

**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, 2021
- 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 001-37998

JOUNCE THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	45-4870634 (I.R.S. Employer Identification No.)
780 Memorial Drive Cambridge, Massachusetts (Address of principal executive offices)	02139 (Zip Code)

Registrant's telephone number, including area code: (857) 259-3840

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

<u>Title of each class</u>	<u>Trading Symbol(s)</u>	<u>Name of each exchange on which registered</u>
Common Stock, \$0.001 par value per share	JNCE	Nasdaq Global Select Market

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

None

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes No

As of June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's Common Stock held by non-affiliates of the registrant was approximately \$210,613,231, based upon the closing price of the registrant's Common Stock on June 30, 2021.

As of February 28, 2022, there were 51,664,688 shares of common stock, \$0.001 par value per share, outstanding.

Documents Incorporated by Reference

Portions of the registrant's Definitive Proxy Statement on Schedule 14A relating to its 2022 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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References to Jounce

Throughout this Annual Report on Form 10-K, the “Company,” “Jounce,” “Jounce Therapeutics,” “we,” “us,” and “our,” except where the context requires otherwise, refers to Jounce Therapeutics, Inc. and its consolidated subsidiary, and “our board of directors” refers to the board of directors of Jounce Therapeutics, Inc.

Cautionary Note Regarding Forward-Looking Statements and Industry Data

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words “aim,” “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “goal,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “target,” “will” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- the timing, progress, and results of preclinical studies and clinical trials for our current and future product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our research and development programs;
- our plans and expectations in light of the COVID-19 pandemic and its impacts on our operations and global healthcare systems;
- the timing, scope, or likelihood of regulatory filings and approvals, including, as applicable, timing of our investigational new drug applications for, biologics license application filing for, and final Food and Drug Administration approval of our current and future product candidates;
- our ability to use our Translational Science Platform to identify targets for future product candidates and to match immunotherapies to select patient subsets;
- our ability to identify, develop and advance future product candidates into, and successfully complete, clinical studies;
- our ability to develop combination therapies, whether on our own or in collaboration with third parties, for our current and future product candidates;
- our expectations regarding the size of the patient populations for our product candidates, if approved for commercial use, and any product candidates we may develop;
- our commercialization and marketing capabilities and strategy;
- the pricing and reimbursement of our current and future product candidates, if approved;
- the implementation of our business model and our strategic plans for our business, our current and future product candidates, and our technology;
- our ability to develop and commercialize a companion diagnostic or complementary diagnostic for our current and future product candidates;
- the rate and degree of market acceptance and clinical utility of our current and future product candidates;
- the potential benefits of our exclusive license of GS-1811, formerly JTX-1811, to Gilead Sciences, Inc.;
- our ability to establish or maintain future collaborations or strategic relationships or obtain additional funding;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering our current and future product candidates, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- our competitive position, and developments and projections relating to our competitors and our industry;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and

- the impact of laws and regulations.

There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the section entitled “Risk Factors” in Part I, Item 1A that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K may include industry and market data, which we may obtain from our own internal estimates and research, as well as from industry and general publications and research, surveys, and studies conducted by third parties. Industry publications, studies, and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that such studies and publications are reliable, we have not independently verified market and industry data from third-party sources.

Summary of Risk Factors

Below is a summary of the principal risk factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading “Risk Factors” and should be carefully considered, together with other information in this Form 10-K and our other filings with the SEC, before making an investment decision regarding our common stock.

- We are early in our development efforts. If we are unable to advance our product candidates through clinical development, advance future product candidates to clinical development or obtain marketing approval and ultimately commercialize any product candidates, our business will be materially harmed.
- The ongoing COVID-19 pandemic has adversely affected, and may continue to adversely affect, our business, including our clinical trials, supply chain and preclinical studies.
- Clinical product development involves a lengthy and expensive process, with an uncertain outcome. We will incur additional costs in connection with, and may experience delays, in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- If we encounter difficulties enrolling or retaining patients in our clinical trials, our clinical development activities could be delayed or otherwise be adversely affected.
- Because we rely on third-party manufacturing and supply partners, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.
- We rely and expect to continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, our business could be substantially harmed.
- We currently face and will face significant competition. If our competitors develop and market products that are more effective, safer or less expensive than any of our product candidates, our commercial opportunities will be negatively impacted.
- We rely on our Translational Science Platform to identify and develop product candidates. Our competitive position could be materially harmed if our competitors develop a platform similar to our Translational Science Platform and develop rival product candidates.
- We will depend on Gilead to develop, manufacture and commercialize GS-1811 and may depend on additional third parties for the development and commercialization of other product candidates.
- We may develop companion diagnostics and/or complementary diagnostics for our product candidates. If we are unable to successfully develop such companion diagnostics or complementary diagnostics, or experience significant delays in doing so, we may not realize the full commercial potential of our current or future product candidates.

- We have accumulated significant losses since our inception and anticipate that we will continue to incur substantial net losses in the foreseeable future.
- We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- If we are unable to obtain, maintain and protect our intellectual property rights for our product candidates or if our intellectual property rights are inadequate, our competitive position could be harmed.
- If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.
- We are highly dependent on our key personnel, and if we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.
- The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

Website and Social Media Disclosure

From time to time, we may use our website (www.jouncetx.com), investor and media relations website (<http://ir.jouncetx.com>), Facebook page (<https://www.facebook.com/jouncetx>), LinkedIn page (<https://www.linkedin.com/company/3494537/>) and Twitter feed (<https://twitter.com/JounceTx>) as channels for the distribution of information. The information we post through these channels may be deemed material. Accordingly, investors should monitor these channels, in addition to following our press releases, Securities and Exchange Commission filings and public conference calls and webcasts. The contents of our website and social media channels are not, however, a part of this report.

PART I

Item 1. Business Overview

We are a clinical-stage immunotherapy company dedicated to transforming the treatment of cancer by developing therapies that enable the immune system to attack tumors and provide long-lasting benefits to patients. Our strategy is to use a biomarker-driven approach from discovery through clinical development. We have developed a suite of integrated technologies that comprise our Translational Science Platform, enabling us to comprehensively interrogate the cellular and molecular composition of tumors. By focusing on specific cell types, both immune and non-immune, within tumors, we can prioritize targets and then identify related biomarkers designed to match the right therapy to the right patient. Our pipeline is focused on product candidates to address PD-(L)1-inhibitor resistant and PD-(L)1 inhibitor sensitive tumors, which represent significant opportunities requiring different biological approaches. We aim to develop product candidates that address the unmet medical need of patients in both of these populations.

Our highest priority program, JTX-8064, is being developed for patients with either PD-(L)1-inhibitor resistant or PD-(L)1 inhibitor sensitive tumors. JTX-8064 is the first tumor-associated macrophage candidate to emerge from our Translational Science Platform. JTX-8064 is a monoclonal antibody that binds to Leukocyte Immunoglobulin Like Receptor B2, or LILRB2 (also known as ILT4), which is a cell surface receptor expressed on macrophages and other myeloid cells. Our INNATE clinical trial is a Phase 1/2 clinical trial of JTX-8064 as a monotherapy and in combination with our PD-1 inhibitor, pimiralisib, in patients with solid tumors. In January 2021, we began enrollment in the dose-escalation portion of the INNATE trial and enrollment was completed in July and October 2021 for monotherapy and combination therapy, respectively. JTX-8064 has been well-tolerated to date with no observed dose limiting toxicities. We selected 700 mg as our recommended phase 2 dose for further evaluation. We initiated enrollment in August 2021 and October 2021 in the phase 2 monotherapy and combination therapy portions, respectively. The INNATE trial is comprised of one monotherapy and seven combination indication-specific expansion cohorts and is designed to demonstrate proof-of-concept. Once proof-of-concept is established, we plan to move JTX-8064 rapidly into registrational trials on a cohort by cohort basis.

The expansion cohorts are studying tumor types in three groups of patients: (i) PD-(L)1 inhibitor experienced patients whose tumors progressed on or after treatment with a PD-(L)1 inhibitor (including, non-small cell lung cancer, or NSCLC), (ii) PD-(L)1 inhibitor naïve patients whose tumors are historically resistant to PD-(L)1 inhibitors (including, ovarian cancer), and (iii) PD-(L)1 inhibitor naïve patients whose tumors are historically more sensitive to PD-(L)1 inhibitors (including, front line PD-L1 positive head and neck squamous cell carcinoma). Proof-of concept expansion cohorts have the potential to enroll up to 29 patients per combination therapy cohort and 47 patients in the monotherapy cohort if pre-specified criteria are met. We expect to report preliminary clinical and biomarker data from INNATE in 2022.

Vopratelimab is a clinical-stage monoclonal antibody that binds to and activates the Inducible T cell CO-Stimulator, or ICOS, a protein on the surface of certain T cells commonly found in many solid tumors. We are currently enrolling patients in the SELECT trial, a randomized phase 2 proof-of-concept trial outside the United States evaluating vopratelimab in combination with pimiralisib compared to pimiralisib alone in biomarker-selected, immunotherapy-naïve second-line NSCLC patients. We identify patients for SELECT using TIS^{vopra}, an 18 gene signature that includes genes relevant to both CD8 and CD4 T cell biology. TIS^{vopra} has been optimized to predict for emergence of ICOS hi CD4 T cells in the peripheral blood, which have been associated with clinical benefit in patients treated with vopratelimab alone or in combination with nivolumab. We expect to report complete clinical data from SELECT in the second half of 2022.

Pimiralisib is a clinical-stage anti-PD-1 monoclonal antibody that we are developing primarily for potential use in combination with our product candidates, as we believe that combination therapy has the potential to be a mainstay of cancer immunotherapy. We presented safety and preliminary efficacy data from our monotherapy Phase 1 clinical trial of pimiralisib in 2019. Based on the results of that clinical trial, we are using pimiralisib in combination with JTX-8064 in INNATE and with vopratelimab in SELECT.

GS-1811, formerly JTX-1811, is the fourth internally developed program to enter the clinic. In August 2020, we entered into an agreement to exclusively license GS-1811 to Gilead Sciences, Inc., or Gilead. GS-1811 is a monoclonal antibody that is designed to selectively deplete T regulatory cells in the tumor microenvironment, or TME, by targeting a receptor called CCR8, which is preferentially expressed on intra-tumoral T regulatory cells. Pursuant to our exclusive license agreement with Gilead, or the Gilead License Agreement, we granted Gilead a worldwide license to develop, manufacture and commercialize GS-1811 and certain derivatives thereof, as well as backup antibodies defined within the agreement. Under the terms of the Gilead License Agreement, we advanced GS-1811 through the clearance of an investigational new drug application, or IND, in June 2021, which triggered a \$25.0 million milestone payment in July 2021, and have transitioned the program to Gilead. Gilead initiated clinical trials of GS-1811 in August 2021. We are entitled to receive additional payments from Gilead upon the achievement of specified clinical, regulatory and sales milestones. We are also eligible to receive tiered royalty payments based on a percentage of annual worldwide net sales ranging from the high-single digits to mid-teens, based on future annual net sales of licensed products, on a licensed product-by-licensed product and country-by-country basis.

JTX-1484 is the most recent product candidate to emerge from our Translational Science Platform. JTX-1484 is a monoclonal antibody designed to block human Leukocyte Immunoglobulin Like Receptor B4, or LILRB4, on various myeloid cells which we believe may lead to reduced immune suppression and enhancement of T cell functionality. We are currently conducting IND-enabling activities for JTX-1484, with the goal of filing an IND in 2023.

With our biomarker-driven approach, we leverage our Translational Science Platform to interrogate cell types within the human TME and to identify and prioritize targets across a broad spectrum of immune and non-immune cell types. In addition, early in the development process, we use our Translational Science Platform to identify potential predictive biomarkers to enable us to enrich our clinical trials for patient populations that may be more likely to respond to a particular immunotherapy. Once clinical data is available for a product candidate, we then use a reverse translational approach to interrogate tumor and blood samples from patients with known outcomes. By using these reverse translational findings, we believe we are better able to design clinical trials and more efficiently develop cancer immunotherapies that potentially provide greater benefit to patients. These biomarker results, coordinated to clinical response, will assist with determining the benefit of proceeding to the use of a companion diagnostic and/or complementary diagnostic for a given therapy.

Our Strategy

We aim to build a multi-product company that discovers, develops and commercializes first-in-class and/or best in class novel therapeutics and combination approaches for patients who are less likely to respond, or who have experienced limited or no response, to currently-approved therapies. Key elements of our strategy include:

- Aggressively develop our product candidates, and potential future product candidates, using a biomarker-driven approach and reverse translational analysis aimed at bringing the right immunotherapy to the right patients;
- Continue investment in our Translational Science Platform to enhance our understanding of the TME, as we look to broaden the benefit of immunotherapy through targeting additional cell types;
- Address the unmet need of cancer patients with tumors unresponsive to T effector cell-directed therapies by focusing our discovery efforts on other cell types within the TME; and
- Expand our pipeline by leveraging our internal discovery platform and/or in-licensing new technologies, product candidates and methodologies.

Immuno-Oncology Overview

The development of immune checkpoint inhibitors introduced a shift in potential cancer treatments, given that earlier treatments historically focused on either killing or arresting the proliferation of the tumor cells themselves. PD-1 and PD-L1 checkpoint inhibitors bind to the PD-1 or PD-L1 receptor on certain T cells and tumor cells, and are approved in multiple cancer types and across different lines of therapy. Even with the success of these antibodies that bind to PD-1 or PD-L1, known as PD-(L)1 inhibitors, there is still a significant unmet medical need for patients who fail to respond to or respond and later relapse on these therapies. We believe that an important approach to meeting this unmet need to is target additional types of immunosuppressive immune cells in the tumor microenvironment.

The interplay between the immune system and cancer is dynamic. As more patients in an expanded set of indications are being exposed to cancer immunotherapies we are learning about the factors that may contribute to a lack of response or a failed response. Biological approaches—beyond those focused on CD8 T cell biology—may be needed to address the unmet medical need of cancer patients who do respond to and relapse after receiving PD-(L)1 inhibitors. Reasons for resistance to immunotherapy may include a lack of appropriate immune cells in the TME, such as the absence of T effector cells, or the presence of immunosuppressive cells, such as T regulatory cells or tumor associated macrophages. Additionally, a tumor may initially respond to a PD-(L)1 inhibitor, but other immune checkpoints may emerge or an acquired resistance to the particular immunotherapy may occur, for example through genetic alterations in key T cell signaling pathways. In these cases, therapeutic approaches that utilize new mechanisms and target cell types other than T effector cells within the TME may restore or broaden the applicability of cancer immunotherapies. We believe LILRB2 may function as an immune checkpoint for macrophages, and its activation, through ligand binding, may suppress anti-tumor immune responses. We believe that by inhibiting LILRB2’s interaction with its ligands, our lead macrophage program, JTX-8064, may have the potential to restore the activity of PD-(L)1 inhibitors in otherwise resistant settings. For patients who have benefited from cancer immunotherapies, data emerging from clinical studies with PD-(L)1 inhibitors suggests the importance of a biomarker-driven patient-enrichment strategy. Additional highlights of the evolving immunotherapy landscape include longer-lasting responses as compared to chemotherapy and that these longer-lasting responses can be improved with combination therapy.










Our Translational Science Platform enables both the identification and prioritization of targets across a broad spectrum of immune and non-immune cell types and the identification of potential biomarkers to inform our clinical development strategy. We believe this platform may position us to address multiple pathways and indications, including those that may be important in colder tumors that are unlikely to respond to current therapies, and to identify the most appropriate indications and most responsive patient populations for our new immunotherapies. By taking this dual approach, we believe we may be able to address areas of unmet need, particularly in the combination setting.

The promise of long-lasting benefit to cancer patients has led to heightened enthusiasm for these types of immunotherapy products and the rapid expansion of the market opportunity. The current market for immunotherapies is estimated to be \$37 billion, and the overall market for immunotherapy is expected to expand over the next five years, with a 2027 market size estimated to be \$76 billion across solid and blood-based tumors according to market reports.

Our Product Pipeline

We are developing a pipeline of immunotherapies that we believe will provide a meaningful and long-lasting benefit to cancer patients. We plan to develop each of these as a single agent and/or in combination with other therapies, as applicable. The following table depicts our current pipeline:

Jounce Immunotherapy Pipeline

Program	Target	Biology	Discovery	Preclinical IND Enabling	Clinical		
					Phase 1	Phase 2	Phase 3
DEVELOPMENT PROGRAMS							
Vopratelimab	ICOS	 CD4 Focused	SELECT (PD-(L)1 naïve patients)				
Pimivalimab	PD-1	 CD8 Focused	SELECT & INNATE				
JTX-8064	LILRB2 (ILT4)	 Macrophage Focused	INNATE (PD-(L)1 experienced & naïve patients)				
GS-1811*	CCR8	 T-Reg Focused					
JTX-1484	LILRB4 (ILT3)	 Myeloid					
DISCOVERY PROGRAMS							
LILRB1 (ILT2)		 Myeloid & Lymphoid					
Bi-Specifics (Not Disclosed)		 Diverse Immune Cell Types					
Other Targets (Not Disclosed)		 PD-(L)1 Resistance Mechanisms					

* Formerly JTX-1811 now out-licensed to Gilead Sciences, Inc.

Development Programs

JTX-8064: An Anti-LILRB2 (ILT4) Antibody Designed to Reprogram Macrophages

JTX-8064 is a humanized IgG4, anti-LILRB2 monoclonal antibody designed to reprogram macrophages. Specifically, it binds to Leukocyte Immunoglobulin Like Receptor B2 (LILRB2/ILT4) and block interactions with its ligands. We are currently assessing JTX-8064 in INNATE, a Phase 1/2 clinical study of JTX-8064 as a monotherapy and in combination with pimivalimab. We began enrolling patients in INNATE in January 2021, and continue enrollment in eight indication-specific expansion cohorts, which are designed to demonstrate proof-of-concept. INNATE will assess pharmacodynamic and potential predictive biomarkers with the aim of informing the future clinical development of JTX-8064. We expect to report preliminary clinical and biomarker data from INNATE in 2022.

JTX-8064 is the first tumor-associated macrophage candidate developed from our Translational Science Platform. When LILRB2 binds to human leukocyte antigen, or HLA, molecules, including HLA-G, on cancer cells and macrophages, it induces an immunosuppressive state in the macrophages. In preclinical studies, JTX-8064 inhibited this immunosuppressive interaction, reprogramming the macrophages to a more immuno-stimulatory state resulting in activation and proliferation of T cells. We believe therapies targeting these innate immune cells may have the potential to benefit patients with tumors that are less likely to respond to existing T cell-focused approaches.

Vopratelimab: An Anti-ICOS Antibody Immunotherapy

Vopratelimab is a clinical-stage monoclonal antibody that binds to and activates ICOS, a protein on the surface of certain T cells. We believe that vopratelimab's mechanism of action engages CD4 T cells and enables a different element of the immune response than PD-(L)1 inhibitors, which act primarily on CD8 T cells. The design of our ongoing Phase 2 SELECT clinical trial was informed by data suggesting that high expression of ICOS per T cell is necessary for vopratelimab to drive the activation of T effector cells. SELECT aims to determine whether vopratelimab can enhance the therapeutic benefit of PD-(L)1 inhibitors in TIS^{vopra} biomarker-selected patients.

We initiated SELECT in October 2020 to assess vopratelimab in combination with pimivalimab compared to pimivalimab alone. SELECT is a randomized trial outside the United States with TIS^{vopra} biomarker-selected, immunotherapy-naive second-line NSCLC patients. The TIS^{vopra} biomarker is a baseline tumor RNA signature with a threshold optimized for the emergence of peripheral ICOS hi CD4 T cells, a vopratelimab pharmacodynamic biomarker associated with clinical benefit and not associated with PD-(L)1 inhibitor therapy. We identified TIS^{vopra} through a reverse translational analysis of tumor biopsies in a subset of patients in our ICONIC Phase 1/2 clinical trial, in whom CD4 T cell populations were analyzed for ICOS levels. This indicated an association between the emergence of ICOS hi CD4 T cells in blood and TIS^{vopra}. When TIS^{vopra} was applied retrospectively to clinical outcomes, it also appeared predictive of improved response rate, six- and nine-month progression free survival and overall survival. We believe selecting patients by using TIS^{vopra} has the potential to identify patients who may be more responsive to vopratelimab, and those who may be more responsive to pimivalimab. Although both trial arms may benefit from TIS^{vopra} patient selection, the SELECT trial is powered to demonstrate the statistical superiority of vopratelimab in combination with pimivalimab compared to pimivalimab alone. We expect to report complete clinical data from SELECT in the second half of 2022.

We also assessed vopratelimab in two Phase 2 trials, EMERGE and ICONIC. Although neither EMERGE nor ICONIC met pre-specified criteria for continuation of enrollment in the patient populations studied, this clinical data informed the biomarker approach we are using in SELECT. Vopratelimab demonstrated an acceptable safety profile in these trials, with no discernible increase in number or severity of adverse events over what would be expected with a PD-(L)1 or CTLA-4 inhibitor alone.

Pimivalimab: An Anti-PD-1 Antibody for Combination Therapy

Combination therapy aimed at multiple targets has become an important element of immunotherapy development efforts with the goal of creating improved, long-lasting responses. PD-(L)1 inhibitors are anticipated to play a key role in combination therapies. For this reason, we are developing our own anti-PD-1 monoclonal antibody, pimivalimab, primarily for use in combination with future product candidates. We believe this will give us greater flexibility to develop our pipeline of therapies. Pimivalimab is currently being used in combination with vopratelimab in SELECT and JTX-8064 in INNATE.

In November 2019, we reported safety and preliminary efficacy data from our Phase 1 clinical trial of pimivalimab. Pimivalimab demonstrated an acceptable safety profile based on a 6-cohort dose-escalation trial. Response Evaluation Criteria in Solid Tumors, or RECIST, responses were observed in three of 18 patients, including one complete response and two partial responses.

JTX-1484: An Anti-LILRB4 Antibody Designed to Reduce Immune Suppression

JTX-1484 is the most recent product candidate to emerge from our Translational Science Platform. JTX-1484 is a monoclonal antibody designed to block human LILRB4 on various myeloid cells which we believe may lead to reduced immune suppression and enhancement of T cell functionality. We are currently conducting IND-enabling activities for JTX-1484, with the goal of filing an IND in 2023.

Discovery Programs

With our focus on bringing the right immunotherapy to the right patients, we continue to invest in our Translational Science Platform as we believe that the systematic interrogation of the immune make-up of human tumors gives us the ability to target different cell types within the TME beyond the T effector cells that are the focus of currently-approved therapies. We can also use our Translational Science Platform and biomarker efforts to inform our clinical strategy by identifying specific patient populations within or across different types of cancer. This may enable us to fully exploit the promise of immunotherapy in cancer by allowing us to pursue tumor types not currently served by therapies that target the T effector arm of the adaptive immune system, as well as potentially convert the TME from an immunosuppressive environment to an immune activating environment and tailor our approach to both PD-(L)1-inhibitor resistant and PD-(L)1-inhibitor sensitive tumors.

We conducted analysis of The Cancer Genome Atlas as well as other public and proprietary databases using our internally generated gene signatures, which represent various immune cells. The immune cell composition of tumors is diverse, both across and within indications. This analysis suggests that a significant number of tumors, including cold tumors in particular, may not benefit from the current T cell focused immunotherapies, such as PD-(L)1 inhibitors.

We are leveraging our Translational Science Platform to systematically and comprehensively interrogate cell types within the TME with the goal of enabling us to develop therapies for patients who have yet to benefit from immunotherapies. We aim to identify targets tied to cell types of interest, including myeloid cells such as macrophages, T regulatory cells and non-immune cells, and design mono- and bi-specific therapies using these targets.

Gilead License Agreement

On August 31, 2020, we entered into an exclusive license agreement with Gilead, or the Gilead License Agreement, granting Gilead a worldwide and exclusive license to develop, manufacture and commercialize GS-1811 and certain derivatives thereof, as well as backup antibodies defined within the agreement. Concurrently with the license agreement, we entered into a stock purchase agreement with Gilead, or the Stock Purchase Agreement, and a registration rights agreement. The agreements with Gilead were subject to review under the Hart-Scott Rodino Antitrust Improvements Act of 1976 and other customary closing conditions, and became effective on October 16, 2020, the closing date of the transaction.

Under the terms of the Gilead License Agreement and Stock Purchase Agreement, respectively, Gilead paid us a one-time, non-refundable upfront payment of \$85.0 million and a payment of \$35.0 million for an equity investment. Gilead has the sole right to develop and commercialize GS-1811. We are entitled to receive payments from Gilead upon the achievement of specified clinical, regulatory and sales milestones, including potential clinical development and regulatory milestone payments up to an aggregate total of \$510.0 million and potential sales milestone payments up to an aggregate total of \$175.0 million. In July 2021, we received a \$25.0 million milestone payment upon IND clearance for GS-1811. We are also eligible to receive tiered royalty payments based on a percentage of annual worldwide net sales ranging from the high-single digits to mid-teens, based on future annual net sales of licensed products, on a licensed product-by-licensed product and country-by-country basis.

Unless terminated earlier in accordance with its terms, the Gilead License Agreement provides that it will expire (i) on a licensed product-by-licensed product and country-by-country basis on the date of the expiration of the royalty term with respect to such licensed product in such country and (ii) in its entirety upon the expiration of all applicable royalty terms with respect to the licensed products in all countries, following which the applicable licenses under the Gilead License Agreement will become fully paid-up, perpetual, irrevocable and royalty-free. Gilead may terminate the Gilead License Agreement for convenience, in its sole discretion, in its entirety or on a product-by-product or region-by-region basis, at any time with prior written notice to us.

