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: 000-28386

CTI BIOPHARMA CORP.

(Exact name of registrant as specified in its charter)

Delaware	**91-1533912**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)
3101 Western Avenue	
Suite 800	
Seattle	
Washington	**98121**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: (206) 282-7100

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

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

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

None.

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

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

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

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

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

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

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

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

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 aggregate market value of the registrant's common equity held by non-affiliates was approximately $210.4 million. Shares of common stock held by each executive officer and director and by each other person who may be deemed to be an affiliate of the registrant have been excluded from this computation. This determination of affiliate status for this purpose is not necessarily a conclusive determination for other purposes.

The number of outstanding shares of the registrant's common stock as of March 17, 2022 was 99,917,628.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to its 2022 annual meeting of stockholders, or the 2022 Proxy Statement, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. We expect to file the 2022 Proxy Statement with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

CTI BIOPHARMA CORP.

TABLE OF CONTENTS

Forward Looking Statements

This Annual Report on Form 10-K and the documents we incorporate by reference herein or therein may contain "forward-looking statements" within the meaning of the United States federal securities laws. All statements other than statements of historical fact are forward-looking statements, including, without limitation:

- our expectations regarding sufficiency of cash resources, cash expenditures, sources of cash flows and other projections, product manufacturing and sales, research and development expenses, selling, general and administrative expenses and additional losses;
- our ability to obtain funding for our operations;
- the commercialization of VONJO as a treatment for myelofibrosis patients with severe thrombocytopenia;
- our ability to develop, commercialize and obtain regulatory approval of pacritinib for other development programs we may pursue in the future;
- the design of our clinical trials and their anticipated enrollment;
- the safety, effectiveness and potential benefits and indications of VONJO and any other product candidates we may develop in the future;
- the rate and degree of market acceptance and clinical utility of VONJO or any other product candidates we may develop in the future;
- the timing of and results from clinical trials and pre-clinical development activities, including those related to VONJO and any other product candidates we may develop in the future;
- our ability to advance product candidates, including VONJO and any other product candidates we may develop in the future, into, and the successful completion of, clinical trials;
- our ability to achieve profitability, including our ability to effectively implement cost reduction strategies and realize anticipated cost savings from those efforts;
- our expectations regarding federal, state and foreign regulatory requirements;
- our and our collaborators' ability to obtain and maintain regulatory approvals, and the timing of such approvals, for VONJO or any other product candidates we may develop in the future;
- our ability to maintain and establish collaborations;
- our expectations regarding market risk, including interest rate changes and foreign currency fluctuations;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- the impact of government laws and regulations;
- our ability to negotiate, integrate, and implement collaborations, acquisitions and other strategic transactions;
- our ability to engage and retain the employees required to advance our development activities and grow our business;
- developments relating to our competitors and our industry, including the success of competing therapies that are or become available;
- our expectations regarding business disruptions and related risks resulting from the ongoing worldwide coronavirus pandemic known as COVID-19; and
- other risks and uncertainties, including those listed under the heading "Risk Factors" in this Annual Report on Form 10-K and in other filings we periodically make with the U.S. Securities and Exchange Commission, or the SEC.

In some cases, forward-looking statements can be identified by terms such as "anticipates," "believes," "continue," "could," "estimates," "expects," "intends," "may," "plans," "potential," "predicts," "projects," "should" or "will" or the

negative thereof, variations thereof and similar expressions. Such statements are based on management's current expectations and are subject to risks and uncertainties, which may cause actual results to differ materially from those set forth in the forward-looking statements. There can be no assurance that such expectations or any of the forward-looking statements will prove to be correct, and actual results could differ materially from those projected or assumed in the forward-looking statements. We urge you to carefully review the disclosures we make concerning risks and other factors that may affect our business and operating results, including those made under Part I, Item 1, "Business," Part I, Item 1A, "Risk Factors," Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," and elsewhere in this Annual Report on Form 10-K and any risk factors contained in subsequent Quarterly Reports on Form 10-Q that we file with the SEC.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

We do not intend to update any of the forward-looking statements after the date of this Annual Report on Form 10-K to conform these statements to actual results or changes in our expectations. Readers are cautioned not to place undue reliance on these forward-looking statements, which apply only as of the date of this Annual Report on Form 10-K.

In this Annual Report on Form 10-K, all references to "we," "us," "our," the "Company" and "CTI" mean CTI BioPharma Corp. and our subsidiaries, except where it is otherwise made clear.

PART I

Item 1. Business

Overview

We are a biopharmaceutical company focused on the acquisition, development and commercialization of novel targeted therapies for blood-related cancers where there is a significant unmet medical need. Our goal is to build a profitable company by generating income from products we develop and commercialize, either alone or with partners. We have one commercially approved product, VONJO™ (pacritinib), which has received accelerated approval in the United States by the U.S. Food and Drug Administration, or the FDA, for the treatment of adult patients with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 x 10^9/L.

Our Strategy

Our objective is to become a leader in the development and commercialization of novel targeted therapeutics for the treatment of blood-related cancers. The key elements of our strategy to achieve these objectives are to:

- **Successfully Commercialize VONJO.** At the time of VONJO's approval by the FDA in February 2022, our commercial and supply infrastructure was in place to enable a prompt commercial launch of VONJO. We continue to focus our efforts on the commercial capabilities that support the ongoing launch of VONJO in the United States through the coordinated efforts of our sales, marketing and market access teams.

- **Evaluate Strategic Product Collaborations to Accelerate Development and Commercialization.** Where we believe it may be beneficial, we intend to evaluate collaborations to broaden and accelerate the clinical trial development and commercialization of VONJO. Collaborations have the potential to generate non-equity based operating capital, supplement our own internal expertise and provide us with access to the marketing, sales and distribution capabilities of our collaborators in specific territories.

- **Identify and Acquire Additional Pipeline Opportunities.** Historically, we have built our candidate pipeline using multiple approaches, including through licensing and acquiring assets that we believe were initially undervalued opportunities. We plan to continue to seek out additional product candidates in an opportunistic manner.

Product and Development Portfolio

The following table summarizes our current product and development portfolio as of the date of this report:

TRIAL/STATUS	INDICATION	OVERVIEW
PACIFICA Phase 3 Ongoing	Myelofibrosis with severe thrombocytopenia	The PACIFICA trial is a randomized, controlled phase 3 study of pacritinib versus Physician's Choice in patients with primary myelofibrosis, post polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis with severe thrombocytopenia (platelet count 50,000/μL)
PERSIST-1 Phase 3 Complete	Myelofibrosis	PERSIST-1 was a randomized (2:1), open-label, multi-center Phase 3 trial evaluating the efficacy and safety of pacritinib compared to Best Availability Therapy, excluding JAK inhibitors, in 327 patients with myelofibrosis, without exclusion for low platelet counts.
PERSIST-2 Phase 3 Complete	Myelofibrosis	PERSIST-2 was a randomized (2:1), open-label, multi-center registration-directed Phase 3 trial evaluating pacritinib compared to Best Available Therapy, including the approved JAK inhibitor dosed according to product label, for patients with myelofibrosis whose platelet counts are less than or equal to 100,000 per microliter (≤100,000/μL).
PAC203 Phase 2 Complete		TRIAL OVERVIEW: PAC203 was a Phase 2 dose-finding study of pacritinib in patients with myelofibrosis who have received prior ruxolitinib.

Oncology Market Overview and Opportunity

According to the American Cancer Society, cancer is the second leading cause of death in the United States, resulting in more than 600,000 deaths annually, or more than 1,600 deaths per day. Approximately 1.9 million new cases of cancer are expected to be diagnosed in 2022 in the United States. While the exact prevalence of myelofibrosis is uncertain, it is estimated that there are approximately 21,000 myelofibrosis patients in the United States, 7,000 of whom have severe thrombocytopenia (defined as platelet counts of less than 50 $x10^9$/L). The most commonly used methods for treating patients with cancer are surgery, radiation and chemotherapy. Patients usually receive a combination of these treatments depending upon the type and extent of their disease.

We believe our expertise in blood-related cancers, together with our ability to identify unique therapies that address unmet medical needs that are potentially less toxic and more effective at treating and curing patients, may fill a significant unmet medical need for cancer patients.

