our IPO, the fair value of shares of our common stock are measured by the stock price on the date of grant.

Recent Accounting Pronouncements

For a description of recent accounting pronouncements, see Note 2 of the notes to our audited financial statements for the year ended December 31, 2022 included elsewhere in this Annual Report on Form 10-K.

Item 7A. Reserved.

Item 8. Financial Statements and Supplementary Data.

INDEX TO FINANCIAL STATEMENTS

Audited Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of PMV Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of PMV Pharmaceuticals, Inc. (the "Company") as of December 31, 2022 and 2021, the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accounting for Research and Development Expenses

Description of the Matter

As disclosed in Note 2 to the financial statements, the Company is required to estimate research and development expenses from its obligations under contracts and purchase orders with vendors, clinical research organizations, clinical manufacturing organizations and others and for clinical site agreements at each balance sheet date. The Company recorded accrued expenses for the research and development expenses, which are included in accrued expenses on the December 31, 2022 balance sheet, and prepaid research and development expenses, which are included in prepaid expenses and other current assets on the December 31, 2022 balance sheet. The amounts recorded for accrued research and development expenses and for the related prepaid expenses, within the aforementioned balance sheet captions, represent the Company's estimate of the unpaid and prepaid research and development expenses based on the progress of the research and development services compared to the amounts paid for those services through December 31, 2022.

Auditing the Company's accrued research and development expenses and related prepaid expenses involved a high degree of subjectivity due to the estimation required by management in determining the progress to completion of services that have been performed that will be invoiced by the vendors, clinical research organizations and consultants and under clinical site agreements subsequent to the date that the financial statements are issued.

How We Addressed the Matter in Our Audit

To test the research and development accruals and prepaid expenses, our audit procedures included, among others, reviewing a sample of agreements with the service providers to corroborate key financial and contractual terms, and testing the accuracy and completeness of the underlying data used in the accrual and prepaid expense computations. We also evaluated management's estimates of the progress of a sample of research and development activities by making direct inquiries of the Company's operations personnel that oversee the external research and development activities and obtaining information directly from a sample of service providers. Additionally, we assessed the historical accuracy of management's estimates when evaluating the current period estimate. To evaluate the completeness of the accruals, we also examined subsequent invoices from the service providers and cash disbursements to the service providers, to the extent such invoices were received, or payments were made prior to the date that the financial statements were issued.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

Philadelphia, Pennsylvania
March 1, 2023

PMV Pharmaceuticals, Inc.
Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 108,297	$ 172,467
Restricted cash	822	822
Marketable securities, current	132,757	124,696
Prepaid expenses and other current assets	5,130	3,301
Total current assets	247,006	301,286
Property and equipment, net	10,955	3,090
Marketable securities, noncurrent	2,495	16,911
Right-of-use assets	9,539	10,060
Other assets	313	221
Total assets	$ 270,308	$ 331,568
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,996	$ 3,189
Accrued expenses	7,308	8,627
Operating lease liabilities, current	528	403
Total current liabilities	10,832	12,219
Operating lease liabilities, noncurrent	13,448	10,790
Total liabilities	24,280	23,009
Commitments and contingencies (see Note 6)		
Stockholders' equity:		
Preferred stock, $0.00001 par value, 5,000,000 shares authorized as of December 31, 2022 and December 31, 2021. No shares issued or outstanding as of December 31, 2022 and December 31, 2021.	—	—
Common stock, $0.00001 par value, 1,000,000,000 shares authorized; 45,771,332 and 45,433,684 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively.	—	—
Additional paid-in capital	487,516	476,363
Accumulated deficit	(241,043)	(167,726)
Accumulated other comprehensive loss	(445)	(78)
Total stockholders' equity	246,028	308,559
Total liabilities and stockholders' equity	$ 270,308	$ 331,568

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

PMV Pharmaceuticals, Inc.
Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Year Ended		
	December 31, 2022	December 31, 2021	December 31, 2020
Operating expenses:			
Research and development	$ 51,988	$ 36,493	$ 23,933
General and administrative	25,052	21,800	11,009
Total operating expenses	77,040	58,293	34,942
Loss from operations	(77,040)	(58,293)	(34,942)
Other income (expense):			
Interest income, net	3,627	449	651
Other income (expense), net	87	21	(143)
Total other income (expense)	3,714	470	508
Loss before (benefit) provision for income taxes	(73,326)	(57,823)	(34,434)
(Benefit) provision for income taxes	(9)	23	6
Net loss	(73,317)	(57,846)	(34,440)
Unrealized (loss) gain on available for sale investments, net of tax	(367)	(78)	3
Comprehensive loss	$ (73,684)	$ (57,924)	$ (34,437)
Net loss per share -- basic and diluted	$ (1.61)	$ (1.28)	$ (2.40)
Weighted-average common shares outstanding	45,594,824	45,137,656	14,364,475

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

PMV Pharmaceuticals, Inc.
Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balances at December 31, 2019	22,866,246	$ 168,933	3,046,200	$ —	$ 4,969	$ (3)	$ (75,440)	$ (70,474)
Issuance of Series D convertible preferred stock, net of issuance costs of $208	5,321,864	69,790	—	—	—	—	—	—
Conversion of convertible preferred stock to common stock	(28,188,110)	(238,723)	28,188,110	—	238,723	—	—	238,723
Exercise of warrants	—	—	9,688	—	194	—	—	194
Issuance of common stock, net of issuance costs of $20,359	—	—	13,529,750	—	223,176	—	—	223,176
Exercise of stock options	—	—	4,070	—	6	—	—	6
Stock-based compensation expense	—	—	—	—	1,933	—	—	1,933
Net loss	—	—	—	—	—	—	(34,440)	(34,440)
Unrealized gain on available for sale marketable securities	—	—	—	—	—	3	—	3
Balance at December 31, 2020	—	$ —	44,777,818	$ —	$ 469,001	$ —	$ (109,880)	$ 359,121
Exercise of stock options and common stock issued under the 2020 ESPP	—	—	655,866	—	2,022	—	—	2,022
Stock-based compensation expense	—	—	—	—	5,340	—	—	5,340
Net loss	—	—	—	—	—	—	(57,846)	(57,846)
Unrealized loss on available for sale marketable securities	—	—	—	—	—	(78)	—	(78)
Balance at December 31, 2021	—	$ —	45,433,684	$ —	$ 476,363	$ (78)	$ (167,726)	$ 308,559
Exercise of stock options and common stock issued under the 2020 ESPP	—	—	337,648	—	958	—	—	958
Stock-based compensation expense	—	—	—	—	10,195	—	—	10,195
Net loss	—	—	—	—	—	—	(73,317)	(73,317)
Unrealized loss on available for sale marketable securities	—	—	—	—	—	(367)	—	(367)
Balance at December 31, 2022	—	$ —	45,771,332	$ —	$ 487,516	$ (445)	$ (241,043)	$ 246,028