Manufacturing

We rely on and will continue to rely on our contract manufacturing organizations, or CMOs, for both drug substance and drug product. While we do not plan to develop our own full-scale manufacturing capabilities, we may consider establishing a small, flexible approach for supporting preclinical IND-enabling studies and early clinical trials. As of now, all of our manufacturing is outsourced to well-established third-party manufacturers. We have entered into long-term contracts with CMOs for drug supply of JTX-8064, vopratelimab and pimivalimab.

Competition

The biotechnology and pharmaceutical industries, and the immunotherapy subsector, are characterized by rapid evolution of technologies, fierce competition and strong defense of intellectual property. While we believe that our product candidates, discovery programs, technology, knowledge, experience, and scientific resources provide us with competitive advantages, we currently face and will face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others.

Any product candidates that we successfully develop and commercialize will compete with currently-approved 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 and the ease of use and effectiveness of any companion diagnostics and/or complementary diagnostics. Potentially competitive therapies fall primarily into the following groups of treatment:

- traditional cancer therapies, including chemotherapy and targeted therapies;
- two anti-ILT4 (LILRB2) specific antibody programs in clinical trials, being developed by Merck & Co., Inc., or Merck, and Immune-Onc Therapeutics, Inc., or Immune-Onc;
- a dual antagonist anti-ILT4/ILT2 (LILRB1) antibody program in a clinical trial, being developed by NGM Biopharmaceuticals, Inc., or NGM;
- three clinical-stage anti-ICOS agonist antibody programs in clinical trials, being developed by Bristol Myers Squibb, or BMS, GlaxoSmithKline plc, or GSK, and Sanofi S.A.;
- a bispecific anti-ICOS and anti-PD-1 antibody program in clinical development being developed by Xencor, Inc.;
- three clinical-stage anti-ILT3 (LILRB4) antibody programs, in clinical trials being developed by Merck, Immune-Onc and NGM;
- approved immunotherapy antibodies, including an approved anti-CTLA 4 antibody (Yervoy[®], marketed by BMS) and approved anti-PD-1/anti-PD-L1 antibodies (Bavencio[®], Keytruda[®], Libtayo[®], Opdivo[®], Tecentriq[®], Imfinzi[®], and Jemperli marketed by Merck KGaA and Pfizer, Inc., Merck, Regeneron Pharmaceuticals, Inc., BMS, Genentech, Inc., AstraZeneca PLC, and GSK, respectively);
- anti-PD-1/anti-PD-L1 immunotherapy antibodies in clinical development;
- other agonist and antagonist immunotherapy antibodies in clinical development; and
- antibody-drug conjugates, bi-specific antibodies, and other therapies targeting T regulatory cells and B cells, macrophages and other immune cell types that are in clinical development.

The availability of reimbursement from government and other third-party payors will also significantly affect the pricing and competitiveness of our products. In addition, our competitors may obtain Food and Drug Administration, or FDA, or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of the companies against which we may compete, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates, novel biological discoveries, including new targets and applications, and other inventions that are important to our business. For our product candidates, generally we intend to first pursue patent protection covering both compositions of matter and methods of use. As we continue the development of our product candidates, we intend to identify additional means of obtaining patent protection that would potentially enhance commercial success, including through additional methods of use and biomarker and companion diagnostic and/or complementary diagnostic related claims.

The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent

protection for any of our product candidates. As of February 28, 2022, with respect to JTX-8064 patent rights, we own three pending U.S. provisional applications, one pending U.S. non-provisional application, twenty-four pending foreign patents and patent applications within two patent families that cover compositions of matter and methods of use, and we own one issued U.S. patent that covers methods of use. As of February 28, 2022, with respect to vopratelimab patent rights, we own seven pending U.S. non-provisional applications, forty pending foreign patents and patent applications, and two pending Patent Cooperation Treaty, or PCT, patent applications within nine patent families that cover compositions of matter and methods of use and ICOS-related biomarkers, and we own two issued U.S. patents and seven issued foreign patents that cover compositions of matter and methods of use. As of February 28, 2022, with respect to pimivalimab patent rights, we own one pending U.S. non-provisional application, twenty pending foreign patents and patent applications, and one pending PCT application within two patent families that cover compositions of matter and methods of use, and we own one issued U.S. patent and two issued foreign patents that cover compositions of matter and methods of use.

We cannot predict whether the patent applications we pursue will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide any proprietary protection from competitors. Even if our pending patent applications are granted as issued patents, those patents, as well as any patents we license from third parties, may be challenged, circumvented or invalidated by third parties.

In addition, we exclusively in-licensed a patent portfolio from Sloan Kettering Institute for Cancer Research, Memorial Sloan Kettering Cancer Center and Memorial Hospital for Cancer, or MSK, and University of Texas MD Anderson Cancer Center, or MD Anderson, consisting of four issued U.S. patents, one issued Australian patent, one issued Japanese patent, one issued Canadian patent, two issued Chinese patents, one issued Hong Kong patent, one issued European patent that has been validated in thirteen European jurisdictions, one pending U.S. patent application, and one pending foreign patent application. This licensed patent portfolio covers methods related to the use of an ICOS agonist in combination with blocking agents of certain T cell inhibitory receptors. The issued patents and the pending patent applications (if issued) licensed from MSK and MD Anderson, if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in 2030, excluding any additional term for patent term adjustments or patent term extensions.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, the patent term that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available. However, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

We also rely on unpatented know-how, inventions and other proprietary information relating to JTX-8064, vopratelimab, pimivalimab, GS-1811, JTX-1484, our future product candidates and our Translational Science Platform. We seek to protect and maintain the confidentiality of proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Our agreements with employees also provide that all inventions conceived by the employee in the course of employment with us or from the employee's use of our confidential information are our exclusive property. However, such confidentiality agreements and invention assignment agreements can be breached, and we may not have adequate remedies for any such breach. For a more comprehensive discussion of the risks related to our intellectual property, please see "Risk Factors—Risks Related to Intellectual Property."

Exclusive License Agreement with Sloan Kettering Institute for Cancer Research, Memorial Sloan Kettering Cancer Center, and Memorial Hospital for Cancer and Allied Diseases

In September 2015, we amended and restated an exclusive license agreement from December 2013 with MSK. Pursuant to this amended and restated license agreement, MSK and MD Anderson granted to us a worldwide exclusive license under certain patents to manufacture, develop and commercialize certain products and services, including those products for which the use in combination with another product for the treatment of any disease is covered by such patents (including, potentially, vopratelimab), and to practice certain methods covered by the patents. Under the license agreement, we are obligated to use commercially reasonable efforts to commercialize at least one licensed product or licensed service as defined in the license agreement.

In connection with the license agreement, we issued to MSK and MD Anderson an aggregate of 60,974 shares of our common stock. We also paid an upfront license fee of \$30,000 to MSK and MD Anderson. Commencing on the third anniversary of the effective date of the license agreement, we must pay an annual maintenance fee ranging in the mid-four figures to the mid-five figures. The annual maintenance fee is fully credited against the royalty payments for the same year or any subsequent year or any other amount due under the license agreement. We are obligated to pay MSK milestone payments of up to \$3,475,000 for the first and second licensed products to achieve certain development and marketing approval milestones, including up to \$2,725,000 for the first licensed product to achieve such developmental and marketing approval milestones. On a country-by-country basis and licensed product-by-licensed product or licensed service-by-licensed service basis, we are also obligated to pay MSK a low single-digit percentage royalty on net sales of licensed products or licensed services, to the extent used in combination with another product for the treatment of any disease covered by the applicable patents, until the earlier of the expiration of the last valid patent claim covering such licensed product or licensed service in such country or twelve years after the first commercial sale of such licensed product or licensed service in such country. If we sublicense our rights under our license agreement with MSK, we would be obligated to pay MSK a low double-digit percentage royalty of the total gross proceeds we receive in consideration of the grant of the sublicense, excluding royalties, research and development funding, payments for equity or debt securities and certain other expenses we have incurred that are reimbursed by the sublicensee.

Unless terminated earlier, the license agreement expires on the date that we no longer have any royalty payment obligations under the license agreement. We may terminate the license agreement for convenience in its entirety upon 30 days' prior written notice to MSK and MD Anderson. Either party may terminate the license agreement in its entirety in the event of an uncured material breach or the bankruptcy, insolvency, dissolution or winding up of the other party which is not dismissed or cured within a set period of time. If we terminate the license agreement because of MSK's and MD Anderson's uncured breach or insolvency, we will retain a non-exclusive, perpetual, irrevocable, fully paid-up, royalty-free worldwide license to the licensed patents. Upon expiration of our obligation to pay royalties for a licensed product or service in a country, our license to the licensed patents for such licensed product or service will become exclusive, perpetual, irrevocable, fully paid-up and royalty-free in such country.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, sales, pricing, reimbursement, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products, including our product candidates. Generally, before a new drug or biologic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

U.S. Drug Development

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Biological products, or biologics, are licensed for marketing under the the Public Health Service Act, or PHSA, and regulated under the FDCA and its implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources.

Our product candidates must be approved by the FDA through either a New Drug Application, or NDA, or Biologics License Application, or BLA, process before they may be legally marketed in the United States. We expect JTX-8064, vopratelimab, pimivalimab, JTX-1484 and future product candidates to be regulated by the FDA as biologics and require the submission of a BLA prior to being marketed in the United States. A company, institution or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically

referred to as a sponsor. A sponsor seeking approval of a new drug or biologic in the United States must generally complete each of the following steps:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP, requirements and other applicable regulations;
- design of a clinical trial protocol and submission to the FDA of an IND application, 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 trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA or BLA;
- determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the application and file it for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with current good manufacturing practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality and purity;
- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA or BLA;
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies and IND

The preclinical developmental stage generally involves laboratory evaluations of product chemistry, formulation and stability, as well as *in vitro* and animal studies to evaluate toxicity, assess the potential for adverse events and, in some cases, establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND.

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational product to humans. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, non-clinical, and/or chemistry, manufacturing, and controls. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators in accordance with GCP requirements, including the requirement that all

research subjects provide their informed consent. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, an IRB for each institution at which the clinical trial will be conducted must review and approve the protocol before a clinical trial commences at such institution, approve the information regarding the trial and the consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization as to whether or not a trial may move forward at designated check points based on available data from the study. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Clinical trials generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, which may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.
- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

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

In August 2018, the FDA released a draft guidance entitled “Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics,” which outlines how developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology biological product development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to product development and reduce developmental costs and time.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from animal or *in vitro* testing or other studies that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects 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 or biologic has been associated with unexpected serious harm to patients. Results from one trial are not necessarily predictive of results from later trials.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to \$10,000 for each day the violation continues.

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

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called “compassionate use,” is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA in 2016, drug and biologic companies must make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

NDA/BLA and FDA Review Process

The results of preclinical studies and clinical trials, together with other detailed information, including proposed labeling, chemistry and manufacturing information, are submitted to the FDA as part of an NDA or BLA. The NDA or BLA is a request for approval to market the drug or biologic for one or more specified indications and must contain proof of safety and efficacy for a drug or safety, purity and potency for a biologic. The FDA must approve the NDA or BLA before a drug or biologic may be marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA or BLA must be accompanied by a user fee. Under federal law, the submission of most applications is subject to an application user fee, which for federal fiscal year 2022 is \$3,117,218 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for federal fiscal year 2022 is \$369,413. These fees may be increased or decreased annually, and fee waivers, reductions or deferrals are available in certain circumstances.

Upon receipt of an NDA or BLA, the FDA conducts a preliminary review of the application within 60 days and it must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File, or RTF, determination to the sponsor. The FDA may request additional information or studies, and the sponsor may resubmit the NDA or BLA with the additional information.

If the submission is found to be complete, the FDA will file the NDA or BLA, triggering a full review. The established goal of the FDA is to review applications within ten months of the filing date for a new molecular-entity NDA or original BLA and within six months from the filing date for a new molecular-entity NDA or original BLA designated for priority review. The FDA does not always meet its goal dates for standard and priority NDAs or BLAs, and the review process is often extended by FDA requests for additional information or clarification.

In connection with its review of an NDA or BLA, the FDA will inspect the manufacturing facilities for the new product and will not approve the product unless the facilities comply with cGMP requirements. The FDA may also refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. Additionally, the FDA may audit data from clinical trials to ensure compliance with GCP requirements and likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the sponsor during the review process.

After evaluating the application and all related information, the FDA will determine whether the expected benefits of the proposed product outweigh its potential risks to patients. The FDA will then issue either a Complete Response Letter, or CRL, or an approval letter. A CRL describes additional work that must be done before the application can be approved, such as requiring additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such data and information are submitted, the FDA may decide that the NDA or BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances. These circumstances are where another product shows clinical superiority to the product with orphan drug exclusivity because it is shown to be safer, more effective or makes a major contribution to patient care. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Competitors may also receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if one of our products is determined to be contained within the scope of the competitor's product for the same indication or disease. If one of our products designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has various programs, including a fast track program, priority review and accelerated approval, that are intended to expedite or facilitate the process for reviewing new drugs and biologics that, generally, are intended to treat a serious or life-threatening condition, demonstrate the potential to address unmet medical needs and that offer meaningful benefits over existing treatments. The fast track program is designed to facilitate the development and review of drugs to treat serious or life-threatening diseases or conditions and fulfill unmet needs. Priority review is designed to give drugs that offer major advances in treatment or provide treatment where no adequate therapy exists. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biologic designated for priority review in an effort to facilitate the review. None of these expedited programs changes the standards for approval, but each may help expedite the development or approval process governing product candidates.

A candidate product may also be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, the investigational product must demonstrate 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, or IMM, which is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug or biologic receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials.

Additionally, a drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program.

Pediatric Information

Under the Pediatric Research Equity Act, an NDA or BLA or supplement to an NDA or BLA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The assessment must also support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act, or FDASIA, requires the submission of a pediatric study plan prior to the assessment of data, which must contain proposed pediatric study, including study design and objectives, any deferral or waiver requests, and any other information required by regulation. The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin.

Post-marketing Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping activities, reporting of adverse experiences, complying with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (known as “off-label use”) and limitations on industry-sponsored scientific and educational activities.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. In September 2021, the FDA published final regulations that describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic.

The FDA may also place other conditions on approvals, including imposing limitations on the uses for which the product may be marketed, requiring that warning statements be included in the product labeling, requiring that additional studies be conducted following approval as a condition of the approval, imposing restrictions and conditions on product distribution, prescribing or dispensing in the form of a REMS or otherwise limiting the scope of any approval. Product approvals may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP regulations. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including recall.

Companion Diagnostics and Complementary Diagnostics

We believe that the success of our product candidates may depend, in part, on the development and commercialization of either a companion diagnostic or complementary diagnostic. Companion diagnostics and complementary diagnostics can identify patients who are most likely to benefit from a particular therapeutic product, identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product, or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics and complementary diagnostics are regulated as medical devices by the FDA and, as such, require either clearance or approval prior to commercialization. The level of risk combined with available controls to mitigate risk determines whether a companion diagnostic device requires Premarket Approval Application approval or is cleared through the 510(k) premarket notification process. Under FDA guidance, for a novel therapeutic product for which a companion diagnostic device is essential for the safe and effective use of the product, the companion diagnostic device should be developed and approved or 510(k)-cleared contemporaneously with the therapeutic. The use of the companion diagnostic device will be stipulated in the labeling of the therapeutic product. This is also true for a complementary diagnostic, although it is not a prerequisite for receiving the therapeutic.

If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, 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. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The level of risk combined with available controls to mitigate risk determines whether a companion diagnostic device requires Premarket Approval Application approval or is cleared through the 510(k) premarket notification process. 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 Device Evaluation and Safety.

In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple drug or biological oncology products, when appropriate. This guidance builds upon existing policy regarding the labeling of companion diagnostics. The 2020 guidance expands on the policy statement in the 2014 guidance by recommending that companion diagnostic developers consider a number of factors when determining whether their test could be developed, or the labeling for approved companion diagnostics could be revised through a supplement, to support a broader labeling claim such as use with a specific group of oncology therapeutic products (rather than listing an individual therapeutic product(s)).

Other Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

For example, in the United States, sales, marketing and scientific and educational programs also must comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid.

Although we would not submit claims directly to payors, manufacturers also can be held liable under the federal False Claims Act, which prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs or biologics, that are false or fraudulent, claims for items or services not provided as claimed or claims for medically unnecessary items or services. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Affordable Care Act. The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects us to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

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.

U.S. Patent Term Restoration and Non-Patent Exclusivity

Depending upon the timing, duration and specifics of FDA approval of any of our product candidates, some 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, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. Assuming grant of the patent for which the extension is sought, the restoration period for a patent covering a product is typically one-half the time between the effective date of the IND and the submission date of the NDA or BLA, plus the time between the submission date of the application and the ultimate approval date. The United States Patent and Trademark Office, or USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Market and data exclusivity provisions under the FDCA also can delay the submission and the approval of certain applications. For drug products, the FDCA provides a five-year period of non-patent or regulatory exclusivity within the United States to the first applicant to gain 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. This interpretation of the FDCA by the FDA was confirmed with the enactment of the Ensuring Innovation Act in April 2021.

An abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009 as part of the Affordable Care Act. Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Complexities associated with the larger, and often more complex, structure of biological products as compared to small molecule drugs, as well as the processes by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biological product is granted twelve years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. It is necessary to determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity and, for subsequent applications, such determinations are made a case-by-case basis with data submitted by the sponsor. As of December 27, 2021, the FDA has approved 33 biosimilar products for use in the United States and two interchangeable biosimilars, including one interchangeable monoclonal antibody.

Pediatric Exclusivity

Pediatric exclusivity is another type of regulatory exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods and, for drug products, existing patents. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued “Written Request” for such a trial. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA’s request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patents that cover the product are extended by six months.

Foreign Regulation

As in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our future products and medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the EU at the EudraCT website: <https://eudract.ema.europa.eu>.

To obtain regulatory approval of an investigational product under European Union regulatory systems, we must submit a marketing authorization application under either a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology. The application used to file the BLA in the United States is similar to that required in the European Union, with the exception of, among other things, region-specific document requirements.

The European Union also provides opportunities for market exclusivity. For example, upon receiving marketing authorization, innovative medicinal products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator’s data to assess a generic or biosimilar application. There is no guarantee that a product will be considered by the European Union’s regulatory authorities to be an innovative medicinal product, and products may not qualify for data exclusivity. Products receiving orphan designation in the European Union can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the European Union for pediatric studies (six months for other products). No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom’s withdrawal from the EU took place on January 31, 2020. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the U.K.’s withdrawal from the EU.

General Data Protection Regulation

The collection, use, 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 U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States, no uniform policy of coverage and reimbursement for drug or biological products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. If we obtain approval in the future to market any our product candidates, we may seek approval and coverage for those products under Medicaid, Medicare and the Public Health Service pharmaceutical pricing program and may seek approval to sell the products to federal agencies. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to pay a rebate for each product reimbursed by the state Medicaid programs. The amount of the rebate for each product is set by law and may be subject to an additional discount if certain pricing increases more than inflation.

Medicare is a federal program that is administered by the federal government. The program covers individuals age 65 and over as well as those with certain disabilities. Medicare Part D provides coverage to enrolled Medicare patients for self-administered drugs (i.e., drugs that are not administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time to time.

Medicare Part B covers most injectable drugs given in an in-patient setting, and some drugs administered by a licensed medical provider in hospital outpatient departments and doctors' offices. Medicare Part B is administered by Medicare Administrative Contractors, which generally have the responsibility of making coverage decision. Subject to certain payment adjustments and limits, Medicare generally pays for Part B covered drugs based on a percentage of a manufacturer-reported average sales price.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. An increasing emphasis on cost containment measures in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally prices tend to be significantly lower.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Affordable Care Act, or ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. 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.

Human Capital

As of December 31, 2021, we had 137 full-time employees. Of these full-time employees, 45 have Ph.D. or M.D. degrees and 108 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.

We are committed to attracting, retaining, developing and motivating a diverse team of highly skilled employees at all levels. The biotechnology industry is very competitive and recruiting and retaining such employees is important to the continued success of our business. We provide our employees with competitive salaries and bonuses, opportunities for equity ownership, including stock-based compensation awards, and development programs that enable continued learning and growth. We also offer comprehensive work-life benefits, including health, dental, income protection, such as life insurance and retirement savings programs. We regularly benchmark these benefits against our industry peers to ensure we remain competitive and attractive to potential new hires. Additionally, we regularly conduct surveys and invite employee questions and feedback to assess employee satisfaction and engagement, and enhance our understanding of the views of our employees and company culture. In response to the COVID-19 pandemic, we increased provided resources, including a home-office stipend, to enable and support employees to work from home full-time or part-time. Our management has continued to assess and respond to the evolving needs of our workforce throughout the pandemic.

We strive to create a workplace that reflects the diversity of cancer patients, and where all feel included and valued because of their differences. Our commitment to diversity, inclusion and equity begins with our management team: six of our ten members are women or from diverse racial and ethnic groups. Our Board of Directors also reflects this commitment: four of our nine members are women and/or from a diverse racial and ethnic group.

Corporate Information

Our principal offices are located at 780 Memorial Drive, Cambridge, MA 02139, and our telephone number is (857) 259-3840.

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012 and we will remain an emerging growth company until December 31, 2022.

We are also a “smaller reporting company,” meaning that the market value of our stock held by non-affiliates is less than \$700 million and our annual revenue was less than \$100 million during our most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than \$250 million or (ii) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we have chosen to present only the two most recent fiscal years of audited financial statements and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Our website address is www.jouncetx.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K. Through our website, we make available, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, any amendments to those reports, proxy and registration statements, and all of our insider Section 16 reports, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the Securities and Exchange Commission, or the SEC. These SEC reports can be accessed through the “Investors & Media” section of our website. The information found on our website (or that may be accessed through links on our website) is not part of this or any other report we file with, or furnish to, the SEC. You should not rely on any such information in making your decision whether to purchase our common stock.

In addition, the SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including us, and any document we file may be viewed at the SEC’s internet address at <http://www.sec.gov> (this website address is not intended to function as a hyperlink, and the information contained in the SEC’s website is not intended to be a part of this filing).

Our code of conduct, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee, Nominating and Corporate Governance Committee and Science and Technology Committee are available through our website at www.jouncetx.com.

Item 1A. Risk Factors

Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Annual Report on Form 10-K and other filings with the Securities and Exchange Commission, or the SEC, press releases, communications with investors, and oral statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events, or otherwise.

Risks Related to Product Development and Regulatory Process

We are early in our development efforts. If we are unable to advance our product candidates through clinical development, advance future product candidates to clinical development or obtain marketing approval and ultimately commercialize any product candidates or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts: JTX-8064, vopratelimab and pimivalimab are our clinical-stage product candidates, and future product candidates, including JTX-1484, are in preclinical or earlier stages of development. We have invested substantially all of our efforts and financial resources in the identification of targets and early stage, preclinical and clinical development of monoclonal antibodies, including the development of JTX-8064, vopratelimab, pimivalimab, GS-1811 and JTX-1484.

Our other efforts have been invested in early stage, preclinical and earlier development programs. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our current and/or future product candidates, which may never occur. We currently generate no revenues from sales of any products, and we may never be able to develop or commercialize a marketable product. Pursuant to our exclusive license agreement with Gilead Sciences, Inc., or Gilead, for the development, manufacture and commercialization of GS-1811, formerly JTX-1811, we received a \$25 million milestone payment in July 2021 upon receiving IND clearance for GS-1811. However, we may never receive any additional payments from Gilead for the achievement of development, regulatory or commercial milestones, or royalties from potential future sales of GS-1811. Our current and future product candidates will require additional preclinical and clinical development, management of clinical, preclinical and manufacturing activities, marketing approval in the United States and other markets, demonstrating effectiveness to pricing and reimbursement authorities, obtaining sufficient manufacturing supply for both clinical development and commercial production, building of a commercial organization, and substantial investment and significant marketing efforts before we generate any revenues from product sales. In addition, our product development programs contemplate the development of companion diagnostics and/or complementary diagnostics, which are assays or tests to identify an appropriate patient population. Complementary diagnostics and companion diagnostics are subject to regulation as medical devices and, if there are no adequate companion diagnostics and/or complementary diagnostics currently on the market for our product candidates, we may advance a diagnostic on our own. That diagnostic would have to be approved or cleared for marketing by the FDA or comparable foreign regulatory agencies before we could commercialize it. The success of our current and future product candidates will depend on several factors, including the following:

- successful completion of preclinical studies and advancement to clinical development of our product candidates;
- acceptance of investigational new drug applications for our planned clinical trials or future clinical trials;
- successful enrollment and completion of clinical trials;
- demonstration of a benefit/risk profile for our current and future product candidates that is sufficient to support a successful biologics license application, or BLA;
- successful development and marketing approval and clearance of companion diagnostics and/or complementary diagnostics for use with our current and future product candidates, if applicable;
- receipt and maintenance of marketing approvals from applicable regulatory authorities;
- approval by national pricing and reimbursement agencies (such as NICE, National Institute for Health Care and Excellence in the United Kingdom);
- establishing agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- launching commercial sales of our current and future product candidates, if and when approved;

- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- enforcing and defending intellectual property rights and claims;
- successful completion of clinical confirmatory trials to verify clinical benefit, if applicable; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

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 our current and future product candidates, which would materially harm our business. If we do not receive marketing approvals for our current and future product candidates, we may not be able to continue our operations.