Pacritinib

Overview

Pacritinib is an oral kinase inhibitor with specificity for JAK2, IRAK1, FLT3 and CSF1R. At clinically relevant concentrations, pacritinib does not inhibit JAK1. The JAK family of enzymes is a central component in signal transduction pathways, which are critical to normal blood cell growth and development, as well as inflammatory cytokine expression and immune responses. Mutations in these kinases have been shown to be directly related to the development of a variety of blood-related cancers, including myeloproliferative neoplasms, leukemia and lymphoma. In addition to myelofibrosis, the kinase profile of pacritinib suggests its potential therapeutic utility in conditions such as acute myeloid leukemia, or AML, myelodysplastic syndrome, or MDS, chronic myelomonocytic leukemia, or CMML, graft versus host disease, or GvHD, and chronic lymphocytic leukemia, or CLL, due to its inhibition of JAK2, IRAK1, FLT3 and CSF1R. We believe pacritinib has the potential to be delivered as a single agent or in combination therapy regimens.

U.S. FDA Approval of VONJO

In September 2020, we reached an agreement with the FDA to submit a New Drug Application, or NDA, for the potential accelerated approval of VONJO as a treatment for myelofibrosis patients with severe thrombocytopenia, and in March 2021 we completed our rolling NDA submission. The NDA was based on the available data from our completed Phase 3 PERSIST-1 and PERSIST-2 trials and the Phase 2 PAC203 dose-ranging trial. In May 2021, the FDA accepted our NDA and granted pacritinib Priority Review, with the Prescription Drug User Fee Act target action date set for November 30, 2021, which was subsequently extended by three months to February 28, 2022. In February 2022, the FDA granted accelerated approval of VONJO for the treatment of adult patients with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 x 10^9/L. As agreed with the FDA, the PACIFICA Phase 3 trial will be completed as a post-marketing requirement.

PERSIST-1 and PERSIST-2 Trials

Pacritinib was evaluated in two Phase 3 clinical trials, collectively known as the PERSIST program, for patients with myelofibrosis. The PERSIST-1 trial evaluated pacritinib in a broad set of patients without limitations on platelet counts, and the PERSIST-2 trial evaluated pacritinib in patients with low platelet counts. Myelofibrosis is a rare blood cancer associated with significantly reduced quality of life and shortened survival. As the disease progresses, the body slows production of important blood cells and within one year of diagnosis, the incidence of disease-related thrombocytopenia (very low blood platelet counts), severe anemia and red blood cell transfusion requirements increase significantly. Among other complications, most patients with myelofibrosis present with enlarged spleens (splenomegaly), as well as many other potentially devastating physical symptoms such as abdominal discomfort, bone pain, feeling full after eating little, severe itching, night sweats and extreme fatigue. Currently patients with very low blood platelets, so called severe thrombocytopenia, (<50,000/µL) have limited or no effective treatment options. Myelofibrosis patients with severe thrombocytopenia have poor survival following discontinuation of therapy with the approved JAK1/JAK2 therapy. We believe pacritinib may offer effective treatment of splenomegaly and disease-related symptoms in patients with severe thrombocytopenia.

PERSIST-1 was a randomized (2:1), open-label, multi-center Phase 3 trial evaluating the efficacy and safety of pacritinib compared to BAT excluding JAK inhibitors, in 327 patients with myelofibrosis, without exclusion for low platelet counts.

In May 2015, data from PERSIST-1 showed that compared to BAT (exclusive of a JAK inhibitor) pacritinib therapy resulted in a significantly higher proportion of patients with SVR and control of disease-related symptoms meeting the primary endpoint of the trial. Additionally, 25 percent of patients treated with pacritinib who were severely anemic and transfusion dependent - requiring at least six units of blood in the 90 days prior to study entry - became transfusion independent, compared to zero patients treated with BAT ($p<0.05$). The most common adverse events, occurring in 10 percent or more of patients treated with pacritinib within 24 weeks, of any grade, were: mild to moderate diarrhea, nausea, anemia, thrombocytopenia and vomiting. Of the patients treated with pacritinib, three discontinued therapy and 13 patients required dose interruption (average one week) for diarrhea. Patients received a daily full dose of pacritinib over the duration of treatment. Gastrointestinal symptoms typically lasted for approximately one week and few patients discontinued treatment due to side effects. There were no Grade 4 gastrointestinal events reported.

The PERSIST-2 trial was a randomized (2:1), open-label, multi-center registration-directed Phase 3 trial evaluating pacritinib compared to BAT, including the approved JAK inhibitor dosed according to product label, for patients with myelofibrosis whose platelet counts are less than or equal to 100,000 per microliter (≤100,000/µL). The PERSIST-2 trial met one of the co-primary endpoints showing a statistically significant SVR in patients treated with pacritinib combining the once- and twice-daily arms compared to BAT. The PERSIST-2 trial did not meet the other co-primary endpoint of greater than 50 percent reduction in TSS. Although secondary objectives could not be evaluated formally due to the study not achieving one of

the primary objectives, when the two pacritinib dosing arms were evaluated separately versus BAT, pacritinib given twice daily showed a higher percent of SVR and TSS responses compared to BAT; whereas, pacritinib given once daily showed only a higher percent SVR responses compared to BAT. The most common treatment-emergent adverse events, occurring in 20 percent or more of patients treated with pacritinib within 24 weeks, of any grade, were gastrointestinal (generally manageable diarrhea, nausea and vomiting) and hematologic (anemia and thrombocytopenia) and were generally less frequent for BID versus QD administration. The most common serious treatment-emergent adverse events (incidence of ≥5 percent reported in any treatment arm irrespective of grade) were anemia, thrombocytopenia, pneumonia and acute renal failure none of which exceeded 8 percent individually in any arm.

In February 2015, we received a recommendation from the Independent Data Monitoring Committee, or IDMC, in place at the time to terminate the PERSIST-1 trial and hold enrollment of new patients in the PERSIST-2 trial. The IDMC's recommendation was based on non-statistically significant safety concerns, including mortality, in patients on pacritinib, particularly those who crossover after 24 weeks. On February 8, 2016, the FDA notified us that a full clinical hold had been placed on pacritinib clinical studies.

PAC203 Trial

In January 2017, the FDA removed the full clinical hold following review of our complete response submission which included, among other items, final Clinical Study Reports for both PERSIST-1 and -2 trials and a dose-exploration clinical trial protocol that the FDA requested. At that time, the PAC203 trial was designed to enroll up to approximately 105 patients with primary myelofibrosis and who had failed prior ruxolitinib therapy across three dose regimens of pacritinib, 100 mg QD, 100 mg BID and 200 mg BID, to evaluate the dose response relationship for safety and efficacy (SVR at 12 and 24 weeks). The 200 mg BID dose was selected as the top dose based upon observations from the completed PERSIST-2 study. In PAC203, the entry criteria were modified to exclude patients with a history of cardiac and/or bleeding events and additional dose modification guidelines were implemented for the management of treatment-emergent cardiac and or bleeding events. The first patient in the PAC203 trial was enrolled in July 2017.

In April 2018, we amended the protocol to expand the sample size to a maximum of 150 patients (or 50 patients per arm) to collect additional data for the safety and efficacy analyses. In July 2018, we announced that the IDMC for the PAC203 trial completed its planned interim data review of the PAC203 trial and that the IDMC did not identify any drug- or dose-related safety concerns and did not identify any concerns about cardiac or bleeding events. Following meetings with the FDA and European Medicines Agency, or EMA, and consultation with the IDMC, we eliminated the interim efficacy analysis and focused the second interim data review, and all subsequent data reviews, on an assessment of safety. The protocol was amended to reflect this change and submitted to FDA. In October 2018, we announced the continuation of the PAC203 Phase 2 study without modification, following a planned second interim data review by the IDMC. The IDMC did not identify significant drug- or dose-related safety concerns and specifically did not identify any concerns around hemorrhagic or cardiac toxicity. A complete dataset from the fully enrolled study (including efficacy, safety, pharmacokinetic and pharmacodynamic data) will be used to determine the optimal dose of pacritinib for further clinical development, as requested by the FDA. The PAC203 study was fully enrolled in December 2018. In January 2019, the IDMC completed its planned third interim safety review and recommended that the study continue without modification.