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

PMV Pharmaceuticals, Inc.
Statements of Cash Flows
(in thousands)

	Year Ended		
	December 31, 2022	December 31, 2021	December 31, 2020
Cash flows from operating activities:			
Net loss	$ (73,317)	$ (57,846)	$ (34,440)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	10,195	5,340	1,933
Depreciation	315	307	318
Amortization (accretion) of premiums on marketable securities	(628)	550	152
Non-cash lease expense	335	974	—
Other, net	(92)	(19)	143
Change in operating assets and liabilities:			
Prepaid expenses and other assets	(1,829)	38	(2,732)
Operating lease liabilities	2,969		
Accounts payable	(389)	191	(1,230)
Accrued expenses	(1,319)	3,894	3,117
Net cash used in operating activities	(63,760)	(46,571)	(32,739)
Cash flows from investing activities:			
Purchases of property and equipment	(7,984)	(1,349)	(148)
Purchases of marketable securities	(229,199)	(256,845)	(14,512)
Maturities of marketable securities	235,815	114,610	42,571
Net cash (used in) provided by investing activities	(1,368)	(143,584)	27,911
Cash flows from financing activities:			
Proceeds from issuance of convertible preferred stock, net issuance costs	—	—	69,790
Proceeds from the issuance of common stock, net	—	—	223,176
Proceeds from the exercise of stock options and common stock issued under the 2020 ESPP	958	2,022	6
Net cash provided by financing activities	958	2,022	292,972
Net decrease in cash, cash equivalents, and restricted cash	(64,170)	(188,133)	288,144
Cash, cash equivalents, and restricted cash			
Cash, cash equivalents, and restricted cash - beginning of period	173,289	361,422	73,278
Cash, cash equivalents, and restricted cash - end of period	$ 109,119	$ 173,289	361,422
Supplemental disclosures of noncash investing activities			
Lease incentives used for leasehold improvements	$ —	$ (88)	$ —
Accrued purchases of property and equipment	$ 196	$ 1,391	$ —
Supplemental disclosures of noncash financing activities			
Conversion of convertible preferred stock to common stock	$ —	$ —	$ 238,723
Conversion of warrant liability to common stock	$ —	$ —	$ 194
Supplemental disclosures of cash flow information			
Cash paid for income tax	$ —	$ 23	$ 6

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

PMV Pharmaceuticals, Inc.
Notes to Financial Statements
December 31, 2022 and 2021
(in thousands except share and per share amounts)

1. Formation and Business of the Company

Organization

PMV Pharmaceuticals, Inc. (the "Company") was incorporated in the state of Delaware in March 2013. Since inception, the Company has devoted substantially all of its time and efforts to performing research and development activities and raising capital. The Company is a precision oncology company pioneering the discovery and development of small molecule, tumor-agnostic therapies targeting p53. The Company's headquarters are located at 1 Research Way, Princeton, New Jersey.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry including, but not limited to, technical risks associated with the successful research, development and manufacturing of product candidates, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Current and future programs will require significant research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

On September 25, 2020, the Company completed an initial public offering (the "IPO") of 13,529,750 shares of common stock, at a public offering price of $18.00 per share including the exercise in full by the underwriters of their option to purchase up to 1,764,750 additional shares of commons stock, for aggregate gross proceeds of $243,536 and its shares started trading on The Nasdaq Global Select Market under the ticker symbol "PMVP." The Company received $223,176 in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by the Company. In connection with the closing of the IPO, all of the Company's outstanding shares of convertible preferred stock automatically converted into 28,188,110 shares of common stock.

The Company has incurred net losses and negative cash flows from operations since its inception. During the year ended December 31, 2022, the Company incurred a net loss of $73,317 and used $63,760 of cash for operations. As of December 31, 2022, the Company had an accumulated deficit of $241,043. Cash, cash equivalents, and marketable securities were $243,549 as of December 31, 2022. Management expects to incur substantial additional operating losses for the next several years and may need to obtain additional debt or equity financings in order to complete development of its products, obtain regulatory approvals, launch and commercialize its products and continue research and development programs. The Company believes it has adequate cash, cash equivalents, and marketable securities to operate for at least the next twelve months from the date of issuance of these financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with United States generally accepted accounting principles ("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 Update ("ASU") of the Financial Accounting Standards Board ("FASB"). The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business. The Company has limited operating history and its prospects are subject to risks, expenses and uncertainties frequently encountered by companies in the biotechnology industry.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of revenues and expenses during the reporting period. The Company bases its estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. Significant estimates and assumptions reflected in these financial statements include, but are not limited to, research and development costs, accrued research and development costs and related prepaid expenses, and the fair values of common stock, convertible preferred stock and stock-based compensation. Actual results could differ materially from those estimates.

Reverse Stock Split

In September 2020, the Company's board of directors and stockholders approved an amendment to the Company's amended and restated certificate of incorporation to affect a 5.2651-for-1 reverse stock split of the Company's common stock and convertible preferred stock, which was effected on September 24, 2020. The par value of the common stock and convertible preferred stock were not adjusted as a result of the reverse stock split. Accordingly, all common stock, convertible preferred stock, stock options, and related per share amounts in these financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split.

Fair Value of Financial Instruments

The Company discloses and recognizes the fair value of its assets and liabilities using a hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The hierarchy gives the highest priority to valuations based upon unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements) and the lowest priority to valuations based upon unobservable inputs that are significant to the valuation (Level 3 measurements). The guidance establishes three levels of the fair value hierarchy as follows:

- Level 1 - Inputs that reflect unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- Level 2 - Inputs other than quoted prices that are observable for the asset or liability either directly or indirectly, including inputs in markets that are not considered to be active.
- Level 3 - Inputs are unobservable in which there is little or no market data available, which require the reporting entity to develop its own assumptions that are unobservable.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

Cash, Cash Equivalents and Marketable Securities

Management considers all highly liquid investments with original maturities of three months or less to be cash equivalents.