The ongoing COVID-19 pandemic has adversely affected, and may continue to adversely affect, our business, including our clinical trials and preclinical studies.

The COVID-19 pandemic has caused many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny and other measures. The COVID-19 pandemic and government and employer measures taken in response have had a significant impact, both direct and indirect, on business and commerce, as supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, have increased dramatically, while demand for other goods and services, such as travel, has fallen. The future progression of the COVID-19 pandemic and its effects on our business and operations are uncertain.

In response to the spread of COVID-19, we have reduced access to our headquarters by recommending our employees who are able to work remotely to continue their work outside of our office. We believe the COVID-19 pandemic has had, and may continue to have, an impact on our clinical trials. For example, we have experienced difficulty sourcing components for sample collection kits, and staffing shortages have had an impact on the pace of enrollment in our trials. As a result of the COVID-19 pandemic, we have experienced and may in the future experience further disruptions that could severely impact our business, clinical trials and preclinical studies, including:

- additional delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays or difficulties in enrolling patients in 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 patient visits and study procedures that are deemed non-essential, which may impact the integrity of subject data and clinical study endpoints;
- delays or difficulties in developing diagnostics or conducting biomarker analysis by third-party vendors who support our clinical trials;
- patients affected by COVID-19 and that the virus could impact pharmacodynamic biomarkers studied in our clinical trials and the interpretation of related data;
- 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;
- additional delays or difficulties in completing the analysis of or reporting results from our clinical trials;
- interruption or delays in the operations of the Food and Drug Administration, or the FDA, or comparable foreign regulatory authorities, which may impact clinical trial timelines or approval timelines;
- interruption of, or delays in receiving, supplies of our product candidates and/or supplies used in the conduct of our clinical trials from our contract manufacturing organizations due to raw materials shortages, staffing shortages, production slowdowns or stoppages, disruptions in delivery systems and government restrictions or limitations, such as those imposed by the Defense Production Act;
- interruption of or delays in the performance of contractual duties by third parties on whom we rely to conduct our clinical trials;

- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people or changes to governmental orders related to the pandemic;
- increased reliance on personnel working from home may negatively impact productivity; and
- difficulties raising capital on favorable terms when needed.

The COVID-19 pandemic continues to evolve. The extent to which the COVID-19 pandemic may further impact our business, clinical trials and preclinical studies and supply chain 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.

Clinical product development involves a lengthy and expensive process, with an uncertain outcome. We will incur additional costs in connection with, and may experience delays, in completing, or ultimately be unable to complete, the development and commercialization of our current and future product candidates, and any companion diagnostics and/or complementary diagnostics.

The risk of failure for our product candidates at any stage of clinical or preclinical development is high. It is impossible to predict when or if our current and future product candidates will prove effective and safe in humans and will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our current and future product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete or may be delayed and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical development and 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.

The FDA or comparable foreign regulatory authorities could change their position on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete more preclinical studies or provide additional data before continuing clinical trials. In the event we are required to satisfy additional FDA requests, the completion of our clinical trials for JTX-8064, vopratelimab and pimivalimab may be delayed. Successful completion of our clinical trials is a prerequisite to submitting a BLA or NDA to the FDA and a Marketing Authorization Application, or MAA, in the European Union for our current and future product candidates and, consequently, the ultimate approval and commercial marketing of our current and future product candidates. We do not know whether any of our clinical trials will be completed on schedule, if at all.

We may experience delays in completing our preclinical studies and initiating or completing clinical trials, and we may experience numerous unforeseen events during, or as a result of, any potential future clinical trials that could delay or prevent our ability to receive marketing approval of our current and future product candidates, including:

- regulators, institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs;
- clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or abandon product development programs;
- the number of patients required for clinical trials or to validate our biomarker-driven strategy may be larger than we anticipate;
- it may be difficult to enroll a sufficient number of patients with a predictive biomarker or enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our third-party contractors, trial sites or investigators may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;

- we may elect to, or regulators or IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unreasonable and significant health risks;
- the cost of clinical trials may be greater than we anticipate;
- the supply or quality of materials or other materials necessary to conduct clinical trials may be insufficient or inadequate due to supply chain interruptions;
- competitors may obtain regulatory approval ahead of us for products or antibodies similar to ours, preventing us from obtaining regulatory approval despite positive clinical data;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us to suspend or terminate the trials, or reports may arise from preclinical or clinical testing of other similar cancer therapies that raise safety or efficacy concerns about our product candidates; and
- the FDA or other regulatory authorities may require us to submit additional data or impose other requirements before permitting us to initiate or continue a clinical trial.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted or ethics committees, or by the FDA or other regulatory authorities, or recommended for suspension or termination by the data safety monitoring board for such trial. Such authorities or we may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical 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, including those issues or effects seen in other drugs or drug candidates in the class to which our drug candidates belong, failure to demonstrate a benefit from using a product, changes in governmental regulations or lack of adequate funding to continue the clinical trial. Many of the factors that result in a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval of our product candidates. Further, regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials or may change the requirements for approval even after such authorities have reviewed and commented on the design for our clinical trials.

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

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- be subject to post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any of our clinical trials will need to be restructured, will be completed on schedule, or will begin as planned, if at all. Any delays in our preclinical or future clinical development programs may harm our business, financial condition and prospects significantly.

Our current and future product candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved pharmaceutical products or investigational new drugs that could halt their clinical development, prevent their marketing approval, limit their commercial potential or result in significant negative consequences.

Although our current and future product candidates will undergo safety testing to the extent possible and, where applicable, under such conditions discussed with regulatory authorities, not all adverse effects of drugs can be predicted or anticipated. In order to obtain marketing approval of a product candidate, we must demonstrate safety in various non-clinical and clinical tests. At the time of initiating human clinical trials, we may not have conducted or may not conduct the types of non-clinical testing ultimately required by regulatory authorities, or future non-clinical tests may indicate that our product candidates are not safe for use. Non-clinical testing and clinical testing are both expensive and time-consuming and have uncertain outcomes.

Immunotherapy, and its method of action of enabling the body's immune system, is powerful and could lead to serious side effects that we only discover in clinical trials. Undesirable or clinically unmanageable side effects could occur and cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Unforeseen side effects from our current and future product candidates could arise either during clinical development or, if such side effects are more rare, after our current and future product candidates have been approved by regulatory authorities and the approved product has been marketed, resulting in the exposure of additional patients. Although we have observed that each of our clinical-stage product candidates has had an acceptable safety profile in studies to date, we cannot predict if future clinical trials of our product candidates, either alone or in combination with other therapies, will demonstrate safety in humans. If any of our current or future product candidates fail to demonstrate safety and efficacy in clinical trials or do not gain marketing approval, we will not be able to generate revenue and our business will be harmed.

We cannot predict whether future safety and toxicology studies may cause undesirable effects. Success in initial tests does not ensure that later testing will be successful. Our product candidates could cause undesirable side effects similar to those toxicities observed in other immunotherapies. It remains possible that new or more severe toxicities could be seen if any product candidate is used in combination with other agents. Such toxicities, if observed, could result in development delays, a determination by the FDA or other regulatory authorities that additional safety testing is required, delay or denial of approval, or limit the labeling and thus overall market scope for such future product candidate.

If unacceptable toxicities arise in the development of our current and future product candidates, we or an existing or future collaborator or licensee could suspend or terminate clinical trials, or the FDA or comparable foreign regulatory authorities could order us, a collaborator or licensee to cease clinical trials or deny approval of our current and future product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, particularly outside of our collaborators or licensees, as toxicities resulting from cancer immunotherapies are not normally encountered in the general patient population or by medical personnel. We expect to have to train medical personnel using any of our product candidates to understand the side effect profile of such product candidates for both our ongoing and planned clinical trials and upon commercialization of such product candidates. The inability to recognize and manage the potential side effects of our product candidates could result in patient deaths. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly.

If we encounter difficulties enrolling or retaining patients in our clinical trials, our clinical development activities could be delayed or otherwise be adversely affected.

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

- the patient eligibility criteria defined in the protocol;
- the development of diagnostics and/or biomarker analysis by third parties;
- our ability to identify and enroll sufficient number of patients with a predictive biomarker;
- the size of the population that we must screen to identify a sufficient number of patients with a predictive biomarker;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions of the potential advantages of the product candidate being studied in relation to other available therapies;
- our ability to obtain and maintain patient consents for participation in our clinical trials and, where appropriate, biopsies to understand our product candidates better and for future patient enrichment efforts; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they are late-stage cancer patients, will not survive the full terms of the clinical trials.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our current and future product candidates. This competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial conducted by another company. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that other companies use for trials in the same indications, which will reduce the number of patients who are available for our clinical trials at such sites. Moreover, because our current and future product candidates represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy, rather than enroll patients in our ongoing or any future clinical trials.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of our current and future product candidates. This may be especially true in light of the COVID-19 pandemic even though the FDA issued guidance on March 18, 2020, and subsequently updated it in 2021, to address the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of the COVID-19 pandemic. Significant clinical trial delays from the pandemic or otherwise also could shorten any periods during which we may have the exclusive right to commercialize our products, allow our competitors to bring products to market before we do or impair our ability to successfully commercialize our products, which would harm our business and results of operations.

We may not be able to conduct clinical trials in some jurisdictions outside of the United States.

We are currently conducting SELECT outside of the United States, and we may conduct future trials in markets outside the United States. Our ability to successfully initiate, enroll and complete a clinical trial in any country outside of the United States is subject to numerous additional risks unique to conducting business in jurisdictions outside the United States, including:

- difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;
- different local standards for the conduct of clinical trials;
- difficulty in complying with various and complex import laws and regulations when shipping drug to certain countries;
- the potential burden of complying with a variety of laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments;
- lack of consistency in standard of care from country to country;
- diminished protection of intellectual property in some countries;
- instability in economic or political conditions, including inflation, recession and actual or anticipated military conflicts, social upheaval or political uncertainty;
- foreign exchange fluctuations;
- cultural differences in medical practice and clinical research; and
- changes in country or regional regulatory requirements.

Additionally, of our sixty-seven active sites in SELECT, fourteen are located in Ukraine, seventeen are located in Russia, and additional sites are located in neighboring countries. The escalation of tensions in the region, including Russia's February 2022 invasion of Ukraine and the resulting imposition of economic and other sanctions by the United States, European Union and many other nations on Russia, individuals in Russia, Russian businesses and the Russian central bank, could disrupt or delay our ability to conduct clinical trial activities, including the evaluation of safety or efficacy data. Although the length and impact of any military action are highly unpredictable, clinical trial sites in Ukraine and other countries may close, and patients could be forced to evacuate or voluntarily choose to relocate far from clinical trial sites, making them unavailable for further dosing or follow-up. The closure of sites, the inability to screen and enroll new patients or any premature discontinuation of treatment by patients already enrolled in our trial could result in the need to enroll additional patients, which would be costly and could delay our anticipated timeline for the completion of the trial. There may also be an impact on the health and safety of our patients, including an increase in the number and severity of adverse events, due to living in a conflict zone and limited or no access to hospitals or healthcare. Airport closures will delay the shipping and processing of trial supplies and patient samples. As a result, there may be delays in treatment or response assessments that could adversely affect the ability to conduct the SELECT trial on the timeline we originally anticipated, the completeness of data and the trial results for SELECT. Any disruptions arising from

the invasion of Ukraine could increase the cost of conducting the trial, which could have a material impact on our financial condition.

Furthermore, the COVID-19 pandemic may also have an impact on our ability to successfully conduct trials outside of the United States. For example, we are conducting SELECT in countries where clinical trial site staff have been diverted to care for COVID-19 patients and where regulatory authorities are short staffed due to the COVID-19 pandemic, and this has impacted enrollment in these countries. If we have difficulty conducting our clinical trials in jurisdictions outside the United States as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which could have a material adverse effect on our business.

We are currently conducting SELECT outside the United States and may conduct future clinical trials for our product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations or the complexity of regulatory burdens may otherwise adversely impact us.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practices, or GCPs, and the FDA must be able to validate the data from the trial through an onsite inspection, if necessary. Generally, the patient population for any clinical trials conducted outside the United States must be representative of the population for which we intend to seek approval in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. Nonetheless, there can be no assurance that the FDA will accept data from trials conducted outside the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our development of any applicable product candidates. Furthermore, certain jurisdictions require data from trials conducted in their country in order to obtain approval in that country.

We rely on our Translational Science Platform to identify and develop product candidates. Our competitive position could be materially harmed if our competitors develop a platform similar to our Translational Science Platform and develop rival product candidates.

We rely on unpatented know-how, inventions and other proprietary information, to maintain our competitive position. We consider know-how to be our primary intellectual property with respect to our Translational Science Platform. Know-how can be difficult to protect. In particular, we anticipate that with respect to this platform, this know-how may over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of skilled personnel.

We cannot rule out that our competitors may have or obtain the knowledge necessary to analyze and characterize tumors for the purpose of identifying and developing products that could compete with the product candidates we develop. Our competitors may also have significantly greater financial, product development, technical, and human resources and access to other human tumors than we do and may have significantly greater experience in using translational science methodology to identify and develop product candidates.

We may not be able to prohibit our competitors from using translational science methods to develop product candidates, including such methods that are the same as or similar to our own. If our competitors use translational science methods to identify and develop products that compete with our current and future product candidates, our ability to develop and market a promising product or product candidate may diminish substantially, which could have a material adverse effect on our business prospects, financial condition, and results of operations.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any of our existing or future collaborators or licensees from obtaining approvals for the commercialization of our current and future product candidates.

Our product candidates and the activities associated with their development and commercialization, including research, testing, manufacturing, labeling, approval and license maintenance, selling, import and export, marketing and distribution are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. Neither we nor any existing or future collaborator or licensee is permitted to market any future product in the United States until we receive approval of a BLA from the FDA. We have never submitted an application for, or received, marketing approval. Obtaining approval of a BLA can be a lengthy, expensive and uncertain process. Even if we believe the preclinical or clinical data for our current and future product candidates are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities.

Marketing approval of a BLA is not guaranteed, and the approval process is expensive and may take several years. The FDA also has substantial discretion in the approval process. Despite the time and expense exerted, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical trials or perform additional preclinical studies and clinical trials. The number of preclinical studies and clinical trials that will be required for FDA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address and the regulations applicable to any particular product candidate. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or deny approval of a product candidate, or we may experience delays or rejections based upon government regulation or changes in regulatory agency policy during the period of product development. Regulatory agencies also may impose significant limitations in the form of narrow indications, warnings, precautions or contraindications with respect to conditions of use or may grant approval subject to the performance of costly post-marketing clinical trials. Regulatory agencies or third-party payors may not approve the price we intend to charge for our future products. Any of the foregoing scenarios could materially harm the commercial prospects for our current and future product candidates.

If our current and future product candidates fail to demonstrate safety and efficacy in clinical trials or do not gain marketing approval, our business will be harmed.

We may seek a Breakthrough Therapy Designation or Fast Track Designation by the FDA for our current and future product candidates, and we may be unsuccessful. If we are successful, the designation may not actually lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our current and future product candidates will receive marketing approval.

We may seek a Breakthrough Therapy Designation or Fast Track Designation for our current and future product candidates. 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. Fast Track Designation may be available 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. Drugs that receive Breakthrough Therapy Designation or Fast Track Designation by the FDA are eligible for accelerated approval and priority review.

The FDA has broad discretion whether or not to grant Breakthrough Therapy Designation or Fast Track Designation. Even if we receive Breakthrough Therapy Designation or Fast Track Designation for a product candidate, such designation may not result in a faster development process, review or approval compared to conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one of our current or future product candidates receives Breakthrough Therapy Designation or Fast Track Designation, the FDA may later decide that the drugs no longer meet the conditions for qualification and rescind the designation.

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

As part of our business strategy, we may seek Orphan Drug Designation for our current and future product candidates, and we may be unsuccessful. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

In Europe, Orphan Drug Designation entitles a party to a number of incentives, such as protocol assistance and scientific advice specifically for designated orphan medicines, and potential fee reductions depending on the status of the sponsor.

Generally, if a drug with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the European Medicines Agency or the FDA from approving another marketing application for the same drug and indication for a set time period, except in limited circumstances.

Even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the drug from competition because different drugs can be approved for the same condition, or the drug may be used off-label. Even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the other drug is clinically superior because it is shown to be safer, to be more effective or to make a major contribution to patient care. In addition, 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 orphan designation. Moreover, 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 quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we may seek Orphan Drug Designation for applicable indications for our current and future product candidates, we may never receive such designations. Even if we do receive such designations, there is no guarantee that we will enjoy the benefits of those designations.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term “same disease or condition” means the designated “rare disease or condition” and could not be interpreted by the Agency to mean the “indication or use.” We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

We may choose not to develop a potential product candidate, or we may suspend or terminate one or more discovery or preclinical programs or our product candidates.

At any time and for any reason, we may determine that one or more of our discovery programs, preclinical programs or product candidates does not have sufficient potential to warrant the allocation of resources toward such program or product candidate. Furthermore, because we have limited financial and personnel resources, we have placed significant focus on the development of our product candidates JTX-8064, vopratelimab and pimivalimab. Accordingly, we may choose not to develop a product candidate or elect to suspend or terminate one or more of our discovery or preclinical programs. If we suspend or terminate a program or product candidate in which we have invested significant resources, we will have expended resources on a program or product candidate that will not provide a full return on our investment. As a result, we may have missed an opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or product candidates. If we do not accurately evaluate the commercial potential or target market for a particular future product candidate, we may relinquish valuable rights to future product candidates through collaboration, licensing or other royalty arrangements.

Obtaining and maintaining marketing approval of our current or future product candidates in one jurisdiction does not mean that we will be successful in obtaining marketing approval of that product candidate in other jurisdictions.

Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing 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 of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials.

Obtaining foreign marketing approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our current and future product candidates will be harmed. Even if we obtain approval for our product candidates and ultimately commercialize them in foreign markets, we would be subject to separate risks and uncertainties, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and the reduced protection of intellectual property rights in some foreign countries.

Our failure to successfully identify, discover, acquire, develop or commercialize additional products or product candidates could impair our ability to grow.

Although a substantial amount of our efforts will focus on the clinical testing and potential approval of our most advanced product candidates, JTX-8064, vopratelimab and pimivalimab, an element of our long-term growth strategy is to in-license products or product candidates for development and commercialization. We may never be able to identify, discover, acquire, develop or commercialize any products or product candidates, which would have a material adverse effect on our business.

Because our internal research capabilities are limited, we may be dependent upon pharmaceutical and biotechnology companies, academic scientists, and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select, and acquire promising pharmaceutical product candidates and products. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. Acquisitions and in-licenses include numerous risks, including potential failure to achieve the expected benefits of the acquisition or license and potential unknown liabilities associated with the product or technology. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses, and technologies, integrate them into our current infrastructure and manage our development efforts.

Even if we receive marketing approval of our current or future product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review.

Any marketing approvals that we receive for our current and future product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or the conditions of approval or contain requirements for potentially costly post-market testing and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA or a comparable foreign regulatory authority approves any of our current or future product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import and export and record keeping for our current and future 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 current good manufacturing practice, or cGMP, and GCPs for any clinical trials that we conduct post-approval. 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 product recalls;
- fines, untitled and warning letters, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications we filed or suspension or revocation of license approvals;
- product seizure or detention, or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

Risks Related to Manufacturing, Commercialization and Reliance on Third Parties

We rely and expect to continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialize our product candidates and our business could be substantially harmed.

We do not have the ability to independently conduct clinical trials. We rely and will rely on medical institutions, clinical investigators, contract laboratories, and other third parties, such as CROs, to conduct or otherwise support our ongoing clinical trials, including processing of human blood and tumor samples and analysis of biomarkers from the clinical trials. We rely and will rely heavily on these parties for execution of clinical trials for our current and future product candidates, and we control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on these third parties including CROs will not relieve us of our regulatory responsibilities. For any violations of laws and regulations during the conduct of our clinical trials, we could be subject to untitled and warning letters or enforcement action that may include civil and criminal penalties up to and including criminal prosecution.

We and our clinical investigators and CROs are required to comply with regulations and requirements, including GCP, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. If we or our clinical investigators or CROs fail to comply with applicable GCP, 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 stockholders that, upon inspection, the FDA will determine that any of our current or future clinical trials will comply with GCP. In addition, our

clinical trials must be conducted with product candidates produced under cGMP regulations. Our failure or the failure of our clinical investigators or CROs to comply with these regulations may require us to repeat clinical trials, which would delay the marketing approval process and could also subject us to enforcement action. We also are required to register certain ongoing clinical trials and provide certain information, including information relating to the trial's protocol, on a government-sponsored database, ClinicalTrials.gov, within specific time frames. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we designed the clinical trials for JTX-8064, vopratelimab and pimivalimab and intend to design the clinical trials for future product candidates, clinical investigators or CROs will conduct all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may also face internal challenges that may materially adversely affect the willingness or ability of such parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If the clinical investigators or CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, marketing approval and commercialization of our current and future product candidates may be delayed, or our development programs may be materially and irreversibly harmed. If we are unable to rely on clinical data collected by our clinical investigators and CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct, and this could significantly delay commercialization and require significantly greater expenditures.

If clinical investigators or CROs 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 are compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such clinical investigators or CROs are associated with may be extended, delayed or terminated. For example, in EMERGE, due to a site error, we enrolled additional patients to achieve the number of patients required for our statistical analysis. If our clinical trials are extended, delayed or terminated, we believe that our financial results and the commercial prospects for our current and future product candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

Furthermore, if clinical investigators or CROs continue to experience adverse impacts from the COVID-19 pandemic or experience adverse impacts from the conflict in Ukraine and surrounding region, including facility closures, staffing shortages, travel restrictions, prioritization of healthcare resources toward pandemic or relief efforts, our clinical development efforts and plans for data disclosures may be delayed.

Because we rely on third-party manufacturing and supply partners, including a single supplier for some of our materials, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.

We rely on third-party contract manufacturers to manufacture our preclinical and clinical trial product supplies. We do not own manufacturing facilities for producing such supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. Our or a third party's failure to execute on our manufacturing requirements, or to do so on commercially reasonable terms and comply with cGMP could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our current or future product candidates under development;
- delay in submitting regulatory applications, or receiving marketing approvals, for our current or future product candidates;
- loss of cooperation of an existing or future collaborator;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities; and
- requirements to cease distribution or to recall batches of our current or future product candidates.

In the event that any of our manufacturers fails to comply with applicable regulatory requirements and facility and process validation tests or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our future product candidates may be unique or proprietary to the original manufacturer, which would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture such future product candidates. In particular, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines, which could negatively affect our ability to develop product candidates in a timely manner or within budget.

Certain raw materials necessary for the manufacture of our product candidates under our current manufacturing process, such as growth media, resins and filters, are available from a single supplier. We do not have agreements in place that guarantee our supply or the price of these raw materials. Any significant delay in the acquisition or decrease in the availability of these raw materials could considerably delay the manufacture of our current and future product candidates, which could adversely impact the timing of any planned trials or the marketing approval of that product candidate.

If any of our third-party manufacturing and supply partners experience adverse impacts from the conflict in Ukraine and surrounding region or the COVID-19 pandemic, including shutdowns, staffing shortages, production slowdowns, disruptions in delivery systems or government restrictions or limitations, our supply chain may be disrupted. For example, one of our pharmaceutical manufacturing partners has advised us of restrictions on shipments to Ukraine and Russia and has suspended certain operations in Ukraine. Additionally, third parties could be required to allocate resources in a way that impacts our operations. Due to the COVID-19 pandemic and under the Defense Production Act, the U.S. government may, among other things, require domestic industries to provide essential goods and services needed for the national defense, such as drug material or other supplies needed to diagnose or treat COVID-19 patients. These impacts may limit our ability to conduct our clinical trials, continue our research and development operations, and manufacture our product candidates for our clinical trials.

We expect to continue to rely on third-party manufacturers if we receive marketing approval for any product candidate. If we are unable to obtain or maintain third-party manufacturing for our current and future product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our current or future product candidates successfully. We do not yet have sufficient information to reliably estimate the cost of the commercial manufacture of any future product candidate.

In addition, in order to conduct clinical trials of our current and future product candidates, we will need to work with third-party manufacturers to manufacture them in large quantities. Our manufacturing partners or our third-party collaborators may be unable to successfully increase the manufacturing capacity of our current and future product candidates in a timely or cost-effective manner, or at all, and labor and material shortages due to the COVID-19 pandemic have adversely impacted the manufacturing capacity of our third-party manufacturers. In addition, quality issues may arise during scale-up activities. If our manufacturing partners or collaborators are unable to successfully scale up the manufacture of our current or future product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and marketing approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

We expect to develop our current and future product candidates in combination with other drugs. If we are unable to enter into a strategic collaboration for, or if we are unable to purchase on commercially reasonable terms, an approved or investigational cancer drug to use in combination with our product candidates, we may be unable to develop or obtain approval for our current and future product candidates in combination with other drugs.