In December 2019, we announced top-line efficacy and safety data for the PAC203 trial. Pacritinib was shown to be generally well tolerated across dosing cohorts. The majority of non-hematological adverse events were mild or moderate in severity and, with the exception of diarrhea, were considered unlikely related to pacritinib. The most common non-hematologic adverse events were gastrointestinal, including diarrhea (23.6%) and nausea (23.6%), and occurred more commonly in patients treated at 200 mg BID (31/54, 57.4%) than at lower doses (100 mg BID: 23/55, 41.8%, 100 mg QD: 22/52, 42.3%). These events were largely grade 1 or 2 in severity. Diarrhea was generally manageable with standard antidiarrheal agents, and only one patient (at 200mg BID) required drug discontinuation due to any gastrointestinal event (diarrhea).

The most common hematologic adverse events were thrombocytopenia and anemia, both occurring at higher frequencies at the 200 mg BID dose (35.2 percent and 24.1 percent respectively); this did not, however, lead to higher rates of Grade 3/4 hemorrhage at higher doses (200 mg BID: 5.6 percent; 100 mg BID: 0 percent; 100 mg QD: 7.7 percent; all Grade 3). Similarly, the highest dose saw no excess in Grade 3/4 cardiac (200 mg BID: 3.7 percent; 100 mg BID: 7.3 percent; 100 mg QD: 5.8; all grade 3). There were 10 Grade 5 (fatal) adverse events: 3 at 200 mg BID (sepsis, respiratory failure, subdural hematoma), 3 at 100 mg BID (disease progression, subdural hemorrhage, heart failure), and 4 at 100 mg QD (disease progression, general physical health deterioration, sepsis, tuberculosis).

The 200 mg BID arm had the highest observed rates of SVR ≥35 percent (200 mg BID: 9.3 percent; 100 mg BID: 1.8 percent; 100 mg QD: 0.0 percent). Of the 5 patients with SVR ≥35 percent at the 200 mg BID dose, 4 had platelet counts

<50,000/μL, representing a 17 percent (4/24) response rate among patients with severe thrombocytopenia. Though a dose response relationship was not observed in total symptom score (TSS) based on the threshold of 50 percent reduction in symptom score, the median percent decrease in TSS (including fatigue) did show deeper reductions with escalating doses, with best response at 200 mg BID. At Week 24, the percent change in TSS from baseline was highest in the 200 mg pacritinib BID group (median -27.3%) compared with the other treatment groups (100 mg pacritinib BID group: median -16.0%; 100 mg pacritinib QD group: median -3.1%). Of the TSS (including fatigue) responders, baseline cytopenias were common: 8 of 12 had hemoglobin <10g/dL, and 4 of 12 had platelet counts <50,000/μL.

PACIFICA Phase 3 Trial

In January 2020, we received the FDA's preliminary comments from a Type A meeting request and reached an agreement on the final design changes to our PACIFICA pivotal Phase 3 clinical trial, including changes to the statistical analysis plan that would allow for a potential accelerated approval pathway for VONJO. We amended our PACIFICA Phase 3 trial protocol, to allow for the primary analysis of Spleen Volume Reduction, or SVR, rate on the first 168 patients, with an end-of-study analysis of Total Symptom Score, or TSS, and Overall Survival, or OS, following the full enrollment of 348 patients. Enrollment in this trial is progressing despite the challenges of conducting clinical trials during the COVID-19 pandemic. As agreed with the FDA, following the accelerated approval of VONJO, we plan to complete the PACIFICA Phase 3 trial as a post-marketing requirement, with expected results in mid-2025.

PRE-VENT Phase 3 Trial

In April 2020, in response to the public health crisis due to the global COVID-19 pandemic, we initiated PRE-VENT, a Phase 3 trial evaluating pacritinib in hospitalized patients with severe COVID-19. PRE-VENT, a randomized, double-blind, placebo-controlled multicenter study will compare pacritinib plus Standard of Care, or SOC, versus placebo plus SOC in hospitalized patients with severe COVID-19, including those with a current or prior diagnosis of cancer. The primary endpoint of the trial will assess the proportion of patients who progress to invasive mechanical ventilation and/or extracorporeal membrane oxygenation or die by Day 28. We commenced enrollment of PRE-VENT in the second quarter of 2020 in the United States and reported top-line data from final analysis from the PRE-VENT trial in October 2021. As a statistically significant improvement in the primary endpoint of progression to invasive mechanical ventilation and/or extracorporeal membrane oxygenation or death by Day 28 was not demonstrated, we decided not to pursue further development of pacritinib for the treatment of severe COVID-19.

aGvHD Phase 1 Trial

In March 2021, results were published from an Investigator Sponsored Phase 1 trial conducted by Joseph Pidala, MD, PhD (Moffitt Cancer Center), and Brian C. Betts, MD (Masonic Cancer Center at the University of Minnesota), evaluating pacritinib for the prevention of acute GvHD, or aGvHD. The results demonstrated that pacritinib, combined with sirolimus and low-dose tacrolimus (PAC/SIR/TAC), has a promising safety profile and exhibits preliminary therapeutic activity in preventing aGvHD after allogeneic hematopoietic cell transplantation from HLA matched related and unrelated donors. Enrollment on the Phase 2 portion of the trial, designed to evaluate the therapeutic effect of pacritinib in combination with sirolimus and low-dose tacrolimus for aGvHD prevention, has recently been suspended due to futility without any report of safety concerns.

License Agreements

Baxalta

In November 2013, we entered into a Development, Commercialization and License Agreement, dated as of November 14, 2013, with Baxter International Inc., or Baxter, for the development and commercialization of pacritinib for use in oncology and potentially additional therapeutic areas, or the Pacritinib License Agreement, which was subsequently amended in June 2015. Baxter assigned its rights and obligations under the Pacritinib License Agreement to Baxalta. Under the Pacritinib License Agreement, we granted to Baxter an exclusive, worldwide (subject to co-promotion rights discussed below), royalty-bearing, non-transferable, and (under certain circumstances outside of the United States) sub-licensable license to our know-how and patents relating to pacritinib.

In October 2016, we entered into the Asset Return and Termination Agreement, or the Baxalta Termination Agreement, with Baxalta. Pursuant to the Baxalta Termination Agreement, the Pacritinib License Agreement was terminated in its entirety (other than with respect to certain customary provisions that survive termination, including those pertaining to confidentiality and indemnification), the Pacritinib License Agreement has no further force or effect, and all rights and obligations of the Company and Baxalta under the Pacritinib License Agreement were terminated.

In October 2016, we resumed primary responsibility for the development and commercialization of pacritinib as a result of the Baxalta Termination Agreement and are no longer eligible to receive cost sharing or milestone payments for pacritinib's development from Baxalta.

Baxalta was acquired by Shire plc in 2016, and Shire plc was subsequently acquired by Takeda Pharmaceutical Company Limited, or Takeda, in 2019. Pursuant to the Baxalta Termination Agreement, we are required to make a milestone payment to Takeda in the amount of approximately $10.3 million upon the first regulatory approval or any pricing and reimbursement approvals of a product containing pacritinib. Subsequent to FDA approval of VONJO in February 2022, the $10.3 million milestone payment has become payable to Takeda.

*S*BIO*

We acquired the compounds SB1518 (which is referred to as "pacritinib") and SB1578, which inhibit JAK2 and FLT3, from S*BIO in May 2012. Under our agreement with S*BIO, we are required to make milestone payments to S*BIO up to an aggregate amount of $132.5 million if certain U.S., EU and Japanese regulatory approvals are obtained and if certain worldwide net sales thresholds are met in connection with any pharmaceutical product containing or comprising any compound that we acquired from S*BIO for use for specific diseases, infections or other conditions. In addition, S*BIO will be entitled to receive royalty payments from us at incremental rates in the low single-digits based on certain worldwide net sales thresholds on a product-by-product and country-by-country basis. Subsequent to FDA approval of VONJO in February 2022, a $25.0 million milestone payment has become payable to S*BIO. At our election, we may pay up to 50% of any milestone payments to S*BIO through the issuance of shares of our common stock or shares of our preferred stock automatically convertible into our common stock.

Teva Pharmaceutical Industries Ltd.