The Company's marketable debt securities have been classified and accounted for as available-for-sale. The Company classifies its marketable debt securities as either short-term or long-term based on each instrument's underlying contractual maturity date. Marketable debt securities with maturities of 12 months or less are classified as short-term and marketable debt securities with maturities greater than 12 months are classified as long-term. The Company's marketable debt securities are carried at fair value, with unrealized gains and losses, net of taxes, reported as a component of accumulated other comprehensive loss in stockholders' equity. Premiums and discounts on marketable debt securities are amortized into earnings over the life of the security and recorded on the interest income, net line of the income statement. For the years ended December 31, 2022, 2021, and 2020, the Company recorded $628 of accretion, $550 of amortization and $152 of amortization, respectively.

Restricted cash as of December 31, 2022 included a $822 deposit at the Company's commercial bank underlying a stand-by letter of credit issued in favor of a landlord (See Note 6) and is classified in current assets.

Comprehensive Loss

The Company presents comprehensive loss in a single statement within its financial statements. Other comprehensive loss consists of unrealized gains and losses on marketable securities, net of tax.

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the circumstances present. The Company accounts for a contract as a lease when it has the right to control the asset for a period of time while obtaining substantially all of the asset's economic benefits. The Company determines the initial classification and measurement of its operating right-of-use ("ROU") assets and operating lease liabilities at the lease commencement date, and thereafter if modified. The lease term includes any renewal options that the Company is reasonably assured to exercise. The Company's policy is to not record leases with a lease term of 12 months or less on its balance sheets. Furthermore, the Company has elected the practical expedient to not separate lease and non-lease components by class of underlying asset for its existing leases. The Company's only existing leases are for office and laboratory space.

The ROU asset represents the right to use the leased asset for the lease term. The lease liability represents the present value of the lease payments under the lease. The present value of lease payments is determined by using the interest rate implicit in the lease, if that rate is readily determinable; otherwise, the Company uses its estimated secured incremental borrowing rate for that lease term.

Lease expense for operating leases is recognized on a straight-line basis over the reasonably assured lease term based on the total lease payments and is included in operating expense in the statements of operations.

Payments due under each lease agreement include fixed and variable payments. Variable payments relate to the Company's share of the lessor's operating costs associated with the underlying asset and are recognized when the event on which those payments are assessed occurs. Variable payments have been excluded from the lease liability and associated right-of-use asset. Neither of the Company's leases contain residual value guarantees.

The interest rate implicit in lease agreements is typically not readily determinable, and as such, the Company utilizes the incremental borrowing rate to calculate lease liabilities, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment.

Property and Equipment

Property and equipment are recorded at cost net of accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets, generally five years, except for leasehold improvements, which are amortized over the shorter of the useful life of the asset or the remaining term of the lease.

Upon retirement or sale of assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss is reflected in operations. Repairs and maintenance costs are charged to operations as incurred.

Impairment of Long-Lived Assets

Long-lived assets, are tested for recoverability whenever events or changes in the business environment indicate that the carrying amount of the assets may not be fully recoverable. Factors considered by the Company when deciding when to perform an impairment review include significant underperformance of the business against expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows resulting from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows resulting from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its current fair value. To date, the Company has not recorded any impairment losses on long-lived assets.

Research and Development Expenses

All costs associated with research and development are expensed as incurred. Research and development expenses include costs directly attributable to the conduct of research and development programs, including compensation costs, which includes allocated stock-based compensation, salary payroll taxes, employee benefits; materials; supplies; depreciation on and maintenance of research equipment; the cost of services provided by outside contractors; and the allocable portions of facility costs, such as rent, utilities, insurance, repairs and maintenance, depreciation, and general support services. The Company records accruals for estimated research and development expenses, comprising payments for work performed by third party vendors, clinical research organizations, clinical manufacturing organizations and others. Some of these vendors bill monthly based on actual services performed, while others bill periodically based upon achieving certain contractual milestones. For the latter, the Company accrues the expenses as goods or services are used or rendered. Research and development activities related to patient enrollment are accrued as patients enter and progress through the trial. In the event that the Company prepays fees, the Company records the prepayment as a prepaid asset and periodically evaluate the prepaid asset in conjunction with the related accrued research and development expenses.

Stock-Based Compensation

The Company's share-based compensation program allows for grants of stock options and restricted stock units. Grants are awarded to employees and non-employees, including directors.

The Company accounts for stock-based employee compensation arrangements in accordance with provisions of ASC 718, *Compensation – Stock Compensation* ("ASC 718"). ASC 718 requires the recognition of compensation expense, using a fair-value based method, for costs related to all share-based payments including stock options. ASC 718 requires companies to estimate the fair value of share-based payment awards on the date of grant using an option pricing or equity valuation model that is applied in a manner consistent with the fair value measurement objectives of ASC 718, is based on established principles of financial theory and reflects all of the substantive terms and conditions of the award. The Company uses the Black-Scholes option-pricing model ("Black-Scholes") to value stock option grants to employees, non-employees and directors. The fair value of the Company's common stock is used to determine the fair value of restricted stock units and stock options.

The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (i) the expected stock price volatility, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) expected dividends. Due to the lack of a public market for the Company's common stock until September 2020 and lack of company-specific historical and implied volatility data, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with expected term assumption. The Company uses the simplified method to calculate the expected term for options granted to employees whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the options due to its lack of sufficient historical data. The risk-free interest rate is based on U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock. The Company recognizes forfeitures as they occur.

Prior to the Company's IPO, due to the absence of an active market for the Company's common stock, the Company utilized methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, Valuation of Privately-Held Company Equity Securities Issued as Compensation, to estimate the fair value of its common stock. In determining the exercise prices for options granted, the Company considered the estimated fair value of the common stock as of the measurement date. Prior to the Initial Public Offering, the estimated fair value of the common stock was determined at each grant date based upon a variety of factors, including the illiquid nature of the common stock, arm's-length sales of the Company's capital stock (including convertible preferred stock), the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event. Other factors considered were the Company's financial position and historical financial performance, the status of technological developments within the Company's research, the composition and ability of the current research and management team, an evaluation or benchmark of the Company's competition, and the current business climate in the marketplace.

The Company's stock-based compensation awards are subject to service-based vesting conditions. Compensation expense related to awards to employees and directors with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is typically the vesting term.

Segment Reporting

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the Company's Chief Operating Decision Maker to make decisions with respect to resource allocation and assessment of performance. To date, the Company has viewed its operations and manages its business as one operating and reporting segment.