We intend to develop our current and future product candidates in combination with one or more other cancer drugs. If the FDA or similar regulatory authorities outside of the United States revoke or do not grant approval of any drugs we use in combination with our current or future product candidates, we will not be able to market any products in combination with such drugs.

If safety or efficacy issues arise with any of these drugs, we could experience significant regulatory delays, and the FDA or similar regulatory authorities outside of the United States may require us to redesign or terminate the applicable clinical trials. If the drugs we use are replaced as the standard of care for the indications we choose for our current or future product candidates, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. In addition, if manufacturing or other issues result in a shortage of supply of the drugs with which we determine to combine with our current or future product candidates, we may not be able to complete clinical development of JTX-8064, vopratelimab, pimivalimab or future product candidates on our current timeline or at all.

Even if our current or future product candidates were to receive marketing approval or be commercialized for use in combination with other existing drugs, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of such existing drugs or that safety, efficacy, manufacturing or supply issues could arise with such drugs.

We may form or seek strategic collaborations to evaluate and, if approved, market our product candidates in combination with another approved or investigational cancer drug. If we are unable to enter into a strategic collaboration on commercially reasonable terms or fail to realize the benefits of any such collaboration, we may be required to purchase an approved cancer drug to use in combination with JTX-8064, vopratelimab and/or pimivalimab. The failure to enter into a successful collaboration or the expense of purchasing an approved cancer drug may delay our development timelines, increase our costs and jeopardize our ability to develop our product candidates.

We are subject to manufacturing risks that could substantially increase our costs and limit the supply of our products.

The process of manufacturing JTX-8064, vopratelimab and pimivalimab or future product candidates is complex, highly regulated and subject to several risks, including:

- Any changes in our manufacturing processes as a result of scaling-up may require additional approvals or may delay the development and marketing approval of our current and future product candidates and ultimately affect our success.
- The third-party manufacturing facilities in which our current and future product candidates are made could be adversely affected by equipment failures, contamination, vendor error, labor shortages, the COVID-19 pandemic, natural disasters, power failures and numerous other factors.
- Any adverse developments affecting manufacturing operations for our current or future product candidates, if any are approved, may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives.
- Biologics, such as JTX-8064, vopratelimab and pimivalimab, that have been produced and are stored for later use may degrade, become contaminated, suffer other quality defects or may not be used within their shelf life, which may cause the affected product candidates to no longer be suitable for their intended use in clinical trials or other development activities. If the defective product candidates cannot be replaced in a timely fashion, we may incur significant delays in our development programs that could adversely affect the value of such product candidates.

We face significant competition and if our competitors develop and market products that are more effective, safer or less expensive than any of our current or future product candidates, our commercial opportunities will be negatively impacted.

The life sciences industry is highly competitive and subject to rapid and significant technological change. We are currently developing therapeutics that will compete with other products and therapies that currently exist or are being developed, such as approved immunotherapy antibodies, the anti-ILT4 antibodies of Merck & Co., Inc. and Immune-Onc Therapeutics, Inc., the dual antagonist anti-ILT4/ILT2 antibody of NGM Biopharmaceuticals, Inc., the anti-ICOS antibodies of Bristol Myers Squibb, GlaxoSmithKline plc, or Sanofi S.A., Xencor, Inc.'s anti-PD-1 and anti-ICOS bispecific antibody, or the anti-ILT3 (LILRB4) antibodies of Merck & Co., Inc., Immune-Onc Therapeutics, Inc. and NGM Biopharmaceuticals, Inc. Products we may develop in the future are also likely to face competition from other products and therapies, some of which we may not currently be aware. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

We have both domestic and international competitors, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, universities and other research institutions and small and other early-stage companies. Many of our competitors have significantly greater financial, manufacturing, marketing, product development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, establishing clinical trial sites, recruiting patients and in manufacturing pharmaceutical products and may succeed in discovering, developing and commercializing products in our field before we do. Currently, Merck & Co., Inc. is conducting Phase 2 trials of its anti-ILT4 antibody and, given its resources, Merck will likely be able to develop its product candidate faster than we are able to develop JTX-8064. We also face competition in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to, or necessary for, our programs.

There are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. These treatments consist both of small molecule drug products, as well as biologics, as approaches to address cancer. These treatments are often combined with one another in an attempt to maximize the response rate and clinical benefit.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, have a broader label, are marketed more effectively, are reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain FDA, European Commission or other marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. Even if our current and future product candidates achieve marketing approval, they may be priced at a significant premium over competitive products, resulting in reduced competitiveness. In addition, if any of our current or future product candidates are approved by the FDA, the approval of a biosimilar product to one of our products could have a material impact on our business.

We will depend on Gilead to develop, manufacture and commercialize GS-1811 and may depend on additional third parties for the development and commercialization of our other product candidate programs. If these programs are not successful, we may not receive significant payments from such third parties or we may not be able to capitalize on the market potential of these product candidates.

In August 2020, we entered into a License Agreement, or the Gilead License Agreement, with Gilead pursuant to which we granted Gilead an exclusive, worldwide license to develop, manufacture and commercialize GS-1811. The Gilead License Agreement provides for potential payments to us from Gilead upon the achievement of specified development, regulatory and sales milestones, and potential royalty-based revenue if GS-1811 is successfully commercialized. In July 2021, we received a milestone payment upon IND clearance of GS-1811. As a result of this license, we will not control the nature, timing or cost of bringing GS-1811 to market. We cannot provide any assurance with respect to the success of the license, and we may never receive any additional milestone or any royalty payments pursuant to the Gilead License Agreement.

We may form or seek other strategic alliances, joint ventures, or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our current and future product candidates that we may develop.

Collaborations and other strategic transactions, including licensing arrangements, involving our product candidates pose the following risks to us:

- Collaborators, including licensors, have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, development and commercialization plans and strategies for GS-1811 are conducted solely by Gilead.
- Collaborators may not pursue development and commercialization of any of our current or future product candidates or may elect not to continue or renew development or commercialization programs 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 program, 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 products or 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 in-license, 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 develop, commercialize, enforce, maintain or defend such intellectual property. For example, Gilead has the first right to enforce, maintain or defend our intellectual property rights for GS-1811 under the Gilead License Agreement.
- Collaborators may not properly enforce, maintain or defend our intellectual property rights or may use our 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 litigation, or other intellectual property proceedings.
- Disputes may arise between a collaborator and us that cause the delay or termination of the research, development or commercialization of our current and future 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.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.
- Collaboration or licensing agreements may restrict our right to independently pursue new product candidates.

As a result, if we enter into additional collaboration agreements and strategic partnerships or license our intellectual property, products or businesses, we may not be able to realize the benefit of, or generate revenues from, such arrangements.

All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of Gilead with respect to the development and commercialization of GS-1811 and would also apply to the activities of any future licensees or collaborators.

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

Our drug development programs and the potential commercialization of our product candidates will require substantial additional resources. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. 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.

We face significant competition in seeking appropriate strategic partners and the negotiation process is time consuming and complex. Whether we reach a definitive agreement for other collaborations will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of our business. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for future 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 them as having the requisite potential to demonstrate safety and efficacy. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may also be restricted under existing agreements from entering into future agreements on certain terms with potential collaborators. For example, under the Gilead License Agreement, we have granted worldwide exclusive rights to Gilead for any antibody or other agent that is specifically directed to CCR8, and this exclusivity would limit our ability to enter into future strategic collaborations with other partners relating to CCR8.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program, delay or reduce the scope of potential commercialization activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all.

The market opportunities for our current and future products, if and when approved, may be limited to those patients who are ineligible for established therapies or for whom prior therapies have failed, and may be small.

Cancer therapies are sometimes characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for third-line use. When cancer is detected early enough, first-line therapy, usually chemotherapy, hormone therapy, surgery, radiation therapy, and, increasingly, immunotherapies or a combination of these, is sometimes adequate to

cure the cancer or prolong life without a cure. Second and third-line therapies are administered to patients when prior therapy is not effective. We expect to initially seek approval of our current and future product candidates as a therapy for patients who have received one or more prior treatments. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first-line therapy, but there is no guarantee that any of our product candidates, even if approved, would be approved for first-line 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 cancers we are targeting, as well as the subset of people with these cancers who have received one or more prior treatments, and who have the potential to benefit from treatment with our current and future product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, and market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our current and future product candidates may be limited or may not be amenable to treatment with any of our products, if and when approved. Even if we obtain significant market share for any of our products, if and when approved, because the potential target populations may be small, we may never achieve profitability without obtaining marketing approval for additional indications, including use as first- or second-line therapy.

We may develop companion diagnostics and/or complementary diagnostics for our current and future product candidates. If we are unable to successfully develop such companion diagnostics or complementary diagnostics, or experience significant delays in doing so, we may not realize the full commercial potential of our current or future product candidates.

Because we are focused on patient selection and enrichment strategies, in which predictive biomarkers may be used to identify the right patients for our product candidates, we believe that our success may depend, in part, on our ability to develop companion diagnostics and/or complementary diagnostics, which are assays or tests to identify an appropriate patient population for our product candidates. There has been limited success to date industry-wide in developing these types of companion diagnostics and/or complementary diagnostics. To be successful, we need to address a number of scientific, technical and logistical challenges. We have not yet initiated development of companion diagnostics and/or complementary diagnostics, and the process of obtaining or creating such a diagnostic is time consuming and costly. We may not be successful in developing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. Companion diagnostics and/or complementary diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval or clearance prior to commercialization. Given our limited experience in developing diagnostics, we expect to rely in part or in whole on third parties for their design and manufacture. If we are unable to engage a third party to assist us, or if we, or any third parties that we engage, are unable to successfully develop companion diagnostics and/or complementary diagnostics for our current and future product candidates, or experience delays in doing so:

- the development of our current and future product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our current and future product candidates may not receive marketing approval if safe and effective use of a product candidate depends on companion diagnostics and/or complementary diagnostics and such a diagnostic is not commercially available or otherwise approved or cleared by the appropriate regulatory authority; and
- we may not realize the full commercial potential of our current and future product candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify, or it takes us longer to identify, patients who are likely to benefit from therapy with our products, if approved.

If any of these events were to occur, our business would be harmed, possibly materially.

If product liability lawsuits are brought against us, we may incur substantial liabilities.

We face an inherent risk of product liability as a result of the clinical testing of our current and future product candidates. 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. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, we may experience financial or reputational losses in the future due to such product liability claims.

Insurance coverage is increasingly expensive. We may not be able to maintain insurance at a reasonable cost or in an amount adequate to satisfy any liability that may arise, if at all. Our insurance policy contains 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.

Adverse events in the field of immuno-oncology could damage public perception of our product candidates and negatively affect our business.

The commercial success of our products will depend in part on public acceptance of the use of cancer immunotherapies. Adverse events in clinical trials of any of our current or future product candidates or other similar products and the resulting publicity, as well as any other adverse events in the field of immuno-oncology that may occur, including in connection with third-party therapies such as approved immunotherapy antibodies, the anti-ILT4 antibodies of Merck & Co., Inc. and Immune-Onc Therapeutics, Inc., the dual antagonist anti-ILT4/ILT2 antibody of NGM Biopharmaceuticals, Inc., the anti-ICOS antibodies of Bristol Myers Squibb, GlaxoSmithKline plc, or Sanofi S.A., Xencor, Inc.'s anti-PD-1 and anti-ICOS bispecific antibody, or the anti-ILT3 (LILRB4) antibodies of Merck & Co., Inc., Immune-Onc Therapeutics, Inc. and NGM Biopharmaceuticals, Inc., could result in a decrease in demand for our product candidates. If public perception is influenced by claims that the use of cancer immunotherapies is unsafe, whether related to our or third-party therapies, our products may not be accepted by the general public or the medical community.

Future adverse events in immuno-oncology or the biopharmaceutical industry could also result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approvals of our products. Any increased scrutiny could delay or increase the costs of obtaining marketing approval for our current and future product candidates.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

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 health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry.

Since its enactment, there have been numerous judicial, administrative, executive and legislative challenges to certain aspects of the ACA, and we expect there be to additional challenges and amendments to the ACA in the future. For example, with enactment of the Tax Cuts for Jobs Act, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimum level of health insurance, became effective in 2019.

The implementation of the ACA is ongoing, and the law appears likely to continue the downward pressure on pharmaceutical pricing. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results. We cannot predict what effect further changes to the ACA would have on our business. 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, companion diagnostics or complementary diagnostics, or additional pricing pressures.

Our future relationships with customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. In addition, we may be subject to transparency laws and patient privacy regulation by the U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include the federal Anti-Kickback Statute, the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 the federal legislation commonly referred to as the Physician Payments Sunshine Act, and analogous state and foreign laws and regulations, any of which may constrain the business or financial arrangements and relationships through which we sell, market and distribute any products for which we obtain marketing approval.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is also uncertain and any investigation or settlement could be time- and resource-consuming, divert management's attention, increase our costs or otherwise have an adverse effect on our business.

If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to various significant penalties, any of which could harm our ability to operate our business and our financial results. In addition, the approval and commercialization of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Risks Related to our Financial Position and Need for Additional Capital

We have accumulated significant losses since our inception and anticipate that we will continue to incur substantial net losses in the foreseeable future.

We are a clinical-stage biopharmaceutical company with a limited operating history, and we are in the early stages of our development efforts. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain marketing approval and become commercially viable. We have financed our operations primarily through the sale of equity securities and through our license and collaboration arrangements with Celgene Corporation and Gilead. Since our inception, most of our resources have been dedicated to the preclinical and clinical development of our product candidates and discovery programs. 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 incurred losses in each year since our inception, except for net income of \$56.8 million for the year ended December 31, 2019 as a result of revenue recognized under our prior agreements with Celgene Corporation, and we incurred a net loss of \$90.9 million for the year ended December 31, 2021. As of December 31, 2021, we had an accumulated deficit of \$241.9 million. We expect to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek marketing approvals for, our current and future product candidates.

Even if we succeed in receiving marketing approval for and commercialize our product candidates, we will continue to incur substantial research and development and other expenditures to develop and market additional potential products. 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 never generated any revenue from product sales and our ability to generate revenue from product sales and become profitable depends on our success on a number of factors.

We have no products approved for commercial sale, have not generated any revenue from product sales, and do not anticipate generating any revenue from product sales until some time after we have received marketing approval for the commercial sale of a product candidate, if ever. Our ability to generate revenue and achieve profitability depends significantly on our success in many factors, including:

- completing clinical development of JTX-8064, vopratelimab and pimivalimab;

- completing preclinical development of JTX-1484;
- completing research, discovery, preclinical and clinical development of future product candidates;
- obtaining marketing approvals for our current and future product candidates for which we complete clinical trials;
- developing a sustainable and scalable manufacturing process for our product candidates, including establishing and maintaining commercially viable supply and manufacturing relationships with third parties;
- launching and commercializing our product candidates for which we obtain marketing approvals, either directly or with a collaborator or distributor;
- obtaining market acceptance of our current and future product candidates as viable treatment options;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring and developing new product candidates;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- obtaining, maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Even if our product candidates or future product candidates that we develop are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. These costs may fluctuate or exceed our expectations and our revenues will depend on many factors that we cannot control or estimate. If we are not able to generate revenue from the sale of any approved products, we may never become profitable.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. As of December 31, 2021, our cash, cash equivalents, short-term and long-term investments were \$220.2 million. We expect to continue to spend substantial amounts to continue the clinical development of JTX-8064, vopratelimab and pimivalimab and preclinical and clinical development of JTX-1484 and future product candidates. If we are able to gain marketing approval for any of our product candidates, we will require significant additional amounts of cash in order to launch and commercialize those product candidates to the extent that such launch and commercialization are not the responsibility of a collaborator or a licensee. In addition, other unanticipated costs may arise. Because the design and outcome of our planned and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our current and future product candidates. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical studies and clinical trials, including the impacts of the COVID-19 pandemic on the timing and progress of our ongoing and planned clinical trials;
- the timing of, and the costs involved in, obtaining marketing approvals for our product candidates if clinical trials are successful;
- the cost of commercialization activities for our product candidates, that are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates for clinical trials in preparation for marketing approval and in preparation for commercialization;
- our ability to establish and maintain strategic licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the timing, receipt, and amount of sales of, or royalties on, our future products, if any;
- the emergence of competing cancer therapies and other adverse market developments; and
- the requirement for and cost of developing companion diagnostics and/or complementary diagnostics.

Until we can generate sufficient product and royalty revenue to finance our cash requirements, which we may never do, we expect to finance our future cash needs through a combination of public or private equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other marketing or distribution arrangements. Based on our research and development plans, we expect that our cash, cash equivalents, short-term and long-term investments as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements through the third quarter of 2023.

If we are unable to obtain adequate financing on favorable terms when needed, we may have to delay, reduce the scope of or suspend one or more of our clinical trials or research and development programs or our commercialization efforts. Further, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic or other macroeconomic conditions.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of private and public equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we are unable to raise additional funds through equity or debt financings when needed, and instead raise additional capital through marketing and distribution agreements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish certain valuable rights to our current and future product candidates, technologies, future revenue streams or discovery programs or grant licenses on terms that may not be favorable to us.

Risks Related to Intellectual Property

If we are unable to obtain, maintain and protect our intellectual property rights for our product candidates or if our intellectual property rights are inadequate, our competitive position could be harmed.

Our commercial success will depend in part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our product candidates. We rely on trade secret, patent, copyright and trademark laws, and confidentiality, licensing and other agreements with employees and third parties, all of which offer only limited protection. We currently, or will in the future, seek to protect our proprietary position by filing and prosecuting patent applications in the United States and abroad related to our current and future product candidates, and any future novel technologies that are important to our business.

The steps we, our licensees or our licensors have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary information or infringement of our intellectual property rights, both inside and outside of the United States. Filing, prosecuting and defending patents on our current and future product candidates throughout the world would be prohibitively expensive, and intellectual property rights in some countries outside the United States can be less extensive than those in the United States.

If we, our licensees or our licensors are unable to obtain and maintain patent protection for our current and future product candidates, or if the scope of the patent protection obtained is not sufficient, our competitors could develop and commercialize products similar or superior to ours, and our ability to successfully commercialize our current and future product candidates and future technologies may be adversely affected.

Our pending applications cannot be enforced against third parties unless and until a patent issues from such applications and, even after issuance, such patents may be challenged in the courts or patent offices in the United States and abroad. We are currently involved in an appeal of an opposition proceeding in the European Patent Office, and this proceeding may be ongoing for a number of years and may divert employee resources from our business. Additionally, this and other such proceedings may result in the loss of patent protection, the narrowing of claims in such patents or the invalidity or unenforceability of such patents, which could limit our ability to stop others from using or commercializing similar or identical products or limit the duration of the patent protection for our current and future product candidates.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. Any efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property we develop or license. Moreover, many countries

have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business and results of operations may be adversely affected.

Furthermore, we cannot predict whether any of our future patent applications will result in the issuance of patents that effectively protect our current and future product candidates, or if any of our issued patents or if any of our licensor's issued patents will effectively prevent others from commercializing competitive products. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult. If we are unable to obtain, maintain, and protect our intellectual property our competitive advantage could be harmed, and it could result in a material adverse effect on our business, financial condition, and the results of operations and prospects.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time, and our current and future product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.

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. We expect to seek patent term extensions of patent terms in the United States for our issued patents, licensed patents and any patents we own in the future and, if available, in other countries where that may be available when we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication. However, the applicable authorities, including the FDA and the United States Patent and Trademark Office, or USPTO, in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. We may not be granted an extension because of, for example, failure to exercise due diligence during the testing phase or regulatory review process, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. If we are unable to obtain patent term extension or the term of any such extension is less than we request, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case, which could result in a material adverse effect on our business, financial condition, results of operation and prospects.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, established legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement the BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We intend to seek market exclusivity for our biological product candidates that is subject to its own BLA for 12 years in the United States, 10 years in Europe and other durations in other markets. However, the term of the patents that cover such product candidates may not extend beyond the applicable market exclusivity awarded by a particular country. For example, in the United States, if all of the patents that cover our particular biologic product expire before the 12-year market exclusivity expires, a third party could submit a marketing application for a biosimilar product four years after approval of our biologic product, and the FDA could immediately review the application and approve the biosimilar product for marketing 12 years after approval of our biologic. Alternatively, a third party could submit a BLA for a similar or identical product any time after approval of our biologic product, and the FDA could immediately review and approve the similar or identical product for marketing and the third party could begin marketing the similar or identical product upon expiry of all of the patents that cover our particular biologic product.

Additionally, there is a risk that this exclusivity could be shortened due to congressional action, potentially creating the opportunity for biosimilar competition sooner than anticipated. The extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If we are unable to protect the confidentiality of our proprietary information and know-how, the value of our technology and products could be adversely affected.

In addition to seeking patent protection, we also rely on other proprietary rights, including protection of trade secrets, know-how and confidential and proprietary information. To maintain the confidentiality of our trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, collaborators and other third parties who have access to our trade secrets. These agreements require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. In addition, in the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information.

Adequate remedies may not exist in the event of unauthorized use or disclosure of our confidential information. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable. In addition, some courts are less willing or unwilling to protect trade secrets. The disclosure of our trade secrets or the independent development of our trade secrets by a competitor or other third party would impair our competitive position and may materially harm our business, financial condition, results of operations and prospects.

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

Our commercial success depends on our ability and the ability of our current or future licensees or collaborators to develop, manufacture, market and sell our product candidates, and to use our related proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and future product candidates. For example, we are aware of third-party patents or patent applications that may be construed to cover the targets of JTX-8064, vopratelimab, pimivalimab or GS-1811. If we are found to infringe a third-party's intellectual property rights, and we are unsuccessful in demonstrating that such intellectual property rights are invalid or unenforceable, we could be required to obtain a license from such third party to continue developing, manufacturing and commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We also could be forced, including by court order, to cease developing, manufacturing, and commercializing our product candidates. In addition, in any such proceeding or litigation, we could be found liable for significant monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Furthermore, we are testing our product candidates, and expect to conduct additional trials of our product candidates, with other products that are covered by patents held by other companies or institutions. In the event that a labeling instruction is required in product packaging recommending that combination, we could be accused of, or held liable for, infringement of the third-party patents covering the product candidate or product recommended for administration with our product candidates. In such a case, we could be required to obtain a license from the other company or institution to use the required or desired package labeling, which may not be available on commercially reasonable terms, or at all.

If we breach any of our license agreements or collaboration agreements, it could have a material adverse effect on our commercialization efforts for our product candidates.

Our commercial success depends on our ability, and at times, the ability of our licensors and current or future licensees and collaborators to develop, manufacture, market, and sell our product candidates, and use our licensors' proprietary technologies without infringing the property rights of third parties. For example, we have entered into an exclusive license agreement with Sloan Kettering Institute for Cancer Research, Memorial Sloan Kettering Cancer Center and Memorial Hospital for Cancer and The University of Texas MD Anderson Cancer Center related to certain uses of our vopratelimab, and we may enter into additional licenses in the future. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our products in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all our licenses.

In addition, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement and defense of patents and patent applications covering the technology that we license to or from third parties. For example, under the Gilead License Agreement, Gilead has the first right to enforce, maintain or defend our intellectual property rights with respect to GS-1811. In such cases, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If Gilead or any other of our licensors or licensees fail to prosecute, maintain, enforce and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize our product candidates that are the subject of such licensed rights could be adversely affected. Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties.

Certain of our license agreements also require us to meet development thresholds to maintain the license, including establishing a set timeline for developing and commercializing products. If we fail to comply with the obligations under our license agreements, including payment and diligence terms, our licensors may have the right to terminate our agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of our license agreements or reduction or elimination of our rights under them may result in our having to negotiate a new or reinstated agreement, which may not be available to us on equally favorable terms, or at all.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

Further, the resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be successful in obtaining necessary rights to our product candidates we may develop or obtain through acquisitions and in-licenses.

We currently have rights to intellectual property, through licenses from third parties, for certain uses of vopratelimab. Because our current and future product candidates may require the use of proprietary rights held by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for our current and future product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities.

If we are unable to successfully obtain required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon or alter our plans for the development or commercialization of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payments and other similar provisions during the patent application process and to maintain patents after they are issued. In certain circumstances, we rely on our licensing partners to take the necessary action to comply with these requirements with respect to our licensed intellectual property. While an unintentional lapse can 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. If we fail to obtain and maintain the patents and patent applications covering our products or procedures, we may not be able to stop a competitor from marketing products that are the same as or similar to our current and future product candidates, which would have a material adverse effect on our business.

Changes to the patent law in the United States and other jurisdictions 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 involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs.

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. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of our business.

Competitors may infringe our licensed patents or any patent we own in the future or misappropriate or otherwise violate our intellectual property rights. We may also be required to defend against claims of infringement and our licensed patents and any patents we own in the future may become involved in priority or other intellectual property related disputes. To counter infringement or unauthorized use, litigation may be necessary to enforce or defend our intellectual property rights or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. Also, third parties may initiate legal proceedings against us or our licensors to assert that we are infringing their intellectual property rights or to challenge the validity or scope of our owned or licensed intellectual property rights. Litigation and other intellectual property related proceedings could result in substantial costs and diversion of management resources, which could harm our business and financial results. Despite our best efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. In addition, an adverse result in any litigation or other intellectual property related proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be disclosed during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments in any such proceedings. If securities analysts or investors perceive these results to be negative, it also could have a material adverse effect on the price of shares of our common stock. Any of the foregoing may have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our collaborators, licensors, employees or we have misappropriated their intellectual property, have wrongfully used or disclosed confidential information of third parties or are in breach of non-competition or non-solicitation agreements with our competitors.