In June 2005, we entered into an acquisition agreement with Cephalon, Inc., or Cephalon, pursuant to which we divested the compound, TRISENOX. Cephalon was subsequently acquired by Teva Pharmaceutical Industries Ltd., or Teva. Under this agreement, we have the right to receive up to $100 million in payments upon achievement by Teva of specified sales and development milestones related to TRISENOX. To date, we have received $60.0 million of such potential milestone payments as a result of Teva having achieved certain sales milestones. The achievement of the remaining milestones is uncertain at this time.

Patents and Other Intellectual Property Rights

We dedicate significant resources to protecting our intellectual property, which is important to our business. We have filed numerous patent applications in the United States and various other countries seeking protection of inventions originating from our research and development, and we have also obtained rights to various patents and patent applications under licenses with third parties and through acquisitions. We have pending patent applications or issued patents in the United States and foreign countries directed to pacritinib and other product candidates. Patent coverage for our individual products extends for varying periods according to the date of the patent filing or grant and the legal term of patents in the various countries where we have obtained patent protection.

Our U.S. and foreign composition of matter patents for pacritinib expire as follows: U.S. patents expire in May 2028 (method) / January 2029 (compound) / March 2030 (salt); foreign patents expire in November 2026 (method and compound) / December 2029 (salt). We expect that any patents issued from our U.S. and foreign patent applications for use of pacritinib for treating transplant rejection will expire in 2036.

Each patent in our portfolio may be eligible for patent term restoration of up to five years under certain circumstances. Also, regulatory exclusivity tied to the protection of clinical data may be complementary to patent protection. During a period of regulatory exclusivity, competitors generally may not use the original applicant's data as the basis for a generic application. In the United States, the data protection generally runs for five years from first marketing approval of a new chemical entity, which period is extended to seven years for an orphan drug indication. Pacritinib has orphan drug designation for myelofibrosis in the United States and the European Union, or EU.

In addition to our patent rights, we rely, to the extent possible, on trade secrets and contractual protections for our know-how and other unpatented technology. Ultimately, to the extent any of our product candidates are not protected by patent rights, our competitors would be free to use inventions embodied in our product candidates to which they have access to compete with us.

The risks and uncertainties associated with our intellectual property, including our patents, are discussed in more detail in Part I, Item 1A, “Risk Factors.”

Manufacturing, Distribution and Associated Operations

Our manufacturing strategy utilizes third party contractors for the procurement and manufacture, as applicable, of raw materials, active pharmaceutical ingredients and finished drug product, as well as for labeling, packaging, storage and distribution of our compounds and associated supply chain operations. As a result of the February 2022 FDA approval of VONJO and the continued expansion of our clinical development activities, we expect that our manufacturing, distribution and related operational requirements will increase correspondingly. Additionally, in October 2016, we resumed primary responsibility for the development and commercialization of pacritinib as a result of the termination of the Pacritinib License Agreement. The development and commercialization of a major product candidate like pacritinib without a collaborative partner has significantly increased our manufacturing, distribution and related operational requirements, and we expect such increases to continue as we advance the clinical development of pacritinib.

Each third party contractor undergoes a formal qualification process by our subject matter experts prior to our entry into any service agreement and initiating any manufacturing work. We currently have a commercial supply arrangement for pacritinib.

Integral to our manufacturing strategy is our quality control and quality assurance program, which includes standard operating procedures and specifications with the goal that our compounds are manufactured in accordance with current Good Manufacturing Practices, or cGMPs, and other applicable global regulations. The cGMP compliance includes strict adherence to regulations for quality control, quality assurance and the maintenance of records and documentation. Manufacturing facilities for products and product candidates must meet cGMP requirements, and commercialized products must have acquired FDA, EMA and any other applicable regulatory approval. In this regard, we expect to continue to rely on contract manufacturers to produce sufficient quantities of our compounds in accordance with cGMPs for use in clinical trials and distribution.

We believe our operational strategy of utilizing qualified outside vendors in the foregoing manner allows us to direct our financial and managerial resources to development and commercialization activities, rather than to the establishment and maintenance of a manufacturing and distribution infrastructure.

Competition

Competition in the pharmaceutical and biotechnology industries is intense. We face competition from a variety of companies focused on developing oncology drugs. We compete with large pharmaceutical companies and with other specialized biotechnology companies. In addition to the specific competitive factors discussed below, new anti-cancer drugs that may be developed and marketed in the future could compete with our various compounds.

Pacritinib may face competition from the currently approved JAK1/JAK2 inhibitors, Jakafi® / Jakavi® (ruxolitinib) and Inrebic® (fedratinib) as well as BESREMi® (ropeginterferon alfa-2b-njft). In August 2019, Celgene (which was subsequently acquired by Bristol Myers Squibb) announced FDA approval of Inrebic® for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis, and in February 2021 Bristol Myers Squibb announced the European Commission, or EC, approval of Inrebic®. In November 2021, PharmaEssentia announced FDA approval of BESREMi® for the treatment of adults with polycythemia vera. Pacritinib may also face competition from momelotinib, which Sierra Oncology acquired from Gilead. In June 2019, Sierra Oncology announced that momelotinib was granted fast track designation by the FDA and launched a Phase 3 clinical trial in November 2019. In June 2021, Sierra Oncology announced that the Phase 3 trial enrollment has been completed and in January 2022, Sierra Oncology announced top-line data from the Phase 3 trial and their intentions to file an NDA in the U.S. for the approval of momelotinib.

Some of our existing or potential competitors have substantially greater financial, technical and human resources than us and may be better equipped to develop, manufacture and market products. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of these competitors have products that have been approved or are in development and operate large, well-funded research and development programs.

Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before us may achieve a significant competitive advantage if their products work through a similar mechanism as our

products and if the approved indications are similar. A number of biotechnology and pharmaceutical companies are developing new products for the treatment of the same diseases being targeted by us. In some instances, such products have already entered late-stage clinical trials or received FDA or EC approval. However, cancer drugs with distinctly different mechanisms of action are often used together in combination for treating cancer, allowing several different products to target the same cancer indication or disease type. Such combination therapy is typically supported by clinical trials that demonstrate the advantage of combination therapy over that of a single-agent treatment.

We believe that our ability to compete successfully will be based on our ability to create and maintain scientifically advanced technology, develop proprietary products, attract and retain scientific personnel, obtain patent or other protection for our products, obtain required regulatory approvals and manufacture and successfully market our products, either alone or through outside parties. We will continue to seek licenses with respect to technology related to our field of interest and may face competition with respect to such efforts. See the risk factor, "*We face direct and intense competition from our competitors in the biotechnology and pharmaceutical industries, and we may not compete successfully against them.*" in Part I, Item 1A, "Risk Factors" of this Annual Report on Form 10-K for additional information regarding the risks and uncertainties we face due to competition in our industry.

Government Regulation

We are subject to extensive regulation by the FDA and other federal, state, and local regulatory agencies. The Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations set forth, among other things, requirements for the testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising and promotion of our products. In addition to FDA regulation, we are also subject to additional legal and regulatory requirements at both the federal and state levels in the United States. Our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in the EU are addressed in a centralized way through the EMA and the EC, but country-specific regulation by the competent authorities of the EU member states remains essential in many respects.

U.S. Regulation

In the United States, the FDA regulates drugs under the FDCA and its implementing regulations, including through review and approval of NDAs. NDAs require extensive studies and submission of a large amount of data by the applicant. There are also additional laws and regulations, administered by the FDA and other government agencies, that are applicable to the development, approval, manufacture, marketing, promotion, sale, pricing and distribution of drugs.

Drug Development

Preclinical Testing. Before testing any compound in human subjects in the United States, a company must generate extensive preclinical data. Preclinical testing generally includes laboratory evaluation of product chemistry and formulation, as well as toxicological and pharmacological studies in several animal species to assess the quality and safety of the product. Animal studies must be performed in compliance with the FDA's Good Laboratory Practice regulations and the U.S. Department of Agriculture's Animal Welfare Act.

IND Application. Human clinical trials in the United States cannot commence until an IND application is submitted and becomes effective. A company must submit preclinical testing results to the FDA as part of the IND application, and the FDA must evaluate whether there is an adequate basis for testing the drug in initial clinical studies in human volunteers. Unless the FDA raises concerns, the IND application becomes effective 30 calendar days following its receipt by the FDA. Once human clinical trials have commenced, the FDA may stop the clinical trials by placing them on "clinical hold" because of concerns about the safety of the product being tested, or for other reasons.