Net Loss per Common Share

Basic net loss per share is computed using the "two-class" method which includes the weighted average number of shares of common stock outstanding during the period and other securities that participate in dividends (a participating security). The Company's convertible preferred stock are participating securities as defined by ASC 260-10, *Earnings per Share*. During the periods where the Company incurs net losses, the Company allocates no loss to participating securities because these securities have no contractual obligation to share in the losses of the Company. Under the two-class method, basic net loss per share applicable to common stockholders is computed by dividing the net loss applicable to common stockholders by the weighted average number of common shares outstanding for the period. Diluted net loss per share is computed similar to basic net loss per share except that the denominator is increased to include the number of additional shares for the potential dilutive effects of a warrant, convertible preferred stock and stock options outstanding during the period calculated in accordance with the treasury stock method, or the two-class method, whichever is more dilutive. The Company allocates net earnings on a *pari passu* (equal) basis to both common and preferred stockholders. Net losses are not allocated to preferred stockholders as they do not have an obligation to share in the Company's net losses. For all periods presented, basic and diluted net loss per share are the same, as any additional share equivalents would be anti-dilutive.

Income Taxes

The Company accounts for income taxes in accordance with ASC 740, *Income Taxes* ("ASC 740"), which requires that deferred tax assets and liabilities be recognized using enacted tax rates for the effect of temporary differences between the book and tax bases of recorded assets and liabilities. Under ASC 740, the liability method is used in accounting for income taxes. Deferred tax assets and liabilities are determined based on the differences between financial reporting and the tax basis of assets and liabilities and are measured using the enacted tax rates and law that will be in effect when the differences are expected to reverse. ASC 740 also requires that deferred tax assets be reduced by a valuation allowance if it is more likely than not that some or all of the deferred tax assets will not be realized. The Company evaluates annually the realizability of the deferred tax assets by assessing the valuation allowance and by adjusting the amount of such allowance, if necessary. The factors used to assess the likelihood of realization include forecast of future taxable income and available tax planning strategies that could be implemented to realize the net deferred tax assets. In 2022 and 2021, the Company recorded a full valuation allowance for the deferred tax assets based on the historical loss and the uncertainty regarding the ability to project future taxable income. In future periods if the Company is able to generate income, the Company may reduce or eliminate the valuation allowance.

The Company accounts for uncertain tax positions in accordance with ASC 740. ASC 740 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax provision that an entity takes or expects to take in a tax return. Additionally, ASC 740 provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosures, and transition. Under ASC 740, an entity may only recognize or continue to recognize tax positions that meet a "more likely than not" threshold. In accordance with this accounting policy, the Company recognizes accrued interest and penalties related to unrecognized tax benefits as a component of income tax.

Recent Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Income Taxes – Simplifying the Accounting for Income Taxes*. The new guidance simplifies the accounting for income taxes by removing several exceptions in the current standard and adding guidance to reduce complexity in certain areas, such as requiring that an entity reflect the effect of an enacted change in tax laws or rates in the annual effective tax rate computation in the interim period that includes the enactment date. The Company adopted this standard as of January 1, 2021. The adoption did not have a material impact on the Company's financial statements.

(in thousands except share and per share amounts)

Concentration of Credit Risk and Other Risks and Uncertainties

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist of cash and cash equivalents and marketable securities. The Company maintains its cash, cash equivalents and marketable securities in accounts at high quality financial institutions. The Company has not experienced any credit losses and does not believe it is exposed to any significant credit risk on these funds. Cash and cash equivalents include a checking account and a money market account held at one financial institution. At times, such deposits may be in excess of insured limits. The Company has not experienced any losses on its deposits of cash and cash equivalents. The Company's marketable debt securities are carried at fair value and include any unrealized gains and losses. Any investments with unrealized losses are considered to be temporarily impaired.

The Company's future results of operations involve a number of risks and uncertainties. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations include, but are not limited to, rapid technological change, uncertainty of market acceptance of the product, competition from substitute products and larger companies, protection of proprietary technology, any future strategic relationships and dependence on key individuals.

Products developed by the Company require clearances from the U.S. Food and Drug Administration or other international regulatory agencies prior to commercial sales. There can be no assurance the Company's product candidates will receive the necessary clearances. If the Company is denied clearance, clearance is delayed or it is unable to maintain clearance, it could have a materially adverse impact on the Company.

3. Financial Instruments and Fair Value Measurements

The Company's financial instruments consist of money market funds, U.S. government debt securities and corporate debt securities. The following tables show the Company's cash equivalents and available-for-sale securities' carrying amounts and fair values as of December 31, 2022 and 2021:

	As of December 31, 2022						
	Carrying Amount	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value	Quoted priced in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Financial assets							
Money market funds	$ 106,861	$ —	$ —	$ 106,861	$ 106,861	$ —	$ —
Corporate securities	103,755	21	(185)	103,591	—	103,591	—
Government securities	31,942	—	(281)	31,661	20,981	10,680	—
Total financial assets	$ 242,558	$ 21	$ (466)	$ 242,113	$ 127,842	$ 114,271	$ —

	As of December 31, 2021						
	Carrying Amount	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value	Quoted Priced in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Financial assets							
Money market funds	$ 40,960	$ —	$ —	$ 40,960	$ 40,960	$ —	$ —
Corporate securities	227,378	3	(19)	227,362	—	227,362	—
Government securities	42,307	—	(62)	42,245	—	42,245	—
Total financial assets	$ 310,645	$ 3	$ (81)	$ 310,567	$ 40,960	$ 269,607	$ —

(in thousands except share and per share amounts)

Cash and Cash Equivalents – As of December 31, 2022, the Company had cash of $1,436 and cash equivalents, consisting of money market funds, of $106,861. As of December 31, 2021, the Company had cash of $3,507 and cash equivalents of $168,960. Cash equivalents consisted of money market funds of $40,960 and corporate debt securities of $128,000. Money market funds are classified within level 1 of the fair value hierarchy because they are valued using quoted market prices in active markets, whereas corporate debt securities are classified within level 2 of the fair value hierarchy because they are valued using inputs other than quoted prices that are observable for the asset or liability either directly or indirectly.

Marketable Securities – Marketable securities of $135,252 as of December 31, 2022, consisted of corporate debt securities of $103,591 and government debt securities of $31,661. There were $132,757 current marketable securities and $2,495 noncurrent marketable securities as of December 31, 2022. Marketable securities of $141,607 as of December 31, 2021, consisted of corporate debt securities of $99,362 and government debt securities of $42,245. There were $124,696 current marketable securities and $16,911 noncurrent marketable securities as of December 31, 2021.

As of December 31, 2022 and 2021, aggregated gross unrealized losses of available-for-sale investments were not material, and accordingly, no allowance for credit losses was recorded.