Many of our employees, our collaborators' employees and our licensors' employees, including our senior management, are currently or previously were employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property of any such individual's current or former employer. In addition, we could be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or

competitors, that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, we may lose valuable intellectual property rights or personnel or sustain monetary damages. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Any of the foregoing may have a material adverse effect on our business, financial condition, results of operations and prospects.

Issued patents covering our current and future product candidates could be found invalid or unenforceable if challenged in court or before the USPTO or comparable foreign authority.

If we or one of our licensing partners initiate legal proceedings against a third party to enforce a patent covering one of our current or future product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. The outcome following legal assertions of invalidity and unenforceability is unpredictable. If a third party 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 our current and future product candidates. Such a loss of patent protection could have a material adverse impact on our business.

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

We are highly dependent on our key personnel, and if we are not successful in attracting, motivating 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, motivate and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, particularly our chief executive officer, Richard Murray, and our scientific and medical personnel. The loss of the services of any of our executive officers, key employees, and scientific and medical advisors, and our inability to find suitable replacements, could result in delays in product development and harm our business.

Our Cambridge, Massachusetts headquarters is located in a region that is home to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel is intense and the turnover rate can be high, which may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We expect that we will need to recruit talent from outside of our region and doing so may be costly and difficult.

To induce valuable employees to remain at our Company, in addition to salary and cash incentives, we have provided equity awards that vest over time. The value to employees of these equity grants that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, meaning that such employees could leave our employment at any time, with or without notice. We do not maintain “key man” insurance policies on the lives of all of these individuals or the lives of any of our other employees.

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, 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. If any of our product candidates receives appropriate regulatory approval, 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 collaborative arrangements regarding the sales and marketing of our products; however, we cannot assure stockholders that we will be able to establish or maintain such collaborative arrangements, on favorable terms if at all. We cannot assure stockholders 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 current or future product candidates.

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

We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and comparable

foreign regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; anti-corruption and anti-bribery laws, including the Foreign Corrupt Practices Act, and various other anti-corruption laws in countries outside of the United States; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. We have adopted a code of conduct applicable to all of our employees and require all employees, including management, to participate in anti-corruption training, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could result in significant penalties and could have a material adverse effect on our ability to operate our business and our results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could 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 involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations 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.

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.

We may evaluate various acquisitions and additional 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 product 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, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

Our internal information technology systems, or those used by our CROs or other third parties, may fail or suffer security breaches and cyber-attacks, which could compromise our intellectual property or other sensitive information, could result in a material disruption of our business or could subject us to regulatory actions that could result in significant fines.

We, our CROs and other third parties rely significantly upon information technology systems, and despite the implementation of security measures, our internal information technology systems are vulnerable to damage from computer viruses and unauthorized access. A system failure or a security breach could result in a material disruption of our business operations. We, our CROs, contractors and other third parties rely on information technology networks and systems to process, personal identifying information and payroll data, including operational and financial transactions and records. In particular, we rely on third parties for many aspects of our business, including manufacturing product candidates and conducting clinical trials. The secure maintenance of this information is critical to our business and reputation. Companies have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access. These threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack. Cyber threats may be generic, or they may be custom-crafted against our information systems. Over the past few years, cyber-attacks have become more prevalent and much harder to detect and defend against. Additionally, our increased reliance on personnel working from home could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with regulators, CROs, clinical trial sites or third-party manufacturing and supply partners.

Our network and storage applications and those of CROs and other third parties may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. We have experienced and may in the future experience such unauthorized access. While we continue to invest in data protection and information technology, including providing an information security training and compliance program to our employees, there can be no assurance that our efforts will prevent service interruptions or identify breaches in our systems. It is often difficult to anticipate or immediately detect such incidents and the damage caused by them. These data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. A security breach, cyber-attack or unauthorized access of our clinical data or other data could damage the integrity of our clinical trials, impact our regulatory filings, cause significant risk to our business, compromise our ability to protect our intellectual property, and subject us to regulatory actions, including under privacy or security rules under federal, state or other international laws protecting confidential information, that could be expensive to defend and could result in significant fines or other penalties. Although we maintain a cyber risk management insurance policy, cyber-attacks could cause us to incur significant remediation costs, disrupt key business operations and divert attention of management and key information technology resources. Furthermore, our insurance premiums increase annually, and such insurance may not continue to be available on reasonable terms or be sufficient in amount to cover one or more large claims. Our network security and data recovery measures and those of our CROs, licensees, collaborators, contractors and vendors may not be adequate to protect against such security breaches and disruptions.

We, or the third parties upon whom we depend, may be adversely affected by unforeseen or catastrophic events, including the emergence of a pandemic or other natural disasters, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

The COVID-19 pandemic has had adverse effects on our business, including difficulty sourcing the components of sample collection kits for our clinical trials, and may have further adverse effects, the extent or nature of which we are not able to predict at this time. In addition, other unforeseen or catastrophic events could severely disrupt our operations and our supply chain, and have a material adverse effect on our business. If a natural disaster, power outage, weather event related to climate change or other event occurred that damaged critical infrastructure, such as our headquarters or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material adverse effect on our business.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

Our general business strategy may be adversely affected by any economic downturn, volatile business environment or unpredictable and unstable conditions in global credit and financial markets. We cannot assure stockholders that deterioration of the global credit and financial markets would not negatively impact our stock price, our current portfolio of cash equivalents or investments, or our ability to meet our financing objectives. Foreign currency fluctuations could result in increased operating expenses and other obligations incident to doing business in another country. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure

any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans.

Risks Related to our Common Stock

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

Our stock price has been and is likely to continue to be volatile. For example, during 2021, our stock price ranged from \$5.03 to \$14.84. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of our clinical trials or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

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

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes has been limited by “ownership changes” and may be further limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the IRC, if a corporation undergoes an “ownership change” (generally defined as a greater than 50 percent change (by value) in the ownership of its equity over a three-year period), the corporation’s ability to use its pre-change net operating loss, or NOL, carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. An IRC Section 382 study, completed in August 2016, identified three previous ownership changes for purposes of IRC Section 382. No additional ownership changes were identified in a study completed in November 2021. As a result of these ownership changes, our net operating loss and tax credit carryforwards allocable to the periods preceding each such ownership change are subject to limitations under IRC Section 382. We may experience ownership changes in the future as a result subsequent shifts in our stock ownership, some of which are outside our control, which may also be subject to limitations by “ownership changes” in the future, which could result in increased tax liability to us.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. As described below in “Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition,” the Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. In addition, state NOLs generated in one state cannot be used to offset income generated in

another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Act, which significantly reformed the IRC. The Tax Act, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for NOLs arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such NOLs may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress's response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the CARES Act was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of NOLs, which was enacted as part of the Tax Act. It also provides that NOLs arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30% to 50% of adjusted taxable income.

Regulatory guidance under the Tax Act, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. In addition, state tax legislation or administrative guidance conforming to or decoupling from particular provisions of the Tax Act, the FFCR Act and the CARES Act could affect our business or financial condition.

We are incurring and will continue to incur significantly increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives.

As a public company, we are incurring and will continue to incur significant legal, accounting and other expenses, particularly after we are no longer an emerging growth company. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, as well as various requirements imposed by the Sarbanes-Oxley Act, rules subsequently adopted by the SEC and Nasdaq to implement provisions of the Sarbanes-Oxley Act, and the Dodd-Frank Wall Street Reform and Consumer Protection Act. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

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

Certain stockholders hold a substantial number of shares of our common stock. If such stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our stock incentive plans will become eligible for sale in the public market extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act, and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates. Any sales of securities by these stockholders who have exercised registration rights could have a material adverse effect on the trading price of our common stock.

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 or our guidance.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements 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. Accordingly, our revenue may depend on development funding and the achievement of development and clinical milestones under current and any potential future license and collaboration agreements and sales of our products, if approved. 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.

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 and future product candidates, 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 and future product candidates, which may vary depending on FDA 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;
- the timing and outcomes of clinical trials for our current product candidates or competing product candidates;
- competition from existing and future products that may compete with our current and 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 any of our current or future product candidates;
- the level of demand for our current and future product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- our ability to commercialize our current and future product candidates, if approved;
- the success of our exclusive license to Gilead and our ability to establish and maintain other 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;
- the impact of the COVID-19 pandemic, including precautions to mitigate the spread of COVID-19; and
- the changing and volatile global economic 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. 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 revenue and/or earnings guidance we may provide.

Moreover, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us as pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely, in part, on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which, in turn, could cause our stock price to decline.

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

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15 percent of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Our bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our bylaws, provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. Any person purchasing or otherwise acquiring any interest in any shares of our capital stock shall be deemed to have notice of and to have consented to this provision of our bylaws.

This exclusive forum provision would not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, which provides for exclusive jurisdiction of the federal courts. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act, inasmuch as Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder, provided, that with respect to claims under the Securities Act, our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. Stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near the State of Delaware. The Court of Chancery may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Alternatively, if a court were to find this provision of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs, which could have a material adverse effect on our business, financial condition or results of operations.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

We lease a facility containing our research and development, laboratory and office space, which consists of approximately 51,000 square feet located at 780 Memorial Drive, Cambridge, Massachusetts. Our lease expires on March 31, 2025. This facility is our corporate headquarters. We believe that our facilities are sufficient to meet our current needs.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information and Holders

Our common stock trades on the Nasdaq Global Select Market under the symbol “JNCE”. As of February 28, 2022, we had approximately 13 holders of record of our common stock. This number does not include beneficial owners whose shares were held by nominees in street name.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently 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 to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects, then applicable contractual restrictions and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Recent Sales of Unregistered Securities

None.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. [Reserved]

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

The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this Annual Report on Form 10-K, including those factors set forth in the section entitled "Cautionary Note Regarding Forward-Looking Statements and Industry Data" and in the section entitled "Risk Factors" in Part I, Item 1A.

Overview

We are a clinical-stage immunotherapy company dedicated to transforming the treatment of cancer by developing therapies that enable the immune system to attack tumors and provide long-lasting benefits to patients. Our strategy is to use a biomarker-driven approach from discovery through clinical development. We have developed a suite of integrated technologies that comprise our Translational Science Platform, enabling us to comprehensively interrogate the cellular and molecular composition of tumors. By focusing on specific cell types, both immune and non-immune, within tumors, we can prioritize targets and then identify related biomarkers designed to match the right therapy to the right patient. Our pipeline is focused on product candidates to address PD-(L)1-inhibitor resistant and PD-(L)1 inhibitor sensitive tumors, which represent significant opportunities requiring different biological approaches. We aim to develop product candidates that address the unmet medical need of patients in both of these populations.

Our highest priority program, JTX-8064, is being developed for patients with either PD-(L)1-inhibitor resistant or PD-(L)1 inhibitor sensitive tumors. JTX-8064 is the first tumor-associated macrophage candidate to emerge from our Translational Science Platform. JTX-8064 is a monoclonal antibody that binds to Leukocyte Immunoglobulin Like Receptor B2, or LILRB2 (also known as ILT4), which is a cell surface receptor expressed on macrophages and other myeloid cells. Our INNATE clinical trial is a Phase 1/2 clinical trial of JTX-8064 as a monotherapy and in combination with our PD-1 inhibitor, pimiralisib, in patients with solid tumors. In January 2021, we began enrollment in the dose-escalation portion of the INNATE trial and enrollment was completed in July and October 2021 for monotherapy and combination therapy, respectively. JTX-8064 has been well-tolerated to date with no observed dose limiting toxicities. We selected 700 mg as our recommended phase 2 dose for further evaluation. We initiated enrollment in August 2021 and October 2021 in the phase 2 monotherapy and combination therapy portions, respectively. The INNATE trial is comprised of one monotherapy and seven combination indication-specific expansion cohorts and is designed to demonstrate proof-of-concept. Once proof-of-concept is established, we plan to move JTX-8064 rapidly into registrational trials on a cohort by cohort basis.

The expansion cohorts are studying tumor types in three groups of patients: (i) PD-(L)1 inhibitor experienced patients whose tumors progressed on or after treatment with a PD-(L)1 inhibitor (including, non-small cell lung cancer, or NSCLC), (ii) PD-(L)1 inhibitor naïve patients whose tumors are historically resistant to PD-(L)1 inhibitors (including, ovarian cancer), and (iii) PD-(L)1 inhibitor naïve patients whose tumors are historically more sensitive to PD-(L)1 inhibitors (including, front line PD-L1 positive head and neck squamous cell carcinoma). Proof-of concept expansion cohorts have the potential to enroll up to 29 patients per combination therapy cohort and 47 patients in the monotherapy cohort if pre-specified criteria are met. We expect to report preliminary clinical and biomarker data from INNATE in 2022.

Vopratelimab is a clinical-stage monoclonal antibody that binds to and activates the Inducible T cell CO-Stimulator, or ICOS, a protein on the surface of certain T cells commonly found in many solid tumors. We are currently enrolling patients in the SELECT trial, a randomized phase 2 proof-of-concept trial outside the United States evaluating vopratelimab in combination with pimiralisib compared to pimiralisib alone in biomarker-selected, immunotherapy-naïve second-line NSCLC patients. We identify patients for SELECT using TIS^{vopra}, an 18 gene signature that includes genes relevant to both CD8 and CD4 T cell biology. TIS^{vopra} has been optimized to predict for emergence of ICOS hi CD4 T cells in the peripheral blood, which have been associated with clinical benefit in patients treated with vopratelimab alone or in combination with nivolumab. We expect to report complete clinical data from SELECT in the second half of 2022.

Pimiralisib is a clinical-stage anti-PD-1 monoclonal antibody that we are developing primarily for potential use in combination with our product candidates, as we believe that combination therapy has the potential to be a mainstay of cancer immunotherapy. We presented safety and preliminary efficacy data from our monotherapy Phase 1 clinical trial of pimiralisib in 2019. Based on the results of that clinical trial, we are using pimiralisib in combination with JTX-8064 in INNATE and vopratelimab in SELECT.

GS-1811, formerly JTX-1811, is our fourth internally developed program to enter the clinic. In August 2020, we entered into an agreement to exclusively license GS-1811 to Gilead Sciences, Inc., or Gilead. GS-1811 is a monoclonal antibody that is designed to selectively deplete T regulatory cells in the tumor microenvironment, or TME, by targeting a receptor called CCR8, which is preferentially expressed on intra-tumoral T regulatory cells. Pursuant to our exclusive license agreement with Gilead,

or the Gilead License Agreement, we granted Gilead a worldwide license to develop, manufacture and commercialize GS-1811 and certain derivatives thereof, as well as backup antibodies defined within the agreement. Under the terms of the Gilead License Agreement, we advanced GS-1811 through the clearance of an investigational new drug application, or IND, in June 2021, which triggered a \$25.0 million milestone payment in July 2021, and have transitioned the program to Gilead. Gilead initiated clinical trials of GS-1811 in August 2021. We are entitled to receive additional payments from Gilead upon the achievement of specified clinical, regulatory and sales milestones. We are also eligible to receive tiered royalty payments based on a percentage of annual worldwide net sales ranging from the high-single digits to mid-teens, based on future annual net sales of licensed products, on a licensed product-by-licensed product and country-by-country basis.

JTX-1484 is the most recent product candidate to emerge from our Translational Science Platform. JTX-1484 is a monoclonal antibody designed to block human LILRB4 on various myeloid cells which we believe may lead to reduced immune suppression and enhancement of T cell functionality. We are currently conducting IND-enabling activities for JTX-1484, with the goal of filing an IND in 2023.

With our biomarker-driven approach, we leverage our Translational Science Platform to interrogate cell types within the human TME and to identify and prioritize targets across a broad spectrum of immune and non-immune cell types. In addition, early in the development process, we use our Translational Science Platform to identify potential predictive biomarkers to enable us to enrich our clinical trials for patient populations that may be more likely to respond to a particular immunotherapy. Once clinical data is available for a product candidate, we then use a reverse translational approach to interrogate tumor and blood samples from patients with known outcomes. By using these reverse translational findings, we believe we are better able to design clinical trials and more efficiently develop cancer immunotherapies that potentially provide greater benefit to patients. These biomarker results, coordinated to clinical response, will assist with determining the benefit of proceeding to the use of a companion diagnostic and/or complementary diagnostic for a given therapy.

Beyond our product candidates, we continue to advance and build our discovery pipeline. We are discovering and developing next-generation immunotherapies by leveraging our Translational Science Platform to systematically and comprehensively interrogate cell types within the tumor microenvironment. Our broad discovery pipeline includes multiple programs targeting myeloid cells such as macrophages, T regulatory cells and non-immune cells. We believe that the use of our Translational Science Platform to efficiently identify novel immuno-oncology targets and advance them from discovery to investigational new drug application, or IND, stage is a sustainable approach that we plan to continually apply across our broad discovery pipeline and target selection process.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, developing our Translational Science Platform and conducting research, preclinical studies and clinical trials. We do not have any products approved for sale. We are subject to a number of risks comparable to those of other similar companies, including dependence on key individuals; the need to develop commercially viable products; competition from other companies, many of which are larger and better capitalized; and the need to obtain adequate additional financing to fund the development of our products. We have funded our operations primarily through proceeds received from public offerings and private placements of our stock totaling \$389.5 million and payments from license and collaboration agreements totaling \$385.0 million.

Due to our significant research and development expenditures, we have accumulated substantial losses since our inception. As of December 31, 2021, we had an accumulated deficit of \$241.9 million. We expect to incur substantial additional losses in the future as we expand our research and development activities.

The spread of COVID-19 during 2020 and 2021 has caused disruption on a global scale and we continue to monitor the impacts of the COVID-19 pandemic on our business. As of March 2, 2022, we have not experienced a significant financial impact directly related to the COVID-19 pandemic but have experienced some disruptions to clinical operations and to our supply chain. As the pandemic continues to unfold, the extent of its effect on our operational and financial performance will depend in large part on future developments, which cannot be predicted with confidence at this time.

Financial Operations Overview

Revenue

For the year ended December 31, 2021, we recognized \$26.9 million of license and collaboration revenue under the Gilead License Agreement primarily relating to a \$25.0 million milestone achievement for FDA clearance of the IND for GS-1811 and \$1.9 million related to the completion of research and transition services. For the year ended December 31, 2020, we recognized \$62.3 million of license and collaboration revenue under the Gilead License Agreement for the GS-1811 license and performance of research and transition services.

In the future, we may generate revenue from product sales or collaboration agreements, strategic alliances and licensing arrangements, including potential milestone payments and royalties under the Gilead License Agreement. We expect that our revenue will fluctuate from quarter-to-quarter and year-to-year as a result of the timing and amount of license fees, milestones, reimbursement of costs incurred and other payments, if any, and product sales, to the extent any products are successfully commercialized. If we or third parties fail to complete the development of our product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Operating Expenses

Research and Development Expenses

Research and development expenses represent costs incurred by us for the discovery, development and manufacture of our current and future product candidates and include: external research and development expenses incurred under arrangements with third parties, including contract research organizations, contract manufacturing organizations, academic and non-profit institutions and consultants; salaries and personnel-related costs, including non-cash stock-based compensation expense; license fees to acquire in-process technology and other expenses, which include direct and allocated expenses for laboratory, facilities and other costs.

We use our employee and infrastructure resources across multiple research and development programs and for identifying, testing and developing product candidates from our Translational Science Platform. We manage certain activities such as contract research and manufacture of our product candidates and discovery programs through our third-party vendors.

At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales of our product candidates. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- addition and retention of key research and development personnel;
- establishing an appropriate safety profile with IND-enabling toxicology studies and clinical trials;
- the cost to acquire or make therapies to study in combination with our immunotherapies;
- successful enrollment in and completion of clinical trials, including the impacts of the COVID-19 pandemic on the timing and progress of our ongoing and planned clinical trials;
- establishing agreements with third-party contract manufacturing organizations for clinical supply for our clinical trials and commercial manufacturing, if our product candidates are approved;
- receipt of marketing approvals from applicable regulatory authorities;
- commercializing products, if and when approved, whether alone or in collaboration with others;
- the cost to develop companion diagnostics and/or complementary diagnostics as needed for each of our development programs;
- the costs associated with the development of any additional product candidates we acquire through third-party collaborations or identify through our Translational Science Platform;
- the terms and timing of any collaboration, license or other arrangement, including any milestone payments thereunder;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our products, if and when approved; and
- continued acceptable safety profiles of the products following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. We plan to increase our research and development expenses for the foreseeable future as we advance our product candidates through clinical trials and continue the enhancement of our Translational Science Platform and the progression of our pipeline.

Due to the inherently unpredictable nature of preclinical and clinical development, we do not allocate all of our internal research and development expenses on a program-by-program basis as they primarily relate to personnel and lab consumables costs that are deployed across multiple programs under development. Our research and development expenses also include external costs, which we do track on a program-by-program basis following the program’s nomination as a development candidate. We began incurring such external costs for vopratelimab in 2015, pimivalimab in 2016, JTX-8064 in 2017, GS-1811 in 2019 and JTX-1484 in 2021.

Included below are external research and development and external clinical and regulatory costs for JTX-8064, vopratelimab (which includes our SELECT trial), pimivalimab, GS-1811, JTX-1484 and our pre-development candidates:

<i>(in thousands)</i>	Year Ended December 31,	
	2021	2020
Vopratelimab	\$ 18,942	\$ 24,117
JTX-8064	18,903	1,674
Pimivalimab	2,603	2,866
GS-1811	2,405	7,007
JTX-1484	170	—
Pre-development candidates	1,683	1,328
Total external research and development and clinical and regulatory costs	<u>\$ 44,706</u>	<u>\$ 36,992</u>

Research and development activities account for a significant portion of our operating expenses. As we continue to implement our business strategy, we expect our research and development expenses to increase over the next several years. We expect that these expenses will increase as we:

- continue our clinical development of JTX-8064, including our INNATE trial as a monotherapy and in combination with pimivalimab;
- continue our clinical development of vopratelimab, including our SELECT trial of vopratelimab and pimivalimab;
- continue advancing programs through IND-enabling activities;
- continue to identify and develop potential predictive biomarkers and companion diagnostics and/or complementary diagnostics for our product candidates; and
- continue to develop and enhance our Translational Science Platform and advance our pipeline of immunotherapy programs and our early research activities into IND-enabling activities.

Product candidates in later stages of clinical development generally incur higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

General and Administrative Expenses

General and administrative expenses consist of salaries and personnel-related costs, including non-cash stock-based compensation expense, for our personnel in executive, business development, legal, finance and accounting, human resources and other administrative functions, consulting fees, facility costs not otherwise included in research and development expenses, fees paid for accounting and tax services, insurance expenses and legal costs. Legal costs include general corporate legal fees, patent legal fees and related costs. We anticipate that our general and administrative expenses will increase in the future to support our continued operations.

Other Income, Net

Other income, net, consists primarily of interest and investment income on our cash, cash equivalents and investments.

Critical Accounting Policies and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. We base our estimates on historical experience, known facts and trends, and other market specific or relevant assumptions we believe to be reasonable under the circumstances. On an ongoing basis, we evaluate our estimates in light of changes in circumstance, facts or experience. Actual results may differ from these estimates under different assumptions or conditions.

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

Revenue Recognition

We recognize revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. In applying ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the promises and performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy the performance obligations. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract, determine those that are performance obligations and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The terms of our license agreements include upfront and license fees, milestones and other contingent payments for the achievement of defined certain clinical, regulatory and sales-based milestone events, as well as royalties on sales of commercialized products. Arrangements that include upfront payments may require deferral of revenue recognition to a future period until obligations under such arrangements are fulfilled. The event-based milestone payments represent variable consideration, and we use the “most likely amount” method to estimate this variable consideration. Given the high degree of uncertainty around the occurrence of these events, we determined the milestone and other contingent amounts to be fully constrained until the uncertainty associated with these payments is resolved. Revenue will be recognized from sales-based royalty payments when or as the sales occur. We will re-evaluate the transaction price in each reporting period as uncertain events are resolved and other changes in circumstances occur.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. 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. This process involves reviewing open contracts and purchase orders, communicating with internal personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We periodically confirm the accuracy of our estimates with our service providers and make adjustments if necessary. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. The financial terms of agreements with these service providers are subject to negotiation, vary from contract-to-contract and may result in uneven payment flows. In circumstances where amounts have been paid in excess of costs incurred, we record a prepaid expense.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-based Compensation

We account for stock-based payments in accordance with ASC Topic 718, *Compensation—Stock Compensation*. This guidance requires all stock-based payments to employees, including grants of employee stock options, restricted stock awards and restricted stock units, to be recognized as expense in the consolidated statements of operations and comprehensive income (loss) based on their grant date fair values. For stock options granted to employees and to members of our board of directors for their services on the board of directors, we estimate the grant date fair value of each stock option using the Black-Scholes option-pricing model. For restricted stock awards and restricted stock units granted to employees, we estimate the grant date fair value of each award using intrinsic value, which is based on the value of the underlying common stock less any purchase price. For stock-based payments subject to service-based vesting conditions, we recognize stock-based compensation expense equal to the grant date fair value of stock-based payment on a straight-line basis over the requisite service period.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the calculation of expected term of the stock-based payment, (ii) the risk-free interest rate, (iii) the expected stock price volatility and (iv) the expected dividend yield. We use the simplified method as prescribed by SEC Staff Accounting Bulletin No. 107 to calculate the expected term for stock options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. We determine the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. Because there had been no public market for our common stock prior to our IPO, there is a lack of historical and implied volatility data. Accordingly, we base our estimates of expected volatility on a combination of our own historical volatility and historical volatility of a group of publicly-traded companies with characteristics similar to ours, including stage of product development and therapeutic focus within the life sciences industry. Historical volatility is calculated over a period of time commensurate with the expected term of the stock-based payment. We use an assumed dividend yield of zero as we have never paid dividends on our common stock, nor do we expect to pay dividends on our common stock in the foreseeable future.