Clinical Trials. Clinical trials involve the administration of the drug to healthy human volunteers or to patients, under the supervision of a qualified investigator. The conduct of clinical trials is subject to extensive regulation, including compliance with the FDA's bioresearch monitoring regulations and Good Clinical Practice, or GCP, requirements, which establish standards for conducting, recording data from and reporting the results of, clinical trials, and are intended to assure that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected. Clinical trials must be conducted under protocols that detail the study objectives, parameters for monitoring safety, and the efficacy criteria, if any, to be evaluated. Each protocol is reviewed by the FDA as part of the IND application. In addition, each clinical trial must be reviewed, approved, and conducted under the auspices of an institutional review board, or IRB, at the institution conducting the clinical trial. Companies sponsoring the clinical trials, investigators, and IRBs also must comply with

regulations and guidelines for obtaining informed consent from the study subjects, complying with the protocol and investigational plan, adequately monitoring the clinical trial and timely reporting adverse events. Foreign studies conducted under an IND application must meet the same requirements that apply to studies being conducted in the United States. Data from a foreign study not conducted under an IND application may be submitted in support of an NDA if the study was conducted in accordance with GCP and the FDA is able to validate the data.

A study sponsor is required to submit certain details about active clinical trials and clinical trial results to the National Institutes of Health for public posting on http://clinicaltrials.gov. Human clinical trials typically are conducted in three sequential phases, although the phases may overlap with one another:

- Phase 1 clinical trials include the initial administration of the investigational drug to humans, typically to a small group of healthy human subjects, but occasionally to a group of patients with the targeted disease or disorder. Phase 1 clinical trials generally are intended to determine the metabolism and pharmacologic actions of the drug, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness.
- Phase 2 clinical trials generally are controlled studies that involve a relatively small sample of the intended patient population, and are designed to develop data regarding the product's effectiveness, to determine dose response and the optimal dose range and to gather additional information relating to safety and potential adverse effects.
- Phase 3 clinical trials are conducted after preliminary evidence of effectiveness has been obtained, and are intended to gather the additional information about safety and effectiveness necessary to evaluate the drug's overall risk-benefit profile, and to provide a basis for physician labeling. Generally, Phase 3 clinical development programs consist of expanded, large-scale studies of patients with the target disease or disorder to obtain statistical evidence of the efficacy and safety of the drug, or the safety, purity, and potency of a biological product, at the proposed dosing regimen.

The sponsoring company, the FDA or the IRB may suspend or terminate a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Further, success in early-stage clinical trials does not assure success in later-stage clinical trials. Data obtained from clinical activities are not always conclusive and may be subject to alternative interpretations that could delay, limit or prevent regulatory approval.

The FDA and IND application sponsor may agree in writing on the design and size of clinical trials intended to form the primary basis of an effectiveness claim in an NDA application. This process is known as a Special Protocol Assessment, or SPA. These agreements may not be changed after the clinical trials begin, except in limited circumstances. The existence of a SPA, however, does not assure approval of a product candidate. For additional information relating to drug development, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Drug Approval

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical trials, together with other detailed information, including information on the manufacture and composition of the investigational product, are submitted to the FDA in the form of an NDA requesting approval to market the product for one or more indications. The testing and approval process requires substantial time, effort and financial resources. Submission of an NDA requires payment of a substantial review user fee to the FDA. The FDA will review the application and may deem it to be inadequate to support commercial marketing, and there can be no assurance that any product approval will be granted on a timely basis, if at all. The FDA may also seek the advice of an advisory committee, typically a panel of clinicians practicing in the field for which the product is intended, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee. Companies are not permitted to market drugs in the United States until receiving approval of an NDA or BLA from the FDA.

The FDA has various programs, including breakthrough therapy, fast track, priority review and accelerated approval, that are intended to expedite or simplify the process for reviewing drugs and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that may be eligible for one or more of these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that provide meaningful benefit over existing treatments.

Before approving a NDA, the FDA usually will inspect the facility or the facilities where the product is manufactured, tested and distributed and will not approve the product unless cGMP compliance is satisfactory. If the FDA evaluates the NDA and the manufacturing facilities as acceptable, the FDA may issue an approval letter, or in some cases, a complete response letter. A complete response letter contains a number of conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter. The

approval letter authorizes commercial marketing of the drug for specific indications. As a condition of approval, the FDA may require post-marketing testing and surveillance to monitor the product's safety or efficacy, or impose other post-approval commitment conditions.

In some circumstances, post-marketing testing may include post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, which are used primarily to gain additional experience from the treatment of patients in the intended population, particularly for long-term safety follow-up. In addition, the FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, to ensure that the benefits outweigh the risks. A REMS can include medication guides, physician communication plans and elements to assure safe use, such as restricted distribution methods, patient registries or other risk mitigation tools.

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes or making certain additional labeling claims, are subject to further FDA review and approval. Obtaining approval for a new indication generally requires that additional clinical trials be conducted. For additional information relating to drug development, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Post-Approval FDA Requirements

Holders of an approved NDA are required to: (i) report certain adverse reactions to the FDA; (ii) comply with certain requirements concerning advertising and promotional labeling for their products; and (iii) continue to have quality control and manufacturing procedures conform to cGMP after approval. The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing and distribution facilities; this latter effort includes assessment of compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in the area of production, quality control and distribution to maintain cGMP compliance. Future FDA inspections may identify compliance issues at manufacturing facilities that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal of the product from the market. Failure to comply with applicable U.S. requirements may subject us to administrative or judicial sanctions, such as clinical holds, FDA refusal to approve pending NDAs or supplemental applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution. For additional information relating to post-approval requirements, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Advertising and Promotion

Under the FDCA and other laws, we are prohibited from promoting our products for off-label uses, or uses not approved by the FDA. This means that in the U.S., we may not make claims about the safety or effectiveness of our products and may not proactively discuss or provide information on the uses of our products that are not approved by the FDA, unless otherwise allowed by the FDA by policy or other guidance. Marketing of prescription drugs is also subject to additional laws and regulations through federal and state agencies tasked with consumer protection. After approval in the U.S., we must comply with these law and regulations, as well as FDA's regulation of drug promotion and advertising, including restrictions on off-label promotion. For additional information relating to restrictions related to advertising and promotion, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Health Care Fraud and Abuse

As a result of approval for VONJO in the United States, our operations and business arrangements with third-parties (including but not limited to researchers, healthcare professionals, consultants, payors, and customers) are subject to additional healthcare laws, regulations and enforcement by federal and state governments in the United States. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, price reporting, and physician sunshine laws.

Anti-Kickback Laws

The Anti-Kickback Statute prohibits companies and individuals from offering, paying, soliciting, or receiving remuneration to induce or reward referrals of business that will be paid for by federal health care programs, such as Medicare and Medicaid. We are also required to comply with other state anti-kickback statutes and other limitations on gifts and payments to physicians and reporting of payments to certain third parties, among other requirements. Failure to abide by anti-kickback statutes can result in civil and criminal enforcement actions and/or sanctions. Likewise, federal and state false claims laws, including the federal False Claims Act and similar state statutes, prohibit knowingly submitting, or causing to be submitted, false claims or false or fraudulent statements material to a false claim to government health care programs. Pharmaceutical companies are frequent targets of false claims lawsuits, which may result in treble damages, penalties, and

potential exclusion from participation in government healthcare programs. The civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Anti-kickback laws, false claims laws, and civil monetary penalty statutes often overlap and may also be enforced in conjunction. For additional information relating to our obligations under health care fraud and abuse laws, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act of 1977, or FCPA, and similar worldwide anti-bribery laws in non-U.S. jurisdictions generally prohibit companies and their intermediaries from making improper payments to non-U.S. officials for the purpose of obtaining or retaining business. The United States Department of Justice and Securities and Exchange Commission jointly enforce the FCPA, and those agencies have, in recent years, emphasized FCPA enforcement against pharmaceutical companies. In some countries, we may interact with health care professionals or other officials that meet the definition of a foreign government official for the purposes of the FCPA. We are subject to the FCPA's prohibitions against unauthorized payments or offers of payments by our employees or agents. If we were determined to have violated the FCPA, we could be subject to substantial fines, penalties, and other legal or equitable sanctions. For additional information relating to our obligations under the FCPA and anti-bribery laws, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Third-Party Reimbursement