4. Property and Equipment, Net

	December 31,	
	2022	2021
Machinery & equipment	$ 2,448	$ 2,261
Computers	13	8
Furniture & fixtures	69	9
Leasehold improvements	409	161
Assets not placed in service	10,200	2,519
Total property and equipment	13,139	4,958
Less: Accumulated depreciation	(2,184)	(1,868)
Property and equipment, net	$ 10,955	$ 3,090

Depreciation expense for the years ended December 31, 2022, 2021, and 2020 was $315, $307, and $318, respectively.

5. Accrued Expenses

Accrued expenses consists of the following:

	December 31,	
	2022	2021
Accrued compensation	$ 2,897	$ 3,797
Accrued research and development costs	4,259	4,734
Other accrued liabilities	152	96
Total	$ 7,308	$ 8,627

6. Commitments and Contingencies

Operating Leases

In June 2015, the Company executed a noncancelable operating lease for approximately 13,000 square feet of laboratory, research and development, and office space in Cranbury, New Jersey for an initial base rent of $20.00 per square foot. This location operates as the Company's current headquarters.

In June 2017, the Company obtained an additional noncancelable operating lease for about 6,000 square feet of laboratory space in the same corporate center at an initial rental rate at $22.00 per square foot. As a result of the additional space, both leases expired June 2022. In January 2022, the Company signed a lease extension for both leases for up to one additional year through June 2023, with the option to terminate upon 120 days of written notice, with an increase in base rent as per the lease extension. Both leases include a common area maintenance expense for $3.00 per square foot with an increase of 3% on the first month of each calendar year during the lease term and a management fee of 3% of the base rent. The Company is obligated to pay, on a pro-rata basis, real estate taxes and operating costs related to the premises.

In August 2018, the Company executed two noncancelable operating leases. One lease for approximately 6,000 square feet for vivarium, laboratory and general office space in South Brunswick, New Jersey. The initial annual base rent is $15.50 per square foot and a management fee of 3% of the base rent. The Company is obligated to pay, on a pro-rata basis, insurance premiums, real estate taxes and operating costs related to the premises. The lease expired in July 2022. In January 2022, the Company signed a lease extension for up to one additional year through July 2023, with the option to terminate upon 120 days of written notice, with an increase in base rent as per the lease extension. The second lease is for office space in Lexington, Massachusetts, that expires August 2023, with an option to renew for a one-time, three-year extension. The initial annual base rent is $28.50 per square foot and will increase $1.00 per square foot at the end of each rent year.

In 2018, the Company received a lease incentive for the buildout of 420 Bedford Street in Lexington, MA. The Company was given an allowance for $165 on behalf of the lessor for construction of office space. Management recognizes this allowance as a lease incentive in its Right-of-Use asset and straight-lines the allowance throughout the term of the lease. As of December 31, 2022, the remaining rent incentive pertaining to the Lexington, MA lease totaled $25.

In January 2021, the Company signed a lease for 50,581 square feet of office and laboratory space at 1 Research Way in Princeton, New Jersey. That lease term extends through 2032, has a five-year extension option, and is intended to replace the Company's two existing facilities and the space is expected to become the Company's future headquarters. Payment under this lease will total $19,889 through May 2032. The Company received a lease incentive of $4,046 from the lessor for a buildout of laboratory, vivarium, and office space, to be reimbursed to the Company in 2022 and 2023. Management estimated the timing and amounts of reimbursements and included them as a reduction of lease payments when initially measuring the lease liability and right-of-use asset upon commencement. As of December 31, 2022, $2,969 of reimbursements were received.

The components of lease cost for the year ended December 31, 2022, and 2021, are as follows:

	Year Ended December 31,	
(in thousands)	**2022**	**2021**
Operating lease cost	$ 2,215	$ 1,691
Variable lease cost	991	704
Total lease cost	$ 3,206	$ 2,395

Amounts reported in the balance sheet for leases where the Company is the lessee as of December 31, 2022, and 2021, were as follows, in thousands:

	Year Ended December 31,	
Operating Leases:	**2022**	**2021**
Right-of-use assets, operating leases	$ 9,539	$ 10,060
Operating lease liabilities, current	$ 528	$ 403
Operating lease liabilities, non-current	13,448	10,790
Total operating lease liabilities	$ 13,976	$ 11,193
Weighted-average remaining lease term (years)	9.08	10.02
Weighted-average discount rate	5.75%	5.75%

Other information related to leases for the year ended December 31, 2022, and 2021, are as follows, in thousands:

	Year Ended December 31,	
	2022	**2021**
Net cash paid (received) for amounts included in the measurement of lease liabilities	$ (1,089)	$ 717
Leased assets obtained in exchange for new or modified operating lease liabilities	987	10,318

Future minimum lease payments, net of reimbursements, remaining as of December 31, 2022 under operating leases by fiscal year were as follows, in thousands:

Fiscal year	
2023	$ 1,219
2024	1,814
2025	1,869
2026	1,925
2027	1,983
Thereafter	9,494
Total minimum lease payments	$ 18,304
Less: Amounts representing imputed interest	(4,328)
Present value of lease liabilities	$ 13,976

Rent expense recorded for the years ended December 31, 2022 and 2021 was $2,215 and $1,691, respectively.

The Company currently subleases the office space at 420 Bedford Street in Lexington, MA to another company. This sublease agreement expires in August, 2023. In April 2021, the Company entered into a sublease agreement with the previous tenants of the office space at 1 Research Way in Princeton, NJ, from April 2021 to July 2021. For the year ended December 31, 2022 and 2021, sublease income for the Company was $107 and $116, respectively

Contingencies

From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of its business activities. The Company accrues a liability for such matters when future expenditures are probable and such expenditures can be reasonably estimated.

(in thousands except share and per share amounts)

7. Convertible Preferred Stock

In July 2020, the Company issued 5,321,864 shares of Series D Preferred Stock at a price of $13.1533 per share, resulting in gross proceeds of $70,000. In connection with the IPO on September 25, 2020, all of the Company's convertible preferred stock, including Series D Preferred Stock, outstanding at the time of the IPO automatically converted into an aggregate of 28,188,110 shares of common stock.

8. Stockholders' Equity

The Company is authorized to issue up to 1,000,000,000 shares of common stock with a par value of $0.00001 per share, and 5,000,000 shares of preferred stock with a par value of $0.00001 per share. As of December 31, 2022 and 2021, there were 45,771,332 and 45,433,684 shares of common stock issued and outstanding, respectively.

Common stockholders are entitled to receive dividends if and when declared by the board of directors subject to the rights of any preferred stockholders. As of December 31, 2022, no dividends on common stock had been declared by the Company.