We account for forfeitures of all stock-based payments when such forfeitures occur.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, which provides for deferred taxes using an asset and liability approach. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

We account for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors, including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

<i>(in thousands)</i>	Year Ended December 31,		\$ Change
	2021	2020	
Revenue:			
License and collaboration revenue—related party	\$ 26,907	\$ 62,339	\$ (35,432)
Operating expenses:			
Research and development	88,979	78,690	10,289
General and administrative	28,984	28,766	218
Total operating expenses	117,963	107,456	10,507
Operating loss	(91,056)	(45,117)	(45,939)
Other income, net	199	1,289	(1,090)
Loss before provision for income taxes	(90,857)	(43,828)	(47,029)
Provision for income taxes	15	14	1
Net loss	<u>\$ (90,872)</u>	<u>\$ (43,842)</u>	<u>\$ (47,030)</u>

License and Collaboration Revenue

For the year ended December 31, 2021, we recognized \$26.9 million of license and collaboration revenue under the Gilead License Agreement related to the achievement of a \$25.0 million clinical development and regulatory milestone for FDA clearance of the IND for GS-1811 and \$1.9 million related to the completion of research and transition services. For the year ended December 31, 2020, we recognized \$62.3 million of license and collaboration revenue under the Gilead License Agreement for the GS-1811 license and performance of research and transition services.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2021 and 2020:

<i>(in thousands)</i>	Year Ended December 31,		\$ Change
	2021	2020	
Employee compensation	\$ 30,780	\$ 27,880	\$ 2,900
External clinical and regulatory	27,935	25,340	2,595
External research and development	16,771	11,652	5,119
Lab consumables	6,151	6,042	109
Facility costs	5,329	5,522	(193)
Other research	2,013	2,254	(241)
Total research and development expenses	<u>\$ 88,979</u>	<u>\$ 78,690</u>	<u>\$ 10,289</u>

Research and development expenses increased by \$10.3 million from \$78.7 million for the year ended December 31, 2020 to \$89.0 million for the year ended December 31, 2021. The increase in research and development expenses was primarily attributable to:

- \$2.9 million of increased employee compensation costs primarily attributable to increased payroll and stock-based compensation;
- \$2.6 million of increased external clinical and regulatory costs primarily attributable to increased costs for our INNATE and SELECT clinical trials, partially offset by decreased costs for our Phase 2 EMERGE trial; and
- \$5.1 million of increased external research and development costs associated with manufacturing activities for our development programs, partially offset by reduced IND-enabling activities during the year ended December 31, 2021.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2021 and 2020:

<i>(in thousands)</i>	Year Ended December 31,		\$ Change
	2021	2020	
Employee compensation	\$ 15,123	\$ 15,137	\$ (14)
Professional services	4,895	4,927	(32)
Facility costs	4,133	4,332	(199)
Other	4,833	4,370	463
Total general and administrative expenses	<u>\$ 28,984</u>	<u>\$ 28,766</u>	<u>\$ 218</u>

General and administrative expenses increased by \$0.2 million from \$28.8 million for the year ended December 31, 2020 to \$29.0 million for the year ended December 31, 2021. The increase in general and administrative expenses was primarily attributable to increased other administrative costs for the year ended December 31, 2021.

Other Income, net

Other income, net, decreased by \$1.1 million from \$1.3 million for the year ended December 31, 2020 to \$0.2 million for the year ended December 31, 2021. The decrease in other income, net is attributable to decreased rates of return on our investments.

Liquidity and Capital Resources

Sources of Liquidity

We have funded our operations primarily through proceeds received from public offerings and private placements of our stock totaling \$389.5 million and payments from license and collaboration agreements totaling \$385.0 million. As of December 31, 2021, we had cash, cash equivalents and investments of \$220.2 million.

On November 4, 2021, we entered into a new Sales Agreement (the “2021 Sales Agreement”) with Cowen and Company, LLC, or Cowen, pursuant to which we may offer and sell shares of our common stock with an aggregate offering price of up to \$75.0 million under an ATM offering program (the “2021 ATM Offering”). The 2021 Sales Agreement provides that Cowen will be entitled to a sales commission equal to 3.0% of the gross sales price per share of all shares sold under the 2021 ATM Offering. No sales were made under the 2021 ATM Offering during the year ended December 31, 2021.

During the first quarter of 2021, we completed a follow-on public offering of its common stock, selling an aggregate of 5,750,000 shares of common stock at a public offering price of \$11.25 per share for net proceeds of \$60.6 million.

On December 17, 2019, we entered into a Sales Agreement with Cowen, pursuant to which we could offer and sell shares of our common stock with an aggregate offering price of up to \$50.0 million under an “at the market” offering program (the “2019 ATM Offering”). During the first quarter of 2021, the Company sold an aggregate of 3,156,200 shares at an average price of \$9.87 per share for net proceeds of \$30.2 million, which completed the sale of all available amounts under the 2019 ATM Offering.

Funding Requirements

Our plan of operation is to continue implementing our business strategy, the research and development of our current product candidates, our preclinical development activities, the expansion of our research pipeline and the enhancement of our internal research and development capabilities. Due to the inherently unpredictable nature of preclinical and clinical development and given the early stage of our programs and 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 products, if and when approved. 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 products, if and when approved, 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 since inception. We have incurred an accumulated deficit of \$241.9 million through December 31, 2021. We expect to incur substantial additional losses in the future as we expand our research and development activities and continue to advance our programs. Based on our research and development plans, we expect that our existing cash, cash equivalents and investments of \$220.2 million will enable us to fund our operating expenses and capital expenditure requirements through the third quarter of 2023 and we will require additional funding to continue our operations beyond the third quarter of 2023. However, we have based this estimate on assumptions that may prove to be incorrect, and we could exhaust 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, including the impacts of the COVID-19 pandemic on the timing and progress of our ongoing and planned clinical trials;
- the cost to access, acquire or develop therapies to study in combination with our immunotherapies;
- successful enrollment in and completion of clinical trials;
- the cost to develop companion diagnostics and/or complementary diagnostics as needed for each of our development programs;
- our ability to establish agreements with third-party manufacturers for clinical supply for our clinical trials and, if any of our product candidates are approved, commercial manufacturing;
- the costs associated with the development of any additional product candidates we acquire through acquisition or third-party collaborations or identify through our Translational Science Platform;
- our ability to maintain our current research and development programs and enhancement of our Translational Science Platform;
- addition and retention of key research and development personnel;
- our efforts to enhance operational, financial and information management systems, and hire additional personnel, including personnel to support development of our product candidates;
- the legal patent costs involved in prosecuting patent applications and enforcing patent claims and other intellectual property claims;
- the costs and ongoing investments to in-license or acquire additional technologies, including the in-license of intellectual property related to our potential product candidates; and
- the terms and timing of any other collaboration, license or other arrangement, including the terms and timing of any option and milestone payments thereunder.

A change in the outcome of any of these or other variables with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

In addition to the variables described above, if and when any of our product candidates successfully complete development, we expect to incur substantial additional costs associated with regulatory filings, marketing approval, post-marketing requirements, maintaining our intellectual property rights, and regulatory protection, in addition to other costs. We cannot reasonably estimate these costs at this time.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity or debt financings, collaborations, licensing arrangements and strategic alliances. We currently do not have a credit facility or committed sources of capital. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. We may require additional capital beyond our currently anticipated amounts. Additional capital may not be available on reasonable terms, or at all. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2021 and 2020:

<i>(in thousands)</i>	Year Ended December 31,	
	2021	2020
Net cash (used in) provided by:		
Operating activities	\$ (83,494)	\$ (27,788)
Investing activities	(60,514)	51,298
Financing activities	92,044	70,742
Net increase in cash, cash equivalents and restricted cash	<u>\$ (51,964)</u>	<u>\$ 94,252</u>

Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2021 was \$83.5 million, compared to \$27.8 million for the year ended December 31, 2020. Cash used in operating activities increased by \$55.7 million due to increased net loss during the year ended December 31, 2021 driven by increased operating expenses and reduced revenue recognition under the Gilead License Agreement as compared to the year ended December 31, 2020.

Cash (Used in) Provided by Investing Activities

Net cash used in investing activities for the year ended December 31, 2021 was \$60.5 million, compared to net cash provided by investing activities of \$51.3 million for the year ended December 31, 2020. Cash used in investing activities increased by \$111.8 million due to increased purchases of investments as a direct result of our financing activities during the first quarter of 2021.

Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was \$92.0 million, compared to \$70.7 million for the year ended December 31, 2020. Cash provided by financing activities increased by \$21.3 million due to proceeds received from our follow-on public offering and ATM Offering completed during the first quarter of 2021.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934, as amended, and are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Part IV, Item 15.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by the company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Securities and Exchange Commission’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2021, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management’s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as a process designed by, or under the supervision of, a company’s principal executive officer and principal financial officer, or persons performing similar functions, and effected by a company’s board of directors, management, and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

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

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

Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2021.

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15(d)-15(f) under the Exchange Act) that occurred during the fourth quarter of the year ended December 31, 2021 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****Board of Directors*****Board Composition and Structure***

The Board of Directors is currently comprised of nine members. Below is a list of the names, ages as of February 28, 2022, and classification of the individuals who currently serve as our directors.

Name	Age	Position
Luis A. Diaz, Jr., M.D.	51	Director (Class II)
Barbara Duncan	57	Director (Class II)
J. Duncan Higgons	67	Director (Class I)
Robert Iannone, M.D., M.S.C.E.	54	Director (Class I)
Robert Kamen, Ph.D.	77	Director (Class II)
Perry Karsen	66	Chairman of the Board of Directors (Class III)
Richard Murray, Ph.D.	63	Director (Class III); Chief Executive Officer and President
Jigar Raythatha	45	Director (Class III)
Luisa Salter-Cid, Ph.D.	57	Director (Class I)

Director Biographies

Luis Diaz, Jr., M.D.—Dr. Diaz has served as the head of the solid tumor oncology division and a faculty member at the Memorial Sloan Kettering Cancer Center since December 2016, and was appointed to the National Cancer Advisory Board in September 2021. From 2004 to December 2016, Dr. Diaz was a faculty member and physician at Johns Hopkins University School of Medicine. He is also a founder and board member, and from 2010 to April 2016 served as president, chief executive officer and chief medical officer, of Personal Genome Diagnostics Inc., a private cancer genome analysis company. He received his M.D. from the University of Michigan, where he also received his B.A. in Microbiology. We believe Dr. Diaz is qualified to serve on our board of directors due to his background as a physician focused on oncology and his experience as a faculty member at a major hospital and medical center.

Barbara Duncan—Ms. Duncan served as the chief financial officer of Intercept Pharmaceuticals Inc., a public biopharmaceutical company, from May 2009 to June 2016 and as treasurer from 2010 to June 2016. She has served on the board of directors of Adaptimmune Therapeutics plc since June 2016, Atea Pharmaceuticals, Inc. since October 2020, Fusion Pharmaceuticals Inc. since October 2020 and Ovid Therapeutics, Inc. since June 2017, each of which is a public therapeutics company. She previously served on the board of public companies ObsEva SA from December 2016 to May 2021, Immunomedics, Inc. from March 2019 to October 2020, Aevi Genomic Medicine, Inc. (formerly Medgenics, Inc.) from June 2015 to February 2020 and Innoviva, Inc. from September 2016 to April 2018. Ms. Duncan holds an M.B.A. from the Wharton School of Business and a B.S. from Louisiana State University. We believe Ms. Duncan is qualified to serve on our board of directors because of her experience in the biopharmaceutical industry, her experience in the financial sector and membership on boards of directors of other public and private companies.

J. Duncan Higgons—Mr. Higgons served as chief operating officer of Agios Therapeutics, Inc., a public biopharmaceutical company, from 2009 to January 2016. Mr. Higgons serves on the board of directors of Rheos Medicines, Inc. and PsiOxus Therapeutics Ltd., both of which are private life science companies. He holds a B.Sc. in Mathematics from King's College University of London and a M.Sc. in Economics from London Business School. We believe that Mr. Higgons is qualified to serve on our board of directors due to his leadership and management experience.

Robert Iannone, M.D., M.S.C.E.—Dr. Iannone has served as the Executive Vice President, Research and Development of Jazz Pharmaceuticals plc, a public biopharmaceutical company, since May 2019. Previously, he served as the Chief Medical Officer and Head of Research and Development at Immunomedics, Inc., a public biopharmaceutical company, from April 2018 until May 2019. Dr. Iannone also held leadership roles at AstraZeneca, a global biopharmaceutical company, where, from July 2014 until April 2018, he was employed in the roles of Senior Vice President and Head of Immuno-oncology, Global Medicines Development. Since May 2021, Dr. Iannone has served as a member of the board of directors of iTeos Therapeutics, Inc. Dr. Iannone received a B.S. from The Catholic University of America, an M.D. from the Yale School of Medicine and an M.S.C.E. from the University of Pennsylvania Perelman School of Medicine. We believe Dr. Iannone is qualified to serve on our board of directors due to his background as a physician focused on oncology and his leadership experience in the life sciences industry.

Robert Kamen, Ph.D.—Dr. Kamen has been a venture partner at Third Rock Ventures, LLC, or TRV, since December 2017, and he previously served as an entrepreneur-in-residence at TRV from 2010 through 2017. Dr. Kamen serves on the boards of directors of EpimAb Biotherapeutics, Inc., a clinical-stage biotechnology company specializing in bispecific antibody development, and Harbour BioMed, a global clinical-stage biopharmaceutical company. He served on the board of directors of Neon Therapeutics, Inc., an immuno-oncology company, from 2015 through May 2020. Dr. Kamen holds a Ph.D. in biochemistry and molecular biology from Harvard University and a B.S. in biophysics from Amherst College. We believe that Dr. Kamen is qualified to serve on our board of directors because of his experience in the venture capital and life sciences industries, membership on various other boards of directors, and his leadership and management experience.

Perry Karsen—Mr. Karsen has served as the chairman of our board of directors since April 2016. Mr. Karsen retired from Celgene Corporation at the end of 2015 and currently is a Senior Advisor at Samsara BioCapital as well as the Executive Chair of Autobahn Labs. He serves as the Chair of the Board of Directors of Nitrase Therapeutics (formerly Nitrome Biosciences), and a member of the Boards of Directors for ESCAPE Bio, as Chair of the Board of Directors of Graphite Bio and on the Board of the Gladstone Foundation. Previously, Mr. Karsen served as a director of Jiya Acquisition Corp., a public blank check special purpose acquisition company affiliated with Samsara BioCapital, from November 2020 to September 2021, as well as on the boards of directors of Intellia Therapeutics, Inc. from April 2016 to December 2020, Voyager Therapeutics, Inc. from July 2015 to August 2019, and OncoMed Pharmaceuticals, Inc. from January 2016 to April 2019, each of which is a public life sciences company. Mr. Karsen received a Masters of Management from Northwestern University's Kellogg Graduate School of Management, a Masters of Arts in Teaching of Biology from Duke University and a B.S. in Biological Sciences from the University of Illinois, Urbana-Champaign. We believe Mr. Karsen is qualified to serve on our board of directors because of his executive leadership experience and membership on boards of directors of other public companies.

Richard Murray, Ph.D.—Dr. Murray has served as our president, chief executive officer and a member of our board of directors since July 2014. Prior to joining Jounce, Dr. Murray served as senior vice president of biologics and vaccines research and development at Merck & Co., a global healthcare company, from 2009 to June 2014 where he was responsible for the advancement of biologics and vaccines, including Merck's cancer immunotherapy pipeline. Since June 2019, he has served as a director of Platelet Biogenesis, Inc., a private biotechnology company. Dr. Murray holds a Ph.D. in microbiology and immunology from the University of North Carolina at Chapel Hill and a B.S. in microbiology from the University of Massachusetts, Amherst. We believe that Dr. Murray is qualified to serve on our board of directors due to his operating and historical experience gained from serving as our president, chief executive officer and as a board member, combined with his experience in drug research and development.

Jigar Raythatha—Mr. Raythatha joined TRV as a venture partner in January 2022 and previously served as the president and chief executive officer and a member of the Board of Directors of Constellation Pharmaceuticals, Inc., a public pharmaceutical company, from March 2017 until its acquisition by MorphoSys AG in July 2021. Mr. Raythatha previously served as chief business officer of Jounce from December 2012 until February 2017. He earned an M.B.A. from Columbia University and a B.A. in biochemistry and economics from Rutgers University. We believe that Mr. Raythatha is qualified to serve on our board of directors because of his leadership experience in the life sciences industry.

Luisa Salter-Cid, Ph.D.—Dr. Salter-Cid has served as the Chief Scientific Officer of Pioneering Medicines, a division of Flagship Pioneering, since May 2021. Previously, Dr. Salter-Cid was the Chief Scientific Officer of Gossamer Bio, Inc., a public clinical-stage biopharmaceutical company, from August 2018 through April 2021, and worked at Bristol Myers Squibb in increasing positions of responsibility from 2005 to August 2018, most recently as Vice President and Head of Immunology, small molecule Immuno-Oncology and Genomics Discovery. Dr. Salter-Cid holds a B.S. in Biology from University of Lisbon and a Ph.D. in Immunology from the University of Miami School of Medicine. We believe that Dr. Salter-Cid is qualified to serve on our board of directors because of her leadership experience in the life sciences industry and experience in immuno-oncology.

Executive Officers

The following table sets forth our executive officers as of February 28, 2022.

Name	Age	Position
Richard Murray, Ph.D. ⁽¹⁾	63	President, Chief Executive Officer and Director
Kim C. Drapkin	54	Chief Financial Officer and Treasurer
Hugh M. Cole	56	Chief Business Officer and Head of Corporate Development
Elizabeth G. Trehu, M.D.	61	Chief Medical Officer

(1) Richard Murray, Ph.D. is also a member of the Board of Directors and his biographical information appears above.

Kim C. Drapkin—Ms. Drapkin has served as our chief financial officer since August 2015, and our treasurer since February 2013. From 2009 to August 2015, Ms. Drapkin was the owner of KCD Financial LLC, through which she served as our interim chief financial officer from 2012 to August 2015, and consulted for numerous biotechnology companies. Ms. Drapkin began her career at PricewaterhouseCoopers LLP, is a certified public accountant and holds a B.S. in accounting from Babson College.

Hugh M. Cole—Prior to joining Jounce in August 2017, Mr. Cole served as chief business officer for ARIAD Pharmaceuticals, Inc., an oncology company, from March 2014 to June 2017, where he led numerous business development transactions. Previously, Mr. Cole served as senior vice president, strategic planning and program management at Shire plc, a global biopharmaceutical company, from 2007 to March 2014. Mr. Cole earned his M.B.A. in health care management and finance at the Wharton School of Business and his A.B. in chemistry from Harvard University.

Elizabeth G. Trehu, M.D.—Dr. Trehu joined Jounce as our chief medical officer in November 2015. Prior to joining Jounce, Dr. Trehu served as the chief medical officer of Promedior, Inc., a biotechnology company, from 2012 to November 2015. Dr. Trehu holds an M.D. from the New York University School of Medicine and an A.B. in English from Princeton University.

Code of Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code is posted on the Corporate Governance section of our website, which is located at www.jouncetx.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K. We will provide any person, without charge, a copy of such Code of Business Conduct and Ethics upon written request, which may be mailed to 780 Memorial Drive, Cambridge, MA 02139, Attn: Corporate Secretary.

Additional information required by this Item 10 will be included in the sections captioned “Proposal 1 - Election of Three Class I Directors” and “Corporate Governance” in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, which information is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in the section captioned “Executive and Director Compensation” in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, which information is incorporated herein by reference.

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

The information required by this Item 12 will be included in the section captioned “Principal Stockholders” and “Equity Compensation Plan Information” in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, which information is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required by this Item 13 will be included in the sections captioned “Corporate Governance” and “Transactions with Related Persons” in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, which information is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in the section captioned “Ratification of the Selection of Independent Registered Public Accounting Firm” in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders, which information is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(1) Financial Statements

The following documents are attached hereto and are filed as part of this Annual Report on Form 10-K.

Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)	F-1
Consolidated Balance Sheets	F-2
Consolidated Statements of Operations and Comprehensive Loss	F-3
Consolidated Statements of Stockholders' Equity	F-4
Consolidated Statements of Cash Flows	F-5
Notes to Consolidated Financial Statements	F-6

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

The exhibits filed or furnished as part of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signatures, which Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Jounce Therapeutics, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts
March 2, 2022

Jounce Therapeutics, Inc.
Consolidated Balance Sheets
(amounts in thousands, except par value amounts)

	December 31,	
	2021	2020
Assets:		
Current assets:		
Cash and cash equivalents	\$ 95,529	\$ 147,493
Short-term investments	83,037	58,985
Prepaid expenses and other current assets	12,261	4,913
Total current assets	190,827	211,391
Property and equipment, net	4,882	7,336
Long-term investments	41,657	6,710
Operating lease right-of-use asset	11,877	14,856
Other non-current assets	3,453	3,943
Total assets	<u>\$ 252,696</u>	<u>\$ 244,236</u>
Liabilities and stockholders' equity:		
Current liabilities:		
Accounts payable	\$ 1,674	\$ 2,036
Accrued expenses	13,467	12,044
Deferred revenue, current—related party	—	1,931
Operating lease liability, current	3,695	3,271
Other current liabilities	62	42
Total current liabilities	18,898	19,324
Operating lease liability, net of current portion	9,993	13,618
Total liabilities	28,891	32,942
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, \$0.001 par value: 5,000 shares authorized at December 31, 2021 and 2020; no shares issued or outstanding at December 31, 2021 and 2020	—	—
Common stock, \$0.001 par value: 160,000 shares authorized at December 31, 2021 and 2020; 51,265 and 41,729 shares issued at December 31, 2021 and 2020, respectively; 51,265 and 41,729 shares outstanding at December 31, 2021 and 2020, respectively	51	42
Additional paid-in capital	465,865	362,270
Accumulated other comprehensive (loss) income	(238)	(17)
Accumulated deficit	(241,873)	(151,001)
Total stockholders' equity	223,805	211,294
Total liabilities and stockholders' equity	<u>\$ 252,696</u>	<u>\$ 244,236</u>

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

Jounce Therapeutics, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(amounts in thousands, except per share amounts)

	Year Ended December 31,	
	2021	2020
Revenue:		
License and collaboration revenue—related party	\$ 26,907	\$ 62,339
Operating expenses:		
Research and development	88,979	78,690
General and administrative	28,984	28,766
Total operating expenses	117,963	107,456
Operating loss	(91,056)	(45,117)
Other income, net	199	1,289
Loss before provision for income taxes	(90,857)	(43,828)
Provision for income taxes	15	14
Net loss	<u>\$ (90,872)</u>	<u>\$ (43,842)</u>
Net loss per share, basic and diluted	\$ (1.82)	\$ (1.24)
Weighted-average common shares outstanding, basic and diluted	49,931	35,426
Comprehensive loss:		
Net loss	\$ (90,872)	\$ (43,842)
Other comprehensive loss:		
Unrealized loss on available-for-sale securities	(221)	(71)
Comprehensive loss	<u>\$ (91,093)</u>	<u>\$ (43,913)</u>

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

Jounce Therapeutics, Inc.
Consolidated Statements Stockholders' Equity
(amounts in thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2019	33,738	\$ 34	\$ 281,664	\$ 54	\$ (107,159)	\$ 174,593
Issuance of common stock from at the market offering, net of issuance costs	2,074	2	14,511	—	—	14,513
Issuance of common stock under a stock purchase agreement	5,540	6	55,724	—	—	55,730
Exercise of stock options	128	—	600	—	—	600
Vesting of restricted stock awards and restricted stock units	249	—	—	—	—	—
Stock-based compensation expense	—	—	9,771	—	—	9,771
Other comprehensive loss	—	—	—	(71)	—	(71)
Net loss	—	—	—	—	(43,842)	(43,842)
Balance at December 31, 2020	<u>41,729</u>	<u>42</u>	<u>362,270</u>	<u>(17)</u>	<u>(151,001)</u>	<u>211,294</u>
Issuance of common stock from at the market offering, net of issuance costs	3,156	3	30,218	—	—	30,221
Issuance of common stock from secondary public offering, net of issuance costs	5,750	6	60,632	—	—	60,638
Exercise of stock options	403	—	1,268	—	—	1,268
Vesting of restricted stock awards and restricted stock units	227	—	—	—	—	—
Stock-based compensation expense	—	—	11,477	—	—	11,477
Other comprehensive loss	—	—	—	(221)	—	(221)
Net loss	—	—	—	—	(90,872)	(90,872)
Balance at December 31, 2021	<u>51,265</u>	<u>\$ 51</u>	<u>\$ 465,865</u>	<u>\$ (238)</u>	<u>\$ (241,873)</u>	<u>\$ 223,805</u>

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

Jounce Therapeutics, Inc.
Consolidated Statements of Cash Flows
(amounts in thousands)

	Year Ended December 31,	
	2021	2020
Operating activities:		
Net loss	\$ (90,872)	\$ (43,842)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	11,477	9,771
Depreciation expense	2,827	3,401
Net amortization of premiums and discounts on investments	921	47
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(7,331)	(236)
Other non-current assets	490	(1,469)
Accounts payable	(329)	(296)
Accrued expenses and other current liabilities	1,443	3,047
Deferred revenue—related party	(1,931)	1,931
Other liabilities	(189)	(142)
Net cash used in operating activities	<u>(83,494)</u>	<u>(27,788)</u>
Investing activities:		
Purchases of investments	(130,272)	(85,895)
Proceeds from maturities of investments	70,131	137,287
Purchases of property and equipment	(373)	(94)
Net cash (used in) provided by investing activities	<u>(60,514)</u>	<u>51,298</u>
Financing activities:		
Proceeds from at the market offering, net of issuance costs	90,826	14,412
Proceeds from issuance of common under a stock purchase agreement, at fair value	—	55,730
Proceeds from exercise of stock options	1,218	600
Net cash provided by financing activities	<u>92,044</u>	<u>70,742</u>
Net (decrease) increase in cash, cash equivalents and restricted cash	(51,964)	94,252
Cash, cash equivalents and restricted cash, beginning of period	148,763	54,511
Cash, cash equivalents and restricted cash, end of period	<u>\$ 96,799</u>	<u>\$ 148,763</u>
Non-cash investing and financing activities:		
Stock option exercise receivables in prepaid expenses and other current assets	\$ 50	\$ —
Issuance costs in accounts payable and accrued expenses	\$ —	\$ 33
Discount on common stock issued under a stock purchase agreement	\$ —	\$ (20,730)
Supplemental cash flow information:		
Cash paid for lease liabilities	\$ 4,896	\$ 4,024
Cash paid for income taxes	\$ 8	\$ 45

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

Jounce Therapeutics, Inc.
Notes to Consolidated Financial Statements

1. Nature of Business

Jounce Therapeutics, Inc. (the “Company”) is a clinical-stage immunotherapy company dedicated to transforming the treatment of cancer by developing therapies that enable the immune system to attack tumors and provide long-lasting benefits to patients. The Company is subject to a number of risks similar to those of other clinical-stage companies, including dependence on key individuals; the need to develop commercially viable products; competition from other companies, many of which are larger and better capitalized; and the need to obtain adequate additional financing to fund the development of its products.