The coverage and reimbursement status of VONJO is subject to significant uncertainty. Sales of and revenue from VONJO will depend on coverage and reimbursement decisions by third-party payors, including government health programs, managed care organizations, and private health insurers. Prices at which we or our customers seek reimbursement for VONJO can be subject to challenge, reduction, or denial by payors. Government health programs, private insurers, are increasingly trying to reduce the costs of pharmaceuticals, and any future legislative, regulatory, or contractual developments could affect the coverage and reimbursement status of VONJO. For additional information relating to product reimbursement, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Data Privacy and Protection

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, or HITECH, and implementing regulations, create requirements relating to the privacy and security of individually identifiable health information. HIPAA regulations govern the manner in which certain health information may be used and disclosed, and require the adoption of administrative, physical, and technical safeguards to protect such information. HIPAA and HITECH requirements are applicable to covered entities, which are (1) health plans, (2) health care clearinghouses, and (3) health care providers who electronically transmit certain health information. Those requirements are also applicable, in many instances, to business associates of covered entities. In some cases, depending on our business operations and contractual agreements, including through the conduct of clinical trials, we are subject to HIPPA requirements. Non-compliance with these laws and regulations can result in significant fines, penalties, damages, loss of goodwill or business opportunities, and reputational harm. There are also additional federal, state, and local privacy laws and regulations in the U.S. that may apply to us now or in the future and that require that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, in June 2018, California enacted the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020. The law requires businesses collecting information about California consumers to disclose what personal information is collected about a consumer and the purposes for which that personal information is used, disclose what personal information is sold or shared for a business purpose, and to whom, and delete information or stop selling such information upon request (subject to exceptions). For additional information relating to our obligations under data privacy laws, see Part I, Item 1A, "Risk Factors" in this Annual Report on Form 10-K.

Non-U.S. Regulation

Before our medicinal products can be marketed outside of the United States, they must be subject to regulatory approval similar to that required in the United States. The requirements governing the conduct of clinical trials, including requirements to conduct additional clinical trials, product licensing, safety reporting, post-authorization requirements, marketing and promotion, interactions with healthcare professionals, pricing and reimbursement may vary widely from country to country. No action can be taken to market any product in a country until an appropriate approval application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain countries, the sales price of a product must also be approved. The pricing

review period often begins after market approval is granted. Even if a product is approved by a regulatory authority, satisfactory prices may not be approved for such product.

Conduct of clinical trials in the European Union

Similar to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls. The conduct of clinical trials is currently governed by the EU Clinical Trials Directive 2001/20/EC, or Clinical Trials Directive, and will be replaced by the EU Clinical Trials Regulation (EU) No. 536/2014, or CTR, once the latter comes into effect. The CTR introduces a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU. It entered into force on January 31, 2022.

Under the current regime, which will expire after a transition period of one or three years, as outlined below in more detail, before a clinical trial can be initiated, it must be approved in each EU Member State where the trial is to be conducted. The approval must be obtained from two separate entities: the National Competent Authority, or NCA, and one or more Ethics Committees. The NCA of the EU Member States in which the clinical trial will be conducted must authorize the conduct of the trial, and the independent Ethics Committee must grant a positive opinion in relation to the conduct of the clinical trial in the relevant EU Member State before the commencement of the trial. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be submitted to or approved by the relevant NCA and Ethics Committees. Under the current regime, all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the NCA and to the Ethics Committees of the EU Member State where they occur.

A more unified procedure will apply under the new CTR. A sponsor will be able to submit a single application for approval of a clinical trial through a centralized EU clinical trials portal. One national regulatory authority (the reporting EU Member State proposed by the applicant) will take the lead in validating and evaluating the application and consult and coordinate with the other concerned EU Member States. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned EU Member States. However, a concerned EU Member State may in limited circumstances declare an “opt-out” from an approval and prevent the clinical trial from being conducted in such EU Member State. The CTR also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database. After several postponements of the effectiveness of the CTR due to technical difficulties with the underlying IT systems, the “go live” of these systems and, accordingly, the coming into force of the regulation, is planned for January 31, 2022. While EU Member States will work in the Clinical Trials Information System, or CTIS, immediately after the system has gone live, the CTR provides for two transition periods for sponsors: For one year, until January 31, 2023, clinical trial sponsors can still choose whether to submit an initial clinical trial application in line with the current system (Clinical Trials Directive) or via CTIS. After January 31, 2023, submission of initial clinical trial applications via CTIS becomes mandatory, and by January 31, 2025, all ongoing trials approved under the current Clinical Trials Directive will be governed by the new Regulation and have to be transitioned to CTIS.

Under both the current regime and the new CTR, national laws, regulations, and the applicable GCP and Good Laboratory Practice standards must also be respected during the conduct of the trials, including the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use guidelines on GCP and the ethical principles that have their origin in the Declaration of Helsinki.

During the development of a medicinal product, the European Medical Agency, or EMA, and national regulators within the EU provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Committee for Medicinal Products for Human Use, or CHMP, on the recommendation of the Scientific Advice Working Party. A fee is incurred with each scientific advice procedure, but is significantly reduced for designated orphan medicines. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application, or MAA, of the product concerned.

In the EU, companies developing a new medicinal product are obligated to study their product in children and must therefore submit a Pediatric Investigation Plan, or PIP, together with a request for agreement to the EMA. The EMA issues a decision on the PIP based on an opinion of the EMA’s Pediatric Committee. Companies must conduct pediatric clinical trials in accordance with the PIP approved by the EMA, unless a deferral (e.g., until enough information to demonstrate its effectiveness and safety in adults is available) or waiver (e.g., because the relevant disease or condition occurs only in adults) has been granted by the EMA. The MAA for the medicinal product must include the results of all pediatric clinical trials performed and details of all information collected in compliance with the approved PIP, unless a waiver or a deferral has been granted, in

which case the pediatric clinical trials may be completed at a later date. Medicinal products that are granted a marketing authorization, or MA, on the basis of the pediatric clinical trials conducted in accordance with the approved PIP are eligible for a six-month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) or, in the case of orphan medicinal products, a two-year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the approved PIP are developed and submitted. An approved PIP is also required when a MA holder wants to add a new indication, medicinal form or route of administration for a medicine that is already authorized and covered by intellectual property rights.

Marketing authorization procedures in the European Union and post-marketing obligations

In the EU and in Iceland, Norway and Liechtenstein (together, the European Economic Area, or EEA), medicinal products may only be placed on the market after a related MA has been granted. MAs for medicinal products can be obtained through several different procedures founded on the same basic regulatory process. These are through the centralized procedure, the mutual recognition procedure, the decentralized procedure, or a national procedure (for medicinal products sold in a single EU Member State only). The centralized procedure provides for the grant of a single MA by the EC that is valid for all EU Member States and, after respective national implementing decisions, in the three additional EEA countries. The centralized procedure is mandatory for certain medicinal products, including for medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products, or ATMP, and medicinal products with a new active substance indicated for the treatment of certain diseases (AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). It is optional for medicinal products containing a new active substance that is not yet authorized in the EEA, and for medicinal products that constitute significant therapeutic, scientific or technical innovations, or for which grant of a MA through the centralized procedure would be in the interest of patients or animal health at EU level. The centralized procedure allows a company to submit a single application to the EMA which will provide a positive opinion regarding the application if it meets certain quality, safety, and efficacy requirements. Based on the positive opinion of the CHMP at EMA, the EC has final authority for granting the MA within 67 days after receipt of the CHMP opinion to grant a centralized MA which is valid in all 28 EU Member States and three of the four European Free Trade Association, or EFTA countries (Iceland, Liechtenstein and Norway).