As of December 31, 2022 and 2021, the Company had reserved shares of common stock for issuance as follows:

	December 31,	
	2022	2021
Options issued and outstanding	5,278,771	4,246,007
Shares available for future stock option and RSU grants	4,618,292	4,951,680
Shares available for employee stock purchase plan	705,559	801,464
Total	10,602,622	9,999,151

9. Stock Plan

2020 Equity Incentive Plan

The 2020 Equity Incentive Plan (the "2020 Plan") was approved by the board of directors on September 24, 2020. The 2020 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock units, restricted stock awards, unrestricted stock awards, cash-based awards and dividend equivalent rights to the Company's officers, employees, directors and consultants. The number of shares of common stock initially reserved for issuance under the 2020 Plan was 4,406,374, which shall be increased, upon approval by the board of directors, on January 1, 2021 and each January 1 thereafter, in an amount equal to the least of (i) 4,406,374 shares of common stock, (ii) five percent (5%) of the outstanding common stock on the immediately preceding December 31, or (iii) such number of common stock determined by the board of directors no later than the immediately preceding December 31. For 2022, the board's compensation committee, as the 2020 Plan administrator, exercised its discretion under clause (iii) to increase the number of shares of common stock reserved for issuance under the 2020 Plan by a lesser amount of 1,363,084 shares, effective as of January 1, 2022. For 2023, the board's compensation committee, as the 2020 Plan administrator, exercised its discretion under clause (iii) to increase the number of shares of common stock reserved for issuance under the 2020 Plan by a lesser amount of 1,830,853 shares, effective as of January 1, 2023. As of December 31, 2022, there were 4,618,292 shares available for issuance under the 2020 Plan.

(in thousands except share and per share amounts)

On September 9, 2022, the Company granted 374,899 Restricted Stock Units (RSUs) to employees pursuant to an employee retention program approved by the Board's compensation committee. The RSU's have graded vesting on an annual basis for two years of continuous service, as per the 2020 Plan.

The table below summarizes the annual grant activity under the 2020 Plan as of December 31, 2022:

	Shares Available for Grant
Balances, December 31, 2021	4,951,680
Shares reserved for issuance	1,363,084
Options granted	(1,419,197)
RSU's granted	(374,899)
Options forfeited / cancelled	97,624
Balances December 31, 2022	4,618,292

2020 Employee Stock Purchase Plan

The 2020 Employee Stock Purchase Plan (the "2020 ESPP") was approved by the board of directors on September 24, 2020. A total of 400,752 shares of common stock were initially reserved for issuance under this plan, which shall be increased, upon approval by the board of directors, on January 1, 2021 and each January 1 thereafter, to the lesser of (i) 801,504 shares of common stock, (ii) 1% of the outstanding shares of common stock on the last day of the immediately preceding fiscal year, or (iii) an amount determined by the board of directors or any of its committees no later than the last day of the immediately preceding fiscal year. For 2022, the board waived the annual increase to the shares reserved under the 2020 ESPP. For 2023, the 2020 ESPP reserved shares were increased under clause (iii) by 457,713 shares, effective as of January 1, 2023. On May 20, 2022, employees exercised their right to purchase 18,454 shares under the 2020 ESPP. On November 21, 2022, employees exercised their right to purchase 30,385 shares under the 2020 ESPP. As of December 31, 2022, 95,905 shares are issued or outstanding, and there were 705,559 shares available for issuance, under the 2020 ESPP.

2013 Equity Incentive Plan

In 2013, the Company adopted the 2013 Stock Plan (the "2013 Plan"). On September 24, 2020, this plan was replaced by the 2020 Plan, and future issuances of incentive instruments will be governed by that plan. Subject to the provisions of the 2020 Plan, the Company had the option to either forfeit or repurchase remaining shares under the 2013 Equity Incentive Plan on or after the registration date. The Company chose to forfeit the remaining shares.

Restricted Stock Units

The following table presents RSU activity under the 2020 Plan as of December 31, 2022:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2021	—	$ —
Granted	374,899	13.6
Unvested shares at December 31, 2022	374,899	$ 13.6

As of December 31, 2022, there was $4,317 of unrecognized compensation cost related to RSUs that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 1.7 years.

Stock Options

The following table summarizes option activity for the year ended December 31, 2022:

	Options Outstanding			
	Number of Options	Weighted Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in 000s)
Balances, December 31, 2021	4,246,007	$ 8.22	6.86	$ 68,506
Options granted	1,419,197	$ 15.83		
Options forfeited / cancelled	(97,624)	$ 20.04		
Options exercised	(288,809)	$ 1.67		
Balances December 31, 2022	5,278,771	$ 10.40	6.82	$ 17,244
At December 31, 2022				
Vested and expected to vest	5,278,771	$ 10.40	6.82	$ 17,244
Exercisable	3,281,213	$ 6.91	5.76	$ 15,520

The weighted average grant date fair value of stock options granted during the year ended December 31, 2022 and 2021 was $10.92 and $20.03, respectively.

The aggregate intrinsic value of options vested and exercisable as of December 31, 2022 and 2021 is calculated based on the difference between the exercise price and the fair value of our common stock. The intrinsic value of options exercised in 2022 and 2021 was $3,764 and $18,534, respectively.

As of December 31, 2022, the total compensation cost related to nonvested service-based awards not yet recognized is $21,005. The weighted-average period over which the nonvested awards is expected to be recognized is 2.8 years.

The Company estimated the fair value of stock options using the Black-Scholes options valuation model. The fair value of employee stock options is being amortized on a straight-line basis over the requisite service period of the awards. The fair value of employee stock options was estimated using the following assumptions:

	Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	1.48% - 4.34%	0.35% - 1.30%	0.31% - 1.51%
Expected life (in years)	5.50 - 6.44	5.50 - 6.44	4.92 - 6.40
Dividend yield	0%	0%	0%
Expected volatility	76.33% - 81.00%	76.50% - 79.90%	70.70% - 77.60%

The weighted average assumptions used to estimate the fair value of stock purchase rights under the 2020 ESPP are as follows:

	Year Ended December 31,	
	2022	2021
Risk-free interest rate	3.44%	0.0004
Expected life (in years)	0.49	0.5
Dividend yield	0%	0%
Expected volatility	77.00%	77.83%

Expected Term: The Company uses the simplified method to calculate expected term described in the SEC's Staff Accounting Bulletin No. 107, which takes into account vesting term and expiration date of the options.

Volatility: Volatility is based on an average of the historical volatilities of comparable publicly traded companies for the expected term.

Risk Free Interest Rate: The risk-free rate is based on the U.S. Treasury yields in effect at the time of grant for periods corresponding with the expected term of the option.