As of December 31, 2021, the Company had cash, cash equivalents, and investments of \$220.2 million. The Company expects that its existing cash, cash equivalents and investments will enable it to fund its expected operating expenses and capital expenditure requirements for at least 12 months from March 2, 2022, the filing date of this Annual Report on Form 10-K. The Company expects to finance its future cash needs through a combination of equity or debt financings, collaborations, licensing arrangements and strategic alliances.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (the “SEC”) and generally accepted accounting principles in the United States of America (“GAAP”) as found in the Accounting Standards Codification (“ASC”) of the Financial Accounting Standards Board (“FASB”). These consolidated financial statements include the accounts of Jounce Therapeutics, Inc. and its wholly-owned subsidiary, Jounce Mass Securities, Inc. All intercompany transactions and balances have been eliminated in consolidation.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company and the Company’s chief operating decision maker, the Company’s chief executive officer, views the Company’s operations and manages its business as a single operating segment. The Company operates only in the United States.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company’s management evaluates its estimates which include, but are not limited to, estimates related to revenue recognized under the Gilead License Agreement (including estimates of standalone selling prices of each performance obligation and internal and external costs expected to be incurred to satisfy performance obligations), accrued expenses, stock-based compensation expense and income taxes. The Company bases its estimates on historical experience and other market specific or other relevant assumptions it believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Fair Value of Financial Instruments

ASC Topic 820, *Fair Value Measurement* (“ASC 820”) establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company’s own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company’s assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

- Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Cash Equivalents

Cash equivalents are highly-liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. These assets include investment in money market funds that invests in U.S. Treasury obligations.

Investments

Short-term investments consist of investments with maturities greater than ninety days and less than one year from the balance sheet date. Long-term investments consist of investments with maturities of greater than one year that are not expected to be used to fund current operations. The Company classifies all of its investments as available-for-sale securities. Accordingly, these investments are recorded at fair value. Realized gains and losses, amortization and accretion of discounts and premiums are included in "Other income, net". Unrealized gains and losses on available-for-sale securities are included in "Other comprehensive income" as a component of stockholders' equity until realized.

Property and Equipment

Property and equipment is recorded at cost and consists of laboratory equipment, furniture and office equipment, computer equipment, leasehold improvements. The Company capitalizes property and equipment that is acquired for research and development activities and that has alternate future use. Expenditures for maintenance and repairs are recorded to expense as incurred, whereas major betterments are capitalized as additions to property and equipment. Leasehold improvements are depreciated over the lesser of their useful life or the term of the lease. Depreciation is calculated over the estimated useful lives of the assets using the straight-line method.

Impairment of Long-lived Assets

The Company reviews its property and equipment whenever events or changes in circumstances indicate that the carrying value of certain assets might not be recoverable and recognizes an impairment loss when it is probable that an asset's realizable value is less than the carrying value.

Leases

The Company accounts for leases in accordance with ASC Topic 842, *Leases*. At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not recognize leases with terms of one year or less on the balance sheet. Options to renew a lease are not included in the Company's initial lease term assessment unless there is reasonable certainty that the Company will renew. The Company monitors its plans to renew its material leases on a quarterly basis.

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

The Company subsequently measures its lease liability at the present value of remaining lease payments, discounted using the IBR for the lease. The right-of-use asset is subsequently measured at the amount of the lease liability, adjusted for prepaid or accrued lease payments and the remaining balance of lease incentives received. The Company recognizes operating lease expense on a straight-line basis over the lease term.

Revenue Recognition

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers* (“ASC 606”). Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. In applying ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the promises and performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies the performance obligations. The Company only applies the five-step model to contracts when it is probable that it will collect the consideration to which it is entitled in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. As part of the assessment, the Company must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. The Company uses key assumptions to determine the standalone selling price, which may include reimbursement rates for personnel costs, development timelines and probabilities of regulatory success. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of promised goods or services to the customer will be one year or less.

Arrangements that include upfront payments may require deferral of revenue recognition to a future period until obligations under these arrangements are fulfilled. The event-based milestone payments represent variable consideration, and the Company uses the “most likely amount” method to estimate this variable consideration. Given the high degree of uncertainty around the occurrence of these events, the Company determined the milestone and other contingent amounts to be fully constrained until the uncertainty associated with these payments is resolved. Revenue will be recognized from sales-based royalty payments when or as the sales occur. The Company will re-evaluate the transaction price in each reporting period as uncertain events are resolved and other changes in circumstances occur. See Note 3, “License and Collaboration Revenue”, for further information on the Company’s application of ASC 606.

Research and Development Expenses

Expenditures relating to research and development are expensed as incurred. Research and development expenses include external expenses incurred under arrangements with third parties, academic and non-profit institutions and consultants; salaries and personnel-related costs, including non-cash stock-based compensation expense; license fees to acquire in-process technology and other expenses, which include direct and allocated expenses for laboratory, facilities and other costs. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

As part of the process of preparing the consolidated financial statements, the Company is required to estimate its accrued research and development expenses as of each balance sheet date. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. This process involves reviewing open contracts and purchase orders, communicating with internal personnel to identify services that have been performed on the Company’s behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual cost. The Company periodically confirms the accuracy of its estimates with its service providers and makes adjustments if necessary. The majority of the Company’s service providers invoice monthly in arrears for services performed or when contractual milestones are met. The financial terms of agreements with these service providers are subject to negotiation, vary from contract-to-contract and may result in uneven payment flows. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

Intellectual Property Expenses

The Company expenses costs associated with intellectual property-related matters as incurred and classifies such costs as general and administrative expenses within the consolidated statements of operations and comprehensive (loss) income.

Stock-based Compensation

The Company accounts for stock-based payments in accordance with ASC Topic 718, *Compensation—Stock Compensation*. This guidance requires all stock-based payments to employees, including grants of employee stock options and restricted stock units (“RSUs”), to be recognized as expense in the consolidated statements of operations and comprehensive loss based on their grant date fair values. For stock options granted to employees and to members of the Company’s board of directors for their services on the board of directors, the Company estimates the grant date fair value of each stock option using the Black-Scholes option-pricing model. For RSUs granted to employees, the Company estimates the grant date fair value of each award using intrinsic value, which is based on the value of the underlying common stock less any purchase price. For stock-based payments subject to service-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock-based payment on a straight-line basis over the requisite service period.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the calculation of expected term of the stock-based payment, (ii) the risk-free interest rate, (iii) the expected stock price volatility and (iv) the expected dividend yield. The Company uses the simplified method as proscribed by SEC Staff Accounting Bulletin No. 107 to calculate the expected term for stock options granted to employees as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The Company determines the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. Because there had been no public market for the Company’s common stock prior to the Company’s initial public offering (“IPO”), there is a lack of Company-specific historical and implied volatility data. Accordingly, the Company bases its estimates of expected volatility based on a combination of the Company’s own historical volatility and historical volatility of a group of publicly-traded companies with similar characteristics to itself, including stage of product development and therapeutic focus within the life sciences industry. Historical volatility is calculated over a period of time commensurate with the expected term of the stock-based payment. The Company uses an assumed dividend yield of zero as the Company has never paid dividends on its common stock, nor does it expect to pay dividends on its common stock in the foreseeable future. The Company accounts for forfeitures of all stock-based payments when such forfeitures occur.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors, including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position.

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive loss. Other comprehensive loss for all periods presented consists of unrealized losses and gains on available-for-sale securities.

Net Loss per Share

Basic net loss per share is calculated based upon the weighted-average number of common shares outstanding during the period, excluding outstanding stock options and RSUs that have been issued but are not yet vested. Diluted net loss per share is calculated based upon the weighted-average number of common shares outstanding during the period plus the dilutive impact of weighted-average common equivalent shares outstanding during the period. The potentially dilutive shares of common stock resulting from the assumed exercise of outstanding stock options and the assumed vesting of RSUs are determined under the treasury stock method.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash, cash equivalents and investments. The Company maintains its cash and cash equivalent balances with high-quality financial institutions and, consequently, the Company believes that such funds are subject to minimal credit risk. The Company's cash equivalents and investments are comprised of money market funds that are invested in U.S. Treasury obligations, corporate debt securities, U.S. Treasury obligations and government agency securities. Credit risk in these securities is reduced as a result of the Company's investment policy to limit the amount invested in any single issuer and to only invest in securities of a high credit quality.

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts or other foreign hedging arrangements.

Recent Accounting Pronouncements, Not Yet Adopted

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. This standard requires that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and it establishes additional disclosure requirements related to credit risks. For available-for-sale debt securities with expected credit losses, this standard now requires allowances to be recorded instead of reducing the amortized cost of the investment. This guidance was originally effective for annual reporting periods beginning after December 15, 2019, including interim periods within those annual reporting periods, and early adoption was permitted. In November 2019, the FASB subsequently issued ASU 2019-10, *Financial Instruments—Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842): Effective Dates*, whereby the effective date of this standard for smaller reporting companies was deferred to annual reporting periods beginning after December 15, 2022, including interim periods within those annual reporting periods, and early adoption is still permitted. Accordingly, the Company will now adopt this standard effective January 1, 2023, and it is currently evaluating the potential impact that ASU 2016-13 may have on the consolidated financial statements.

3. License and Collaboration Revenue

Gilead License Agreement

On August 31, 2020, the Company and Gilead entered into an exclusive license agreement (the "Gilead License Agreement") to license the Company's GS-1811, formerly JTX-1811, program to Gilead. Concurrently with the license agreement, the Company and Gilead entered into a stock purchase agreement (the "Stock Purchase Agreement") and a registration rights agreement (the "Registration Rights Agreement", and together with the Gilead License Agreement and the Stock Purchase Agreement, the "Transaction Agreements"). The transactions with Gilead were subject to review under the Hart-Scott Rodino Antitrust Improvements Act of 1976 and other customary closing conditions, and became effective on October 16, 2020, the closing date of the agreement. Pursuant to the Gilead License Agreement, the Company granted to Gilead a worldwide and exclusive license to develop, manufacture and commercialize GS-1811 and certain derivatives thereof (the "Licensed Products"). Gilead paid the Company a one-time, non-refundable upfront payment of \$85.0 million in October 2020. The Company continued to develop GS-1811 during the initial development term, which included conducting activities defined within the agreement to advance GS-1811 through the clearance of an investigational new drug application ("IND"), which occurred in June 2021, after which the program transitioned to Gilead.

Milestone and Royalties

The Company is entitled to receive payments from Gilead upon the achievement of specified clinical, regulatory and sales milestones, including potential clinical development and regulatory milestone payments up to an aggregate total of \$510.0 million and potential sales milestone payments up to an aggregate total of \$175.0 million.

The Company is also eligible to receive tiered royalty payments based on a percentage of annual worldwide net sales ranging from the high-single digits to mid-teens, based on future annual net sales of the Licensed Products, on a Licensed Product-by-Licensed Product and country-by-country basis.

In June 2021, the Company received clearance of the IND for GS-1811 from the U.S. Food and Drug Administration (“FDA”) and achieved a \$25.0 million milestone under the Gilead License Agreement.

Termination

Gilead may terminate the Gilead License Agreement for convenience, in its sole discretion, in its entirety or on a Licensed Product-by-Licensed Product or region-by-region basis, at any time with prior written notice to the Company. Unless terminated earlier in accordance with its terms, the Gilead License Agreement provides that it will expire (i) on an Licensed Product-by-Licensed Product and country-by-country basis on the date of the expiration of the royalty term with respect to such Licensed Product in such country and (ii) in its entirety upon the expiration of all applicable royalty terms with respect to the Licensed Products in all countries, following which the applicable licenses under the Gilead License Agreement will become fully paid-up, perpetual, irrevocable and royalty-free.

Accounting Analysis

Identification of the Contract(s)

The Company assessed the Gilead License Agreement and concluded that it represents a contract with a customer within the scope of ASC 606. In addition, the Company determined that the Gilead License Agreement and Stock Purchase Agreement should be evaluated as a combined contract in accordance with ASC 606 given that the agreements were executed contemporaneously, negotiated as a package and have the same commercial objective to provide funding to further the Company’s research and development activities.

Identification of Promises and Performance Obligations

The Company determined that the Gilead License Agreement contains the following promises: (i) delivery of a worldwide and exclusive license to develop, manufacture and commercialize GS-1811 (the “GS-1811 License”), (ii) provision of certain research transition activities, specifically outlined within the Gilead License Agreement, related to the advancement of GS-1811 through the clearance of an IND application and transition of the GS-1811 program to Gilead (the “Research and Transition Services”), (iii) appointment of an individual to act as an alliance manager and primary point of contact for Gilead, (iv) appointment of individuals to participate on the Joint Steering Committee (“JSC”), and (v) optional assistance by Jounce after completion of Research and Transition Services upon the request of Gilead.

The Company assessed the above promises and concluded that each of the GS-1811 License and Research and Transition Services is capable of being distinct and distinct within the context of the Gilead License Agreement. Based upon this evaluation, the Company concluded that its promise to deliver the GS-1811 License and promise to perform Research and Transition Services represent separate performance obligations in the Gilead License Agreement.

The Company determined that the appointment of an individual to act as an alliance manager and primary point of contact for Gilead, participation in alliance management meetings and the appointment of individuals to participate on the JSC do not constitute the transfer of a good or service to Gilead and as such, do not represent performance obligations under the contract.

Finally, the Company assessed Gilead’s ability to request optional assistance by Jounce after completion of Research and Transition Services and determined that it was both quantitatively and qualitatively immaterial in the context of the Gilead License Agreement. Accordingly, the Company did not assess the optional assistance as a performance obligation.

Determination of Transaction Price

As noted above, the Company received a non-refundable upfront payment of \$85.0 million upon the execution of the Gilead License Agreement. This upfront payment represents an element of fixed consideration under the Gilead License Agreement.

The Company also evaluated as possible variable consideration the milestones and royalties discussed above. With respect to clinical development and regulatory milestones, based upon the high degree of uncertainty and risk associated with these potential payments, the Company concluded that all such amounts should be fully constrained and are not included in the initial transaction price. As part of the evaluation of the constraint the Company considered certain factors, including that receipt of such milestones is outside the control of the Company and the probability of success criteria is estimated. Each of these variable consideration items was evaluated under the most-likely amount method. As for royalties and sales milestones, the Company determined that the royalties and milestones relate solely to the GS-1811 License, which is a license of intellectual property (“IP”). Accordingly, the Company did not include any potential royalty or sales milestone amounts in the initial transaction price, and the Company will not recognize revenue related to these royalties and sales milestones until the associated sales occur and relevant thresholds are met. The Company will re-evaluate the transaction price in each reporting period as uncertain events are resolved or as other changes in circumstances occur, and if necessary, will adjust its estimate of the transaction price to include milestones as they become probable of occurrence.

The Company assessed proceeds of \$35.0 million received under the Stock Purchase Agreement and determined that the fair value of the equity component was \$55.7 million based on the closing price of \$10.06 per share on October 16, 2020. Pursuant to the agreement, the Company sold 5,539,727 shares of common stock for aggregate cash consideration of \$35.0 million, or \$6.32 per share, which is equal to the daily volume weighted average per share intraday price of the Common Stock on Nasdaq over the 30-trading day period ending on and including August 28, 2020 plus a 30% premium. As a result, the Company determined that the gross proceeds of \$35.0 million received under the Stock Purchase Agreement included a discount to the fair value of the Company’s stock as of October 16, 2020 equal to \$20.7 million. In accordance with ASC 606, the discount amount will be included in the transaction price for revenue recognition, resulting in an initial transaction price of \$64.3 million.

Allocation of Transaction Price to Performance Obligations

The Company allocated the transaction price to each performance obligation on a relative estimated standalone selling price basis. The Company developed the estimated standalone selling price for the GS-1811 License based on the present value of expected future cash flows associated with the license and related clinical development and regulatory milestones. In developing such estimate, the Company applied judgement in determining the timing needed to develop the Licensed Product, the probability of success, and the discount rate. The Company developed the estimated standalone selling price for the Research and Transition Services obligation based on the nature of the services to be performed and the Company’s best estimate of the length of time required to perform the services necessary to achieve clearance of an IND application for the GS-1811 program.

Based on the above considerations, \$60.8 million of the initial transaction price was allocated to the GS-1811 License performance obligation and \$3.5 million was allocated to the Research and Transition Services performance obligation.

Recognition of Revenue

The Company determined that the GS-1811 License is a functional license as the underlying IP has significant standalone functionality. In addition, the Company determined that the GS-1811 License represents a right to use certain of the Company’s IP as it exists at a point in time. Finally, the Company determined that October 16, 2020 represents (i) the date at which the Company made available the IP to Gilead and (ii) the beginning of the period during which Gilead is able to use and benefit from its right to use the IP. Based upon these considerations, the Company recognized the entirety of the initial transaction price allocated to the GS-1811 License performance obligation during the year ended December 31, 2020.

Further, the Company determined the input method under ASC 606 is the most appropriate method of revenue recognition for the Research and Transition Services performance obligation. The method of measuring progress towards delivery of the services incorporated actual internal and external costs incurred, relative to total internal and external costs expected to be incurred to satisfy the performance obligation. The period over which total costs were estimated reflected the Company’s best estimate of the period over which it would perform the research and transition services to achieve clearance of an IND application of the GS-1811 program and transition the program to Gilead.

During the year ended December 31, 2021, the Company recognized \$26.9 million of license and collaboration revenue under the Gilead License Agreement, \$25.0 million of which related to the achievement of a clinical development and regulatory milestone for FDA clearance of the IND for GS-1811 and \$1.9 million of which related to the completion of research and transition services. During the year ended December 31, 2020, the Company recognized \$62.3 million of license and collaboration revenue, \$60.8 million of which related to the GS-1811 License performance obligation and \$1.6 million related to the performance of research and transition services.

The following table presents changes in the Company’s contract liabilities related to the Gilead License Agreement during the year ended December 31, 2021 (in thousands):

	January 1, 2021	Additions	Reductions	December 31, 2021
Contract liabilities:				
Deferred revenue — related party	\$ 1,931	\$ —	\$ (1,931)	\$ —
Total	\$ 1,931	\$ —	\$ (1,931)	\$ —

The reductions to deferred revenue - related party during the year ended December 31, 2021 were comprised of revenue recognized for research and transition services performed during the period.

4. Fair Value Measurements

The Company measures the fair value of money market funds, U.S. Treasuries and government agency securities based on quoted prices in active markets for identical securities. Investments also include corporate debt securities which are valued either based on recent trades of securities in inactive markets or based on quoted market prices of similar instruments and other significant inputs derived from or corroborated by observable market data.

The carrying amounts reflected in the consolidated balance sheets for cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values, due to their short-term nature.

Assets measured at fair value on a recurring basis as of December 31, 2021 were as follows (in thousands):

	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds, included in cash equivalents	\$ 95,529	\$ 95,529	\$ —	\$ —
Investments:				
Corporate debt securities	86,470	—	86,470	—
U.S. Treasuries	30,271	30,271	—	—
Government agency securities	7,953	—	7,953	—
Totals	\$ 220,223	\$ 125,800	\$ 94,423	\$ —

Assets measured at fair value on a recurring basis as of December 31, 2020 were as follows (in thousands):

	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds, included in cash equivalents	\$ 147,492	\$ 147,492	\$ —	\$ —
Investments:				
Corporate debt securities	63,691	—	63,691	—
Government agency securities	2,005	—	2,005	—
Totals	\$ 213,188	\$ 147,492	\$ 65,696	\$ —

There were no changes in valuation techniques during the years ended December 31, 2021 or 2020. There were no liabilities measured at fair value on a recurring basis as of December 31, 2021 or 2020.

5. Investments

Short-term investments consist of investments with maturities greater than ninety days and less than one year from the balance sheet date. Long-term investments consist of investments with maturities of greater than one year that are not expected to be used to fund current operations. The Company classifies all of its investments as available-for-sale securities. Accordingly, these investments are recorded at fair value. Realized gains and losses, amortization and accretion of discounts and premiums are included in other income, net. Unrealized gains and losses on available-for-sale securities are included in other comprehensive income as a component of stockholders' equity until realized.

Cash equivalents, short-term investments and long-term investments as of December 31, 2021 were comprised as follows (in thousands):

	December 31, 2021			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents and short-term investments:				
Money market funds, included in cash equivalents	\$ 95,529	\$ —	\$ —	\$ 95,529
Corporate debt securities	69,316	—	(34)	69,282
U.S. Treasuries	13,777	—	(22)	13,755
Total cash equivalents and short-term investments	178,622	—	(56)	178,566
Long-term investments:				
Corporate debt securities	17,276	—	(88)	17,188
U.S. Treasuries	16,580	—	(64)	16,516
Government agency securities	7,983	—	(30)	7,953
Total long-term investments	41,839	—	(182)	41,657
Total cash equivalents and investments	\$ 220,461	\$ —	\$ (238)	\$ 220,223

Cash equivalents, short-term investments and long-term investments as of December 31, 2020 were comprised as follows (in thousands):

	December 31, 2020			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents and short-term investments:				
Money market funds, included in cash equivalents	\$ 147,492	\$ —	\$ —	\$ 147,492
Corporate debt securities	56,985	9	(13)	56,981
Government agency securities	2,001	4	—	2,005
Total cash equivalents and short-term investments	206,478	13	(13)	206,478
Long-term investments:				
Corporate debt securities	6,727	—	(17)	6,710
Total long-term investments	6,727	—	(17)	6,710
Total cash equivalents and investments	\$ 213,205	\$ 13	\$ (30)	\$ 213,188

As of December 31, 2021 and 2020, the aggregate fair value of securities that were in an unrealized loss position for less than twelve months was \$86.7 million and \$28.3 million, respectively. As of December 31, 2021, the aggregate fair value of securities that were in an unrealized loss position for more than twelve months was \$4.8 million. There were no securities that were in an unrealized loss position for more than twelve months as of December 31, 2020. As of December 31, 2021, the Company did not intend to sell, and would not be more likely than not required to sell, the securities in an unrealized loss position before recovery of their amortized cost bases. Furthermore, the Company determined that there was no material change in the credit risk of these securities. As a result, the Company determined it did not hold any securities with any other-than-temporary impairment as of December 31, 2021.

There were no realized gains and losses on available-for-sale securities during the year ended December 31, 2021 and 2020.

6. Restricted Cash

As of both December 31, 2021 and 2020, the Company maintained non-current restricted cash of \$1.3 million. This amount is included within “Other non-current assets” in the accompanying consolidated balance sheets and is comprised solely of a security deposit required pursuant to the lease for the Company’s corporate headquarters.