The decentralized authorization procedure permits companies to file identical MAAs to the competent authorities in several EU Member States simultaneously if such a medicinal product has not received marketing approval in any EU Member State before. This procedure is available for medicinal products not falling within the mandatory scope of the centralized procedure. The competent authority of a single EU Member State, known as the Reference EU Member State, is appointed to review the application and provide an assessment report. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference EU Member State and concerned EU Member States. The reference EU Member State prepares a draft assessment report and drafts of the related materials within 120 days after receipt of a valid application. The competent authorities of the other EU Member States, the concerned member states, are subsequently required to grant MA for their territories on the basis of this assessment. If an EU Member State cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the EC, whose decision is binding for all EU Member States.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States. The national MA procedure is founded on the same basic EU regulatory process as the other MA procedures discussed herein. The national MA procedure, which is increasingly rare, permits a company to submit an application to the competent authority of a single EU Member State and, if successful, to obtain a MA that is valid only in this EU Member State.

The initial MA granted in the EU is valid for five years. The authorization may be renewed and remain valid for an unlimited period unless the national competent authority or the EC decides on justified grounds to proceed with one additional five year renewal period; applications for renewal must be made to the EMA at least nine months before the five-year period expires. The renewal of a MA is subject to a re-evaluation of the risk-benefit balance of the product by the national competent authorities or the EMA.

Similar to accelerated approval regulations in the United States, conditional MAs can be granted in the EU by the EC in exceptional circumstances. A conditional MA can be granted for medicinal products where, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, a number of criteria are fulfilled; (i) the benefit/risk balance of the product is positive, (ii) it is likely that the applicant will be in a position to provide the comprehensive clinical data, (iii) unmet medical needs will be fulfilled by the grant of the MA and (iv) the benefit to public

health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional MA must be renewed annually.

As in the United States, it may be possible to obtain a period of market and/or data exclusivity in the EU that would have the effect of postponing the entry into the marketplace of a competitor's generic, hybrid or biosimilar product (even if the medicinal product has already received a MA) and prohibiting another applicant from relying on the MA holder's pharmacological, toxicological and clinical data in support of another MA for the purposes of submitting an application, obtaining MA or placing the product on the market. New chemical entities, or NCE, approved in the EU qualify for eight years of data exclusivity and 10 years of marketing exclusivity.

An additional non-cumulative one-year period of marketing exclusivity is possible if, during the data exclusivity period (the first eight years of the 10-year marketing exclusivity period), the MA holder obtains an authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies.

The data exclusivity period begins on the date of the product's first MA in the EU. After eight years, a generic product application may be submitted and generic companies may rely on the MA holder's data. However, a generic product cannot launch until two years later (or a total of 10 years after the first MA in the EU of the innovator product), or three years later (or a total of 11 years after the first MA in the EU of the innovator product) if the MA holder obtains MA for a new indication with significant clinical benefit within the eight-year data exclusivity period. Additionally, another noncumulative one-year period of data exclusivity can be added to the eight years of data exclusivity where an application is made for a new indication for a well-established substance, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication. Another year of data exclusivity may be added to the eight years, where a change of classification of a medicinal product has been authorized on the basis of significant pre-trial tests or clinical trials (when examining an application by another applicant for or holder of market authorization for a change of classification of the same substance the competent authority will not refer to the results of those tests or trials for one year after the initial chance was authorized).

Products may not be granted data exclusivity since there is no guarantee that a product will be considered by the EU's regulatory authorities to include a NCE. Even if a compound is considered to be a NCE and the MA applicant is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the medicinal product if such company can complete a full MA application with their own complete database of pharmaceutical tests, preclinical studies and clinical trials and obtain MA of its product.

PRIME Designation

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies on the basis of compelling non-clinical data and tolerability data from initial clinical trials. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MA application assessment once a dossier has been submitted. Importantly, once a candidate medicine has been selected for the PRIME scheme, a dedicated contact point and rapporteur from the CHMP or from CAT are appointed facilitating increased understanding of the product at EMA's committee level. A kick-off meeting with the CHMP/CAT rapporteur initiates these relationships and includes a team of multidisciplinary experts to provide guidance on the overall development plan and regulatory strategy. PRIME eligibility does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval.

Pricing and reimbursement in the European Union

Even if a medicinal product obtains a MA in the EU, there can be no assurance that reimbursement for such product will be secured on a timely basis or at all. The EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of medicinal products for human use. An EU Member State may approve a specific price or level of reimbursement for the medicinal product, or alternatively, may adopt a system of direct or indirect controls on the profitability of the company responsible for placing the medicinal product on the market, including volume-based arrangements, caps and reference pricing mechanisms.

Reference pricing used by various EU Member States and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical study or other

studies that compare the cost-effectiveness of our product candidates, if any, to other available therapies in order to obtain or maintain reimbursement or pricing approval. There can be no assurance that any country that has price controls or reimbursement limitations for medicinal products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, medicinal products launched in the EU do not follow price structures of the United States and generally published and actual prices tend to be significantly lower. Publication of discounts by third party payers or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries.

The so-called health technology assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including France, Germany, Ireland, Italy and Sweden. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact, and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the regulatory authorities of individual EU Member States. A negative HTA of one of our products by a leading and recognized HTA body could not only undermine our ability to obtain reimbursement for such product in the EU Member State in which such negative assessment was issued, but also in other EU Member States. For example, EU Member States that have not yet developed HTA mechanisms could rely to some extent on the HTA performed in other countries with a developed HTA framework, when adopting decisions concerning the pricing and reimbursement of a specific medicinal product.

On January 31, 2018, the EC adopted a proposal for a regulation on HTA. This legislative proposal is intended to boost EU-level cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The proposal provides that EU Member States will be able to use common HTA tools, methodologies and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement. While EU Member States could choose to delay participation in the joint work until three years after the rules enter into force, it would become mandatory after six years. The EC has stated that the role of the draft HTA regulation is not to influence pricing and reimbursement decisions in the individual EU Member States, but there can be no assurance that the draft HTA regulation will not have effects on pricing and reimbursement decisions. The HTA entered into force on January 11, 2022 and applies as of January 2025 followed by a further three-year transitional period during which EU member states must fully adapt to the new system.

To obtain reimbursement or pricing approval in some countries, including the EU Member States, we may be required to conduct studies that compare the cost-effectiveness of our product candidates to other therapies that are considered the local standard of care. There can be no assurance that any country will allow favorable pricing, reimbursement and market access conditions for any of our products, or that it will be feasible to conduct additional cost-effectiveness studies, if required.

In certain of the EU Member States, medicinal products that are designated as orphan medicinal products may be exempted or waived from having to provide certain clinical, cost-effectiveness and other economic data in connection with their filings for pricing/reimbursement approval.

Post-Approval Regulation

Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the EC and/or the competent regulatory authorities of the individual EU Member States. This oversight applies both before and after grant of manufacturing licenses and MAs. It includes control of compliance with EU good manufacturing practice, or GMP, rules, manufacturing authorizations, pharmacovigilance rules and requirements governing advertising, promotion, sale, and distribution, recordkeeping, importing and exporting of medicinal products.

Failure by us or by any of our third-party partners, including suppliers, manufacturers and distributors to comply with EU laws and the related national laws of individual EU Member States governing the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of MA, statutory health insurance, bribery and anti-corruption or other applicable regulatory requirements may result in administrative, civil or criminal

penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

The holder of a MA for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. These pharmacovigilance rules can impose on holders of MAs the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed medicinal products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies or post-authorization safety studies to obtain further information on a medicine's safety, or to measure the effectiveness of risk-management measures, which may be time consuming and expensive and could impact our profitability. MA holders must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of Periodic Safety Update Reports, or PSURs, in relation to medicinal products for which they hold MAs. The EMA reviews PSURs for medicinal products authorized through the centralized procedure. If the EMA has concerns that the risk benefit profile of a product has varied, it can adopt an opinion advising that the existing MA for the product be suspended, withdrawn or varied. The agency can advise that the MA holder be obliged to conduct post-authorization Phase IV safety studies. If the EC agrees with the opinion, it can adopt a decision varying the existing MA. Failure by the MA holder to fulfill the obligations for which the EC's decision provides can undermine the ongoing validity of the MA.

More generally, non-compliance with pharmacovigilance obligations can lead to the variation, suspension or withdrawal of the MA for the product or imposition of financial penalties or other enforcement measures.