Dividend Yield: The Company has never declared or paid any cash dividends and does not plan to pay cash dividends in the foreseeable future, and therefore, used an expected dividend yield of zero in the valuation model.

Stock-based compensation expense recorded under ASC 718 was allocated to research and development and general and administrative expense as follows:

	For the Years Ended December 31,		
	2022	2021	2020
Research and development	$ 3,466	$ 1,440	$ 836
General and administrative	6,729	3,900	1,097
Total stock-based compensation	$ 10,195	$ 5,340	$ 1,933

Stock-based compensation expense by award type included within the condensed consolidated statements of operations is as follows:

	For the Years Ended December 31,		
	2022	2021	2020
Stock options	$ 9,174	$ 4,938	$ 1,933
Restricted stock units	790	—	—
Employee stock purchase plan	231	402	—
Total stock-based compensation	$ 10,195	$ 5,340	$ 1,933

10. Income Taxes

The income tax (benefit) provision for the years ended December 31, 2022, 2021, and 2020 are as follows (in thousands):

	For the Years Ended December 31,		
	2022	2021	2020
Current:			
Federal	$ -	$ -	$ -
State	(9)	23	6
Total current	(9)	23	6
Deferred:			
Federal	$ -	$ -	$ -
State	-	-	-
Total deferred	-	-	-
Total (benefit) provision	$ (9)	$ 23	$ 6

(in thousands except share and per share amounts)

A reconciliation of income tax computed at the statutory federal income tax rate to the (benefit) provision for income taxes included in the accompanying statements of operations for the Company is as follows:

	For the Years Ended		
	December 31, 2022	December 31, 2021	December 31, 2020
Income tax provision at statutory rate	21%	21%	21%
State income taxes, net of federal benefit	7%	9%	8%
Tax credits	3%	3%	2%
Stock compensation	0%	5%	(1)%
Executive compensation limitation	(1)%	0%	0%
Other	0%	(1)%	0%
Change in valuation allowance	(30)%	(37)%	(30)%
Effective income tax rate	0%	0%	0%

For the years ended December 31, 2022, 2021, and 2020, the Company's effective tax rate is below the federal statutory income tax rate of 21% primarily due to state income taxes, net of federal benefit and the Company's position to establish a full valuation allowance on its deferred tax assets.

The tax effect of temporary differences and carryforwards that give rise to significant portions of the deferred tax assets and liabilities are presented below:

	As of December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 49,451	$ 45,231
Stock compensation	2,905	1,587
Capitalized research expenditures	13,563	-
Research and development credits	6,856	4,593
Accruals and other	911	1,033
Operating lease liabilities	3,969	3,175
Total deferred tax assets	77,655	55,619
Valuation allowance	(74,917)	(52,728)
Deferred tax assets recognized	2,738	2,891
Deferred tax liabilities:		
Right-of-use assets	(2,709)	(2,854)
Fixed assets and depreciation	(29)	(37)
Total deferred tax liabilities	(2,738)	(2,891)
Net deferred tax assets	$ -	$ -

The Company has recorded a valuation allowance for its deferred tax assets that it does not believe will be realizable at a more likely than not level based on analysis of all available sources of taxable income.

(in thousands except share and per share amounts)

As of December 31, 2022 and 2021, the Company had federal net operating loss carryforwards of $174,736 and $159,886, respectively. As of December 31, 2022, the Company had state net operating loss carryforwards for New Jersey, California, Massachusetts, and Arizona of approximately $169,847, $4,912, $5,277, and $46, respectively. At December 31, 2021, the Company had state net operating loss carryforwards for New Jersey, California and Massachusetts of approximately $154,972, $4,912, and $4,640 respectively. Federal net operating loss carryforwards of $27,500 expire beginning in the year 2033. State net operating loss carryforwards begin to expire in the year 2033. Net operating loss carryforwards related to tax years after 2017 of $147,236 do not expire. The Company also has federal and state research and development credit carryforward of approximately $9,749 and $6,588 as of December 31, 2022 and 2021, respectively. The federal credits will begin to expire in 2034 if not utilized. The California state credits carryforward indefinitely and the New Jersey state credits expire starting in 2030. The above net operating losses and research and development credits are subject to Sections 382 and 383 of the Internal Revenue Code. In the event of a change in ownership as defined by these code sections, the usage of the net operating losses and research and development credits may be limited.

The Company accrues interest and penalties related to unrecognized tax benefits in the (benefit) provision for income taxes line item in the statements of operations and comprehensive loss**.** As of December 31, 2022 and 2021, the Company had not accrued any interest or penalties related to uncertain tax positions.

If the ending balance of $2,437 and $1,654 of unrecognized tax benefits as of December 31, 2022 and 2021, respectively, were recognized, none of the recognition would affect the income tax rate. The following table summarized the activity related to the Company's unrecognized tax benefits:

	For the Years Ended	
	December 31, 2022	December 31, 2021
Unrecognized tax benefits, beginning of year	$ 1,654	$ 877
Increases related to prior year tax positions	-	43
Increases related to current year tax positions	783	734
Unrecognized tax benefits, end of year	$ 2,437	$ 1,654

The Company does not anticipate any material change in its unrecognized tax benefits over the next twelve months. The unrecognized tax benefits may change during the next year for items that arise in the ordinary course of business.

The Company files U.S. federal and state income tax returns with varying statutes of limitations. The Company's tax years 2013 to 2021 will remain open for examination by the federal and state authorities for three and four years, respectively, from the date of utilization of any net operating losses and research and development credits.

11. Net Loss per Share

The Company excluded all outstanding stock options and restricted stock units at each period end from the computation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect. The following common stock equivalents were excluded from the calculation of diluted net loss per share:

	As of December 31,	
	2022	2021
Options to purchase common stock	5,278,771	4,246,007
Unvested restricted common stock units	374,899	—
Unvested employee stock purchase plan shares	95,905	47,066
Total	5,749,575	4,293,073

12. Related Parties

The Company has consulting agreements with two members of its board of directors; one of which waived his consulting fees as of September 2021. Total consulting fees paid in in the year ended December 31, 2022, were $111. There were no amounts owed under the consulting agreements as of December 31, 2022.

Total consulting fees paid as of the year ended December 31, 2021, were $110. In May of 2021, two members of the board of directors were awarded 5,781 options of Company stock each, as per their updated Scientific Advisory Board agreements. There were no amounts owed under the consulting agreements as of December 31, 2021.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Our management maintains disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

As of December 31, 2022, the Company conducted an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended ("the Exchange Act"). Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of the end of the period covered by this Annual Report on Form 10-K.