The following table provides a reconciliation of cash, cash equivalents and restricted cash that sums to the total of the same such amounts shown in the consolidated statements of cash flows (in thousands):

	Year Ended December 31, 2021		Year Ended December 31, 2020	
	Beginning of Period	End of Period	Beginning of Period	End of Period
Cash and cash equivalents	\$ 147,493	\$ 95,529	\$ 53,241	\$ 147,493
Restricted cash	1,270	1,270	1,270	1,270
Cash, cash equivalents and restricted cash	<u>\$ 148,763</u>	<u>\$ 96,799</u>	<u>\$ 54,511</u>	<u>\$ 148,763</u>

7. Property and Equipment, Net

Property and equipment, net as of December 31, 2021 and 2020 was comprised as follows (in thousands):

	Estimated Useful Life (in Years)	December 31,	
		2021	2020
Laboratory equipment	5	\$ 11,616	\$ 11,408
Furniture and office equipment	4	1,086	1,071
Computer equipment	3	1,641	1,528
Leasehold improvements	Shorter of useful life or remaining lease term	8,609	8,572
Total property and equipment, gross		22,952	22,579
Less: accumulated depreciation		(18,070)	(15,243)
Total property and equipment, net		<u>\$ 4,882</u>	<u>\$ 7,336</u>

Depreciation expense for the years ended December 31, 2021 and 2020 was \$2.8 million and \$3.4 million, respectively.

8. Accrued Expenses

Accrued expenses as of December 31, 2021 and 2020 were comprised as follows (in thousands):

	December 31,	
	2021	2020
Employee compensation and benefits	\$ 6,844	\$ 6,825
External research and professional services	6,252	4,855
Lab consumables and other	371	364
Total accrued expenses	<u>\$ 13,467</u>	<u>\$ 12,044</u>

9. Common Stock and Preferred Stock

Common Stock

The Company is authorized to issue 160,000,000 shares of common stock. Holders of common stock are entitled to one vote per share. Holders of common stock are entitled to receive dividends, if and when declared by the Board of Directors.

On December 17, 2019, the Company entered into a Sales Agreement with Cowen and Company, LLC (“Cowen”) pursuant to which the Company could offer and sell shares of its common stock with an aggregate offering price of up to \$50.0 million under an “at the market” offering program (the “2019 ATM Offering”). The Sales Agreement provided that Cowen will be entitled to a sales commission equal to 3.0% of the gross sales price per share of all shares sold under the ATM Offering. During the first quarter of 2021, the Company sold an aggregate of 3,156,200 shares at an average price of \$9.87 per share for net proceeds of \$30.2 million, which completed the sale of all available amounts under the 2019 ATM Offering.

In addition, during the first quarter of 2021, the Company completed a follow-on public offering of its common stock, selling an aggregate of 5,750,000 shares of common stock at a public offering price of \$11.25 per share for net proceeds of \$60.6 million, after deducting underwriting discounts and commissions and offering fees.

On November 4, 2021, the Company entered into a new Sales Agreement with Cowen (the “2021 Sales Agreement”), pursuant to which the Company may offer and sell shares of our common stock with an aggregate offering price of up to \$75.0 million under an ATM offering program (the “2021 ATM Offering”). The 2021 Sales Agreement provides that Cowen will be entitled to a sales commission equal to 3.0% of the gross sales price per share of all shares sold under the 2021 ATM Offering. No sales were made under the 2021 ATM Offering during the year ended December 31, 2021.

Preferred Stock

The Company is authorized to issue 5,000,000 shares of undesignated preferred stock in one or more series. As of December 31, 2021, no shares of preferred stock were issued or outstanding.

Shares Reserved for Future Issuance

As of December 31, 2021 and 2020, the Company had reserved for future issuance the following number of shares of common stock (in thousands):

	December 31,	
	2021	2020
Shares reserved for vesting of restricted stock units	833	588
Shares reserved for exercises of outstanding stock options	7,629	6,586
Shares reserved for future issuances under the 2017 Stock Option and Incentive Plan	1,258	1,284
Total shares reserved for future issuance	9,720	8,458

10. Stock-based Compensation

2013 Stock Option and Grant Plan

In February 2013, the board of directors adopted and the Company’s stockholders approved the 2013 Stock Option and Grant Plan (the “2013 Plan”), as amended and restated, under which it could grant incentive stock options (“ISOs”), non-qualified stock options, restricted stock awards (“RSAs”) and restricted stock units (“RSUs”) to eligible employees, officers, directors, and consultants. The 2013 Plan was subsequently amended in January 2015, April 2015, July 2015, March 2016 and October 2016 to allow for the issuance of additional shares of common stock.

2017 Stock Option and Incentive Plan

In January 2017, the board of directors adopted and the Company’s stockholders approved the 2017 Stock Option and Incentive Plan (the “2017 Plan”), which became effective immediately prior to the effectiveness of the Company’s IPO. Upon the adoption of the 2017 Plan, no further awards will be granted under the 2013 Plan.

The 2017 Plan provides for the grant of ISOs, non-qualified stock options, RSAs, RSUs, stock appreciation rights and other stock-based awards. The Company’s employees, officers, directors and consultants and advisors are eligible to receive awards under the 2017 Plan. The terms of awards, including vesting requirements, are determined by the Board of Directors, subject to the provisions of the 2017 Plan.

The Company initially registered 1,753,758 shares of common stock under the 2017 Plan, which was comprised of (i) 1,510,000 shares of common stock reserved for issuance under the 2017 Plan, plus (ii) 243,758 shares of common stock originally reserved for issuance under the 2013 Plan that became available for issuance under the 2017 Plan upon the completion of the Company’s IPO. The 2017 Plan also provides that an additional number of shares will automatically be added to the shares authorized for issuance under the 2017 Plan on January 1, 2018 and each January 1st thereafter. The number of shares added each year will be equal to the lesser of (i) 4% of the outstanding shares on the immediately preceding December 31st or (ii) such amount as determined by the compensation committee of the board of directors. Effective January 1, 2020 and 2021, 1,349,526 and 1,669,162 additional shares, respectively, were automatically added to the shares authorized for issuance under the 2017 Plan.

As of December 31, 2021, there were 1,258,296 shares available for future issuance under the 2017 Plan.

Inducement Stock Options

The Company may grant, upon approval by the compensation committee of the board of directors, awards, including options to purchase shares of common stock, as an inducement to employment in accordance with Nasdaq Listing Rule 5635(c)(4). The securities are issued pursuant to Section 4(a)(2) under the Securities Act of 1933, as amended, relating to transactions by an issuer not involving any public offering. These options are subject to substantially the same terms as options issued pursuant to the 2017 Plan. During the second quarter of 2021, the Company granted an option to purchase 225,000 shares of common stock as an inducement award.

2017 Employee Stock Purchase Plan

In January 2017, the board of directors adopted and the Company’s stockholders approved the 2017 Employee Stock Purchase Plan (the “2017 ESPP”), which became effective upon the closing of the Company’s IPO. The Company initially reserved 302,000 shares of common stock for future issuance under the 2017 ESPP. The 2017 ESPP also provides that an additional number of shares will automatically be added to the shares authorized for issuance under the 2017 ESPP on January 1, 2018 and each January 1st thereafter through January 1, 2027. The number of shares added each year will be equal to the lesser of (i) 1% of the outstanding shares on the immediately preceding December 31st, (ii) 603,000 shares or (iii) such amount as determined by the Compensation Committee of the Board of Directors. Effective January 1, 2020 and 2021, 337,381 and 417,290 additional shares, respectively, were automatically added to the shares authorized for issuance under the 2017 ESPP. No offering periods under the 2017 ESPP had been initiated as of December 31, 2021.

Stock-based Compensation Expense

Total stock-based compensation expense recognized in the consolidated statements of operations and comprehensive (loss) income for the years ended December 31, 2021 and 2020 was as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	\$ 5,560	\$ 4,242
General and administrative	5,917	5,529
Total stock-based compensation expense	<u>\$ 11,477</u>	<u>\$ 9,771</u>

RSU Activity

The Company has also granted RSUs to its employees under the 2017 Plan. The following table summarizes RSU activity for the year ended December 31, 2021 (in thousands, except per share amounts):

	RSUs	Weighted-Average Grant Date Fair Value per Share
Unvested as of December 31, 2020	588	\$ 5.82
Issued	562	\$ 11.17
Vested	(227)	\$ 5.62
Cancelled	(90)	\$ 9.15
Unvested as of December 31, 2021	<u>833</u>	<u>\$ 9.13</u>

The aggregate fair value of RSUs vested during the year ended December 31, 2021, based upon the fair values of the stock underlying the RSUs on the day of vesting, was \$1.5 million. The aggregate fair value of RSUs vested during the year ended December 31, 2020, based upon the fair values of the stock underlying the RSUs on the day of vesting, was \$1.5 million.

As of December 31, 2021, there was unrecognized stock-based compensation expense related to unvested RSUs of \$4.7 million, which the Company expects to recognize over a weighted-average period of approximately 1.5 years.

Stock Option Activity

The fair value of stock options granted to employees and directors during the years ended December 31, 2021 and 2020 was calculated on the date of grant using the following weighted-average assumptions:

	Year Ended December 31,	
	2021	2020
Risk-free interest rate	0.8 %	1.2 %
Expected dividend yield	— %	— %
Expected term (in years)	6.0	6.0
Expected volatility	81.9 %	72.3 %

Using the Black-Scholes option pricing model, the weighted-average grant date fair value of stock options granted to employees and directors during the years ended December 31, 2021 and 2020 was \$7.05 and \$4.25 per share, respectively.

The following table summarizes changes in stock option activity during the year ended December 31, 2021 (in thousands, except per share amounts):

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2020	6,586	\$ 8.30	6.5	\$ 13,110
Granted	1,867	\$ 10.19		
Exercised	(403)	\$ 3.15		
Cancelled	(421)	\$ 11.35		
Outstanding at December 31, 2021	<u>7,629</u>	\$ 8.87	6.4	\$ 16,881
Exercisable at December 31, 2021	<u>5,165</u>	\$ 8.91	5.3	\$ 13,944

The aggregate intrinsic value of stock options exercised during the years ended December 31, 2021 and 2020 was \$3.0 million and \$0.5 million, respectively.

As of December 31, 2021, there was unrecognized stock-based compensation expense related to unvested stock options of \$12.5 million, which the Company expects to recognize over a weighted-average period of approximately 2.5 years.

11. Income Taxes

The provision for income taxes for the years ended December 31, 2021 and 2020 was comprised as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Current taxes:		
Federal	\$ —	\$ —
State	15	14
Total current taxes	15	14
Deferred taxes:		
Federal	—	—
State	—	—
Total deferred taxes	—	—
Total provision for income taxes	<u>\$ 15</u>	<u>\$ 14</u>

A reconciliation of the federal statutory income tax rate to the Company's effective tax rate is as follows:

	Year Ended December 31,	
	2021	2020
Income tax computed at federal statutory tax rate	21.0 %	21.0 %
State taxes, net of federal benefit	6.9 %	4.2 %
Tax credit carryforwards	3.5 %	7.8 %
Permanent items	(0.7)%	(12.4)%
Change in valuation allowance	(30.7)%	(20.4)%
Other	— %	(0.2)%
Effective tax rate	<u>— %</u>	<u>— %</u>

The principal components of the Company's deferred tax assets and liabilities as of December 31, 2021 and 2020 were comprised as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	\$ 45,590	\$ 22,717
Tax credit carryforwards	25,327	21,387
Deferred revenue	—	528
Operating lease liability	3,739	4,614
Intangibles	960	785
Accrued expenses and other	1,843	1,838
Unrealized loss on available-for-sale securities	17	17
Depreciation	583	314
Stock-based compensation	5,207	4,031
Total deferred tax assets	<u>83,266</u>	<u>56,231</u>
Less: valuation allowance	(80,022)	(52,172)
Net deferred tax assets	<u>3,244</u>	<u>4,059</u>
Deferred tax liabilities:		
Operating lease right-of-use asset	(3,244)	(4,059)
Total deferred tax liabilities	<u>(3,244)</u>	<u>(4,059)</u>
Net deferred taxes	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2021, the Company had federal and state net operating loss ("NOL") carryforwards of \$166.1 million and \$169.3 million, respectively. Federal NOLs generated through the year ended December 31, 2017 expire at various dates from 2032 through 2037, and federal NOLs generated in years beginning after December 31, 2017 may be carried forward indefinitely. State NOLs expire at various dates from 2035 through 2038. As of December 31, 2021, the Company had federal research and development tax credit carryforwards of \$19.2 million which expire at various dates from 2032 through 2041. In addition, as of December 31, 2021, the Company had state research and development and investment tax credit carryforwards of \$7.6 million and \$0.1 million, respectively. The state research and development tax credit carryforwards expire at various dates from 2029 through 2036 and the state investment tax credit carryforwards expire at various dates from 2022 through 2024.

Management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which primarily pertain to NOL carryforwards, tax credit carryforwards, the Company's operating lease liability and stock-based compensation. Management has determined that it is more likely than not that the Company will not realize the benefits of its deferred tax assets, and as a result, a valuation allowance of \$80.0 million has been established at December 31, 2021. The increase in the valuation allowance of \$27.8 million during the year ended December 31, 2021 was primarily due to increased net loss during the year ended December 31, 2021 driven by increased operating expenses and reduced revenue recognition under the Gilead License Agreement as compared to the year ended December 31, 2020.

NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (“IRS”) and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the IRC. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the Company’s value immediately prior to the ownership change. An IRC Section 382 study, completed in August 2016, identified three previous ownership changes for purposes of IRC Section 382. As a result of these ownership changes, the Company’s NOL and tax credit carryforwards allocable to the periods preceding each such ownership change are subject to limitations under IRC Section 382. No additional ownership changes were identified in a study completed in November 2021. Subsequent ownership changes may further affect the limitation in future years.

The Company had no unrecognized tax benefits as of either December 31, 2021 or 2020. During the year ended December 31, 2017, the Company completed a study of its research and development credit carryforwards generated during the years ended December 31, 2016 and 2015. The Company has not conducted a study of its research and development credit carryforwards generated during any subsequent years. This study may result in an adjustment to the Company’s research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company’s research and development credit carryforwards, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated statements of operations and comprehensive loss if an adjustment were required.

Interest and penalty charges, if any, related to income taxes would be classified as a component of the provision for income taxes in the consolidated statements of operations and comprehensive loss. As of December 31, 2021, the Company has not incurred any material interest or penalty charges.

The Company files income tax returns in the United States federal tax jurisdiction and the Massachusetts state tax jurisdiction. Since the Company is in a loss carryforward position, it is generally subject to examination by federal and state tax authorities for all tax years in which a loss carryforward is available.

12. Related-party Transactions

In August 2020, the Company entered into the Gilead License Agreement and Stock Purchase Agreement under which it received a non-refundable upfront payment of \$85.0 million and cash consideration of \$35.0 million for Gilead’s purchase of 5,539,727 shares of the Company’s common stock. During the year ended December 31, 2021, the Company recognized \$26.9 million in revenue under the Gilead License Agreement and recorded less than \$0.1 million of reimbursement expenses due from Gilead within prepaid expenses and other current assets in the accompanying consolidated balance sheets. During the year ended December 31, 2020, the Company recognized \$62.3 million in revenue under these arrangements and recorded deferred revenue of \$1.9 million in the accompanying consolidated balance sheets. As of December 31, 2020, the Company had recorded \$0.1 million of reimbursement expenses due from Gilead within prepaid expenses and other current assets in the accompanying consolidated balance sheets.

13. Commitments and Contingencies

Corporate Headquarters Lease

In November 2016, the Company entered into an operating lease agreement (the “Corporate Headquarters Lease”) to occupy 51,000 square feet of laboratory and office space in Cambridge, Massachusetts. This facility serves as the Company’s corporate headquarters. The lease term began on November 1, 2016 and extends to March 31, 2025. The Company has the option to extend the lease term for one consecutive five-year period, at the market rate, by giving the landlord written notice of its election to exercise the extension at least twelve months prior to the original expiration of the lease term. The Company provided the landlord with a security deposit in the form of a letter of credit in the amount of \$1.3 million, which is recorded as restricted cash and included within “Other non-current assets” in the consolidated balance sheets. The Corporate Headquarters Lease also provided the Company with a tenant improvement allowance of \$0.5 million. Leasehold improvements related to this facility are being amortized over the shorter of their useful life or the lease term.

Accounting under ASC 842

As a result of the adoption of ASC 842 on January 1, 2019, the Company recorded a right-of-use asset and a corresponding lease liability on the consolidated balance sheets as of December 31, 2021 and 2020. As there is no rate implicit in the Corporate Headquarters Lease, the Company estimated its incremental borrowing rate based upon a synthetic credit rating and yield curve analysis. Based upon this analysis, the Company calculated a discount rate of 8.0% for the Corporate Headquarters Lease.

As of December 31, 2021, the future minimum lease payments due under the operating lease for the Company’s corporate headquarters are as follows (in thousands):

	Amount
2022	\$ 4,657
2023	4,789
2024	4,925
2025	1,249
Total remaining minimum rental payments	15,620
Less: effect of discounting	(1,932)
Total lease liability	<u>\$ 13,688</u>

The Company recorded operating lease expense for the Corporate Headquarters Lease of \$4.3 million for the year ended December 31, 2021 and \$4.2 million for the year ended December 31, 2020. As of December 31, 2021, the remaining lease term of the Corporate Headquarters Lease was 3.3 years. The Company presents changes in its right-of-use asset and lease liability on a combined net basis within “Other liabilities” in the consolidated statements of cash flows.

License and Collaboration Agreements

The Company has entered into various license agreements for certain technology. The Company could be required to make aggregate technical, clinical development and regulatory milestone payments of up to \$7.9 million and low single-digit royalty payments based on a percentage of net sales of licensed products. As of December 31, 2021, the Company had made \$1.0 million in aggregate milestone payments under these license agreements. The Company may cancel these agreements at any time by providing 30 to 90 days’ notice to the licensors, and all payments not previously due would no longer be owed.

The Company has also entered into collaboration agreements with various third parties for research services and access to proprietary technology platforms. Under these collaboration agreements, the Company could be required to make aggregate technical, clinical development and regulatory milestones payments ranging from \$12.5 million to \$12.9 million per product candidate and low single-digit royalty payments based on a percentage of net sales on a product-by-product basis. As of December 31, 2021, the Company had made \$1.8 million in aggregate milestone payments under these collaboration agreements.

14. 401(k) Savings Plan

The Company has a defined-contribution savings plan under Section 401(k) of the IRC (the “401(k) Plan”). The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis. Beginning on January 1, 2018, the Company matches 50% of an employee’s 401(k) contributions up to a maximum of 6% of the participant’s salary, subject to employer match limitations under the IRC. As such, the Company made \$0.7 million and \$0.6 million in contributions to the 401(k) Plan for the years ended December 31, 2021 and 2020, respectively.

15. Net Loss per Share

The following weighted-average amounts were excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive (in thousands):

	Year Ended December 31,	
	2021	2020
Outstanding stock options	7,388	6,594
Unvested RSUs	791	660
Total	8,179	7,254

EXHIBIT INDEX

Exhibit No.	Description of Exhibit
3.1	Fourth Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 of the Registrant’s Annual Report on Form 10-K (File No. 001-37998) filed March 8, 2018)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 of the Registrant’s Annual Report on Form 10-K (File No. 001-37998) filed March 8, 2018)
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant’s Registration Statement on Form S-1 (File No. 333-215372) filed December 30, 2016)
4.2	Description of Securities (incorporated by reference to Exhibit 4.3 of the Registrant’s Annual Report on Form 10-K (File No. 001-37998) filed February 27, 2020)
10.1#	Jounce Therapeutics, Inc. 2017 Stock Option and Grant Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.1 of the Registrant’s Registration Statement on Form S-1/A (File No. 333-215372) filed January 17, 2017)
10.2#	Form of Restricted Stock Unit Award Agreement under 2017 Stock Option and Incentive Plan (for employees) (incorporated by reference to Exhibit 10.1 of the Registrant’s Quarterly Report on Form 10-Q (File No. 001-37998) filed August 9, 2018)
10.3#	Form of Non-Qualified Stock Option Agreement Inducement Grant for Employees (incorporated by reference to Exhibit 10.1 of the Registrant’s Quarterly Report on Form 10-Q (File No. 001-37998) filed August 5, 2021)
10.4#	Jounce Therapeutics, Inc. 2013 Stock Option and Grant Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant’s Annual Report on Form 10-K (File No. 001-37998) filed March 8, 2018)
10.5#	Jounce Therapeutics, Inc. 2017 Employee Stock Purchase Plan, As Amended (incorporated by reference to Exhibit 10.1 of the Registrant’s Quarterly Report on Form 10-Q (File No. 001-37998) filed November 13, 2017)
10.6*#	Amended and Restated Non-Employee Director Compensation Policy
10.7#	Amended and Restated Employment Agreement between Richard Murray and the Registrant, dated January 6, 2017 (incorporated by reference to Exhibit 10.4 of the Registrant’s Registration Statement on Form S-1/A (File No. 333-215372) filed January 17, 2017)
10.8#	Amended and Restated Employment Agreement between Kim Drapkin and the Registrant, dated January 6, 2017 (incorporated by reference to Exhibit 10.5 of the Registrant’s Registration Statement on Form S-1/A (File No. 333-215372) filed January 17, 2017)
10.9#	Amended and Restated Employment Agreement between Elizabeth Trehu and the Registrant, dated January 6, 2017 (incorporated by reference to Exhibit 10.6 of the Registrant’s Registration Statement on Form S-1/A (File No. 333-215372) filed January 17, 2017)
10.10#	Employment Agreement between Hugh Cole and the Registrant, dated August 14, 2017 (incorporated by reference to Exhibit 10.8 of the Registrant’s Annual Report on Form 10-K (File No. 001-37998) filed March 8, 2018)
10.11#	Form of Director Indemnification Agreement (incorporated by reference to Exhibit 10.12 of the Registrant’s Registration Statement on Form S-1 (File No. 333-215372) filed December 30, 2016)
10.12#	Form of Officer Indemnification Agreement (incorporated by reference to Exhibit 10.13 of the Registrant’s Registration Statement on Form S-1/A (File No. 333-215372) filed January 17, 2017)
10.13#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.14 of the Registrant’s Registration Statement on Form S-1/A (File No. 333-215372) filed January 17, 2017)
10.14	Lease Agreement between ARE-770/784/790 Memorial Drive, LLC and the Registrant, dated November 1, 2016 (incorporated by reference to Exhibit 10.11 of the Registrant’s Registration Statement on Form S-1 (File No. 333-215372) filed December 30, 2016)
10.15†	Amended and Restated Exclusive License Agreement between Sloan Kettering Institute for Cancer Research, Memorial Sloan Kettering Cancer Center and Memorial Hospital for Cancer and the Registrant, dated September 28, 2015 (incorporated by reference to Exhibit 10.9 of the Registrant’s Registration Statement on Form S-1 (File No. 333-215372) filed December 30, 2016)
10.16‡	License Agreement by and between the Registrant and Gilead Sciences, Inc., dated August 31, 2020 (incorporated by reference to Exhibit 10.1 of the Registrant’s Quarterly Report on Form 10-Q (File No. 001-37998) filed on November 6, 2020)
10.17‡	Stock Purchase Agreement by and between the Registrant and Gilead Sciences, Inc., dated August 31, 2020 (incorporated by reference to Exhibit 10.2 of the Registrant’s Quarterly Report on Form 10-Q (File No. 001-37998) filed on November 6, 2020)
10.18‡	Registration Rights Agreement by and between the Registrant and Gilead Sciences, Inc., dated August 31, 2020 (incorporated by reference to Exhibit 10.3 of the Registrant’s Quarterly Report on Form 10-Q (File No. 001-37998) filed on November 6, 2020)
10.19	Sales Agreement, dated of November 4, 2021 by and between the Registrant and Cowen and Company, LLC (incorporated by reference to Exhibit 1.1 of the Registrant’s Current Report on Form 8-K (File No. 001-37998) filed November 4, 2021)
21.1*	List of Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1+	Certifications of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101*	The following materials from the Company’s Annual Report on Form 10-K for the year ended December 31, 2020, formatted in eXtensible Business Reporting Language (XBRL): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations and Comprehensive Income (Loss), (iii) Consolidated Statements of Stockholders’ Equity, (iv) Consolidated Statements of Cash Flows and (v) Notes to Consolidated Financial Statements

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*	Filed herewith
+	Furnished herewith
#	Indicates a management contract or any compensatory plan, contract or arrangement
†	Confidential treatment granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended
‡	Portions of this Exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K

SIGNATURES

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

JOUNCE THERAPEUTICS, INC.

Date: March 2, 2022

By: /s/ Richard Murray
Richard Murray, Ph.D.
President and Chief Executive Officer

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

Signature	Title	Date
<u>/s/ Richard Murray</u> Richard Murray, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 2, 2022
<u>/s/ Kim C. Drapkin</u> Kim C. Drapkin	Treasurer and Chief Financial Officer (Principal Financial and Accounting Officer)	March 2, 2022
<u>/s/ Perry A. Karsen</u> Perry A. Karsen	Chairman of the Board of Directors	March 2, 2022
<u>/s/ Luis A. Diaz, Jr.</u> Luis A. Diaz, Jr., M.D.	Director	March 2, 2022
<u>/s/ Barbara Duncan</u> Barbara Duncan	Director	March 2, 2022
<u>/s/ J. Duncan Higgons</u> J. Duncan Higgons	Director	March 2, 2022
<u>/s/ Robert Iannone</u> Robert Iannone, M.D., M.S.C.E.	Director	March 2, 2022
<u>/s/ Robert Kamen</u> Robert Kamen, Ph.D.	Director	March 2, 2022
<u>/s/ Jigar Raythatha</u> Jigar Raythatha	Director	March 2, 2022
<u>/s/ Luisa Salter-Cid</u> Luisa Salter-Cid, Ph.D.	Director	March 2, 2022