Management's Report on Internal Control Over Financial Reporting

Our management is also responsible for establishing and maintaining for us adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, our management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the *Internal Control—Integrated* Framework (2013 framework) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under this framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

Changes in Internal Control Over Financial Reporting

An evaluation was also performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of any changes in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. That evaluation did not identify any change in our internal control over financial reporting during the fourth quarter of the year ended December 31, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

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 under the captions "Directors and Corporate Governance," "and "Other Matters—Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement for the annual meeting of stockholders to be held in June 2023 to be filed with the SEC on or before April 30, 2023, or the Proxy Statement, and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item will be included under the captions "Executive Compensation," and "Directors and Corporate Governance" in the Proxy Statement 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 under the captions "Beneficial Ownership of Shares of Common Stock" and "Executive Compensation—Equity Compensation Plan Information" in the Proxy Statement 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 under the captions "Certain Relationships and Related Person Transactions" and "Directors and Corporate Governance" in the Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be included under the captions "Ratification of Appointment of Independent Registered Public Accounting Firm" in the Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

EXHIBIT INDEX

Exhibit Number	Description	Form	File No.	Number	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended, as currently in effect.	8-K	001-39539	3.1	September 29, 2020
3.2	Amended and Restated Bylaws of the Registrant, as currently in effect.	8-K	001-39539	3.2	September 29, 2020
4.1	Description of Securities of the Registrant.	10-K	001-39539	4.1	March 3, 2021
4.2	Amended and Restated Investors' Rights Agreement, dated July 17, 2020, by and among the Registrant and certain of its stockholders.	S-1	33-248627	4.1	September 4, 2020
4.3	Specimen common stock certificate of the Registrant.	S-1/A	333-248627	4.2	September 21, 2020
4.4	Form of Indenture.	S-3ASR	333-260012	4.4	October 4, 2021
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-248627	10.1	September 4, 2020
10.2+	2013 Equity Incentive Plan, as amended, and forms of agreement thereunder.	S-1/A	333-248627	10.2	September 21, 2020
10.3+	2020 Equity Incentive Plan and forms of agreements thereunder.	S-1/A	333-248627	10.3	September 21, 2020
10.4+	2020 Employee Stock Purchase Plan and forms of agreements thereunder.	S-1/A	333-248627	10.4	September 21, 2020
10.5+	Employment Offer Letter, dated August 17, 2020, by and between the Registrant and David H. Mack, Ph.D.	S-1	333-248627	10.5	September 4, 2020
10.6+	Employment Offer Letter, dated August 17, 2020, by and between the Registrant and Winston Kung.	S-1	333-248627	10.6	September 4, 2020
10.7+	Employment Offer Letter, dated August 18, 2020, by and between the Registrant and Leila Alland, M.D.	S-1	333-248627	10.7	September 4, 2020
10.8+	Employment Offer Letter, dated February 22, 2021, by and between the Registrant and Deepika Jalota, Pharm.D.	10-K	001-39539	10.8	March 1, 2022
10.9+	Employee Incentive Compensation Plan.	S-1	333-248627	10.9	September 4, 2020
10.10+	Change in Control and Severance Policy.	S-1	333-248627	10.10	September 4, 2020

10.11+	Amended and Restated Change in Control and Severance Policy Participation Agreement, dated August 17, 2020, by and between the Registrant and David H. Mack, Ph.D.	S-1	333-248627	10.11	September 4, 2020
10.12+	Amended and Restated Change in Control and Severance Policy Participation Agreement, dated August 17, 2020, by and between the Registrant and Winston Kung.	S-1	333-248627	10.12	September 4, 2020
10.13+	Amended and Restated Change in Control and Severance Policy Participation Agreement, dated August 18, 2020, by and between the Registrant and Leila Alland, M.D.	S-1	333-248627	10.13	September 4, 2020
10.14+	Amended and Restated Change in Control and Severance Policy Participation Agreement, dated January 14, 2022, by and between the Registrant and Deepika Jalota, Pharm.D.	10-K	001-39539	10.14	March 1, 2022
10.15+*	Amended Outside Director Compensation Policy.				
10.16	Consulting Agreement, dated January 1, 2016, by and between the Registrant and Arnold Levine, Ph.D.	S-1	333-248627	10.16	September 4, 2020
10.17	Consulting Agreement, dated May 21, 2021, by and between the Registrant and Richard Heyman, Ph.D., as amended on July 16, 2021	10-K	001-39539	10.17	March 1, 2022
10.18	Lease Agreement, dated March 3, 2015, by and between the Registrant and Cedar Brook 2005, LP, as amended by the First Amendment to Lease dated April 24, 2017.	S-1	333-248627	10.18	September 4, 2020
10.19	Lease Agreement, dated January 8, 2021, by and between the Registrant and BMR-ONE RESEARCH WAY LLC.	10-K	001-39539	10.19	March 3, 2021
10.20	Open Market Sale Agreement, dated as of October 4, 2021, between the Registrant and Jefferies LLC	S-3ASR	333-260012	1.2	October 4, 2021
21.1	List of Subsidiaries	10-K	001-39539	21.1	March 1, 2022
23.1*	Consent of Independent Registered Public Accounting Firm.				
24.1*	Power of Attorney (contained in the signature page to this Annual Report on Form 10-K).				
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				

32.1*#	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
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.
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.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101)

* Filed herewith.

+ Indicated management contract or compensatory plan.

The certifications attached as Exhibits 32.1 and 32.2 that accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary

The Company has elected not to include summary information.

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 Annual Report to be signed on its behalf by the undersigned, thereunto duly authorized.

PMV PHARMACEUTICALS, INC.

By: /s/ David H. Mack
David H. Mack, Ph.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 David H. Mack, Ph.D. and Winston Kung, jointly and each one of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place, and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ David H. Mack David H. Mack, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2023
/s/ Winston Kung Winston Kung	Chief Operating Officer and Chief Financial Officer (Principal Financial and Accounting Officer)	March 1, 2023
/s/ Richard Heyman Richard Heyman, Ph.D.	Director and Chairman of the Board of Directors	March 1, 2023
/s/ Arnold Levine Arnold Levine, Ph.D.	Director	March 1, 2023
/s/ Carol Gallagher Carol Gallagher, Ph.D.	Director	March 1, 2023
/s/ Laurie Stelzer Laurie Stelzer	Director	March 1, 2023
/s/ Charles M. Baum Charles M. Baum, MD., Ph.D.	Director	March 1, 2023
/s/ Kirsten Flowers Kirsten Flowers	Director	March 1, 2023

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