The manufacturing process for medicinal products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the EC guidelines for GMP. These requirements include compliance with EU GMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Similarly, the distribution of medicinal products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States. The manufacturer or importer must have a qualified person who is responsible for certifying that each batch of product has been manufactured in accordance with GMP, before releasing the product for commercial distribution in the EU or for use in a clinical trial. Manufacturing facilities are subject to periodic inspections by the competent authorities for compliance with GMP.. Companies may be subject to civil, criminal or administrative sanctions. These include suspension of manufacturing authorization in case of non-compliance with the EU or EU Member States' requirements governing the manufacturing of medicinal products.

Sales and Marketing Regulations

In the EU, the advertising and promotion of our products are also subject to EU laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other national legislation of individual EU Member States may apply to the advertising and promotion of medicinal products and may differ from one country to another. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent regulatory authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the MA granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. All advertising and promotional activities for the product must be consistent with the approved SmPC and therefore all off-label promotion is prohibited in the EU. Direct-to-consumer advertising of prescription-only medicines is also prohibited in the EU. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with healthcare professionals.

Anti-Corruption Legislation

Our business activities outside of the United States are subject to anti-bribery or anti-corruption laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct or rules of other countries in which we operate, including the U.K. Bribery Act of 2010.

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

Data Privacy and Protection

The collection and use of personal health data and other personal information in the EU is governed by the provisions of the European General Data Protection Regulation (EU) 2016/679, or GDPR, which came into force in May 2018, and related implementing laws in individual EU Member States.

The GDPR imposes a number of strict obligations and restrictions on the ability to process (processing includes collection, analysis and transfer of) personal data of individuals within the EU and in the EEA, including health data from clinical trials and adverse event reporting. The GDPR also includes requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals prior to processing their personal data or personal health data, notification of data processing obligations to the national data protection authorities, and the security and confidentiality of the personal data. EU Member States may also impose additional requirements in relation to health, genetic and biometric data through their national implementing legislation.

Under the GDPR, personal data can only be transferred within the EU Member States and the three additional EEA countries (Norway, Iceland and Liechtenstein) that have adopted a national law implementing the GDPR. Appropriate safeguards are required to enable cross-border transfers of personal data from the EU and EEA countries to a "third country" (a country outside the EU or EEA). This status has a number of significant practical consequences, in particular for international data transfers, competent supervisory authorities and enforcement of the GDPR.

In conclusion, the GDPR prohibits the transfer of personal data to countries outside of the EU/EEA (including the United States) that are not considered by the EC to provide an adequate level of data protection, except if the data controller meets very specific requirements such as the use of standard contractual clauses, or SCCs, issued by the EC. In this respect, recent legal developments in Europe have created complexity and compliance uncertainty regarding certain transfers of personal data from the EU/EEA. For example, following the Schrems II decision of the Court of Justice of the EU on July 16, 2020, in which the Court invalidated the Privacy Shield under which personal data could be transferred from the EU/EEA to United States entities who had self-certified under the Privacy Shield scheme, there is uncertainty as to the general permissibility of international data transfers under the GDPR. The Court did not invalidate the then-current SCCs, but ruled that data exporters relying on these SCCs are required to verify, on a case-by-case basis, if the law of the third country ensures an adequate level of data protection that is essentially equivalent to that guaranteed in the EU/EEA. In light of the implications of this decision, we may face difficulties regarding the transfer of personal data from the EU/EEA to third countries. However, on June 4, 2021 the EC issued a new set of SCCs for data transfers from controllers or processors in the EU/EEA to controllers or processors established outside the EU/EEA. These SCCs replace the old sets of SCCs that were adopted under the previous European Data Protection Directive 95/46. Since September 27, 2021, it is no longer possible to conclude contracts incorporating these previous versions of the SCCs. In addition, for contracts concluded before September 27, 2021, it is still possible to rely on the previous SCCs until the end of an additional 15 months transitional period (until December 27, 2022), provided that the processing operations which are the subject matter of the contract remain unchanged and reliance on previous SCCs ensures that the transfer is subject to appropriate safeguards. On November 11, 2021, the European Data Protection Board adopted recommendations on such appropriate safeguards that supplement transfer mechanisms. These recommendations aim to assist data exporters with their duty to identify and implement appropriate supplementary measures where they are needed to ensure an essentially equivalent level of protection to the personal data they transfer to third countries.

The GDPR also regulates our response in the event of a data breach impacting any personal data we process, whether on our or our vendors' systems. In addition to the disruptions to our business and impact to our reputation that any such security incident could cause, we may be subject to regulatory fines, class actions, or other costly measures if there is a security breach on our or our vendors' systems. We maintain cyber-liability insurance, however, that insurance may be insufficient to fully cover the losses associated with such a breach, including any resulting regulatory fines

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States may result in significant monetary fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater, other administrative penalties and a number of criminal offenses (punishable by uncapped fines) for organizations and, in certain cases, their directors and officers, as well as civil liability claims from individuals whose personal data was processed. Data protection authorities from the different EU Member States may still implement certain variations, enforce the GDPR and national data protection laws differently, and introduce additional national regulations and guidelines, which adds to the complexity of processing personal data in the EU. Guidance developed at both the EU level and at the national level in individual EU Member States concerning implementation and compliance practices are often updated or otherwise revised.

Furthermore, there is a growing trend towards the required public disclosure of clinical trial data in the EU, which adds to the complexity of obligations relating to processing health data from clinical trials. Such public disclosure obligations are provided in the new EU CTR, EMA disclosure initiatives and voluntary commitments by industry. Failing to comply with these obligations could lead to government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business and operating results. The uncertainty regarding the interplay between different regulatory frameworks, such as the CTR and the GDPR, further adds to the complexity that we face with regard to data protection regulation.

With regard to the transfer of data from the EU to the United Kingdom, or UK, the EU-UK Trade and Cooperating Agreement, or TCA, provided for a transition period of up to six months as of January 1, 2021 to enable the EC to complete its adequacy assessment of the UK's data protection laws. On June 28, 2021 the EC adopted two adequacy decisions for the UK – one under the GDPR and the other for the Law Enforcement Directive. Personal data may now freely flow from the EU to the UK since the UK is deemed to have an adequate data protection level. Additionally, following the UK's withdrawal from the EU and the EEA, companies also have to comply with the UK's data protection laws (including the UK GDPR, which is based on the EU GDPR), the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The adequacy decisions include a 'sunset clause' which entails that the decisions will automatically expire four years after their entry into force.

Other Markets (UK)

The UK formally left the EU on January 31, 2020 and the transition period, during which EU laws continued to apply to the UK, expired on December 31, 2020. This means EU laws now only apply to the UK in respect of Northern Ireland as laid out in the Protocol on Ireland and Northern Ireland. Following the end of the transition period, the TCA applied provisionally from January 1, 2021 and entered into force on May 1, 2021.

The TCA includes provisions affecting the life sciences sector (including on customs and tariffs) but areas for further discussion between the EU and the UK remain. In addition, there are some specific provisions concerning pharmaceuticals. These include the mutual recognition of GMP and issued GMP documents. The TCA does not, however, contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards.

Since January 1, 2021, the EU laws which have been transposed into UK law through secondary legislation continue to be applicable in the UK as "retained EU law". As there is no general power to amend these regulations, the UK government has enacted the Medicines and Medical Devices Act 2021. The purpose of the act is to enable the existing regulatory frameworks in relation to human medicines, clinical trials of human medicines, veterinary medicines and medical devices to be updated. The powers under the act may only be exercised in relation to specified matters and must safeguard public health.

Specified provisions of the Medicines and Medical Devices Act 2021 entered into force on February 11, 2021. The remaining provisions came into effect within two months of February 11, 2021 or will otherwise come into effect as stipulated in subsequent statutory instruments. The Medicines and Medical Devices Act 2021 supplements the UK Medical Devices Regulations 2002, or UK Regulations, which are based on the EU Medical Devices Directive as amended to reflect the UK's post-Brexit regulatory regime. Notably, the UK Regulations do not include any of the revisions that have been made by the EU Medical Devices Regulation (EU) 2017/745, which, since May 26, 2021, now applies in all EU Member States.

The UK's Medicines and Healthcare products Regulatory Agency conducted a comprehensive consultation between September and November 2021 on proposals to develop a new UK regime for medical devices in the UK. The proposals include more closely aligning definitions for medical devices and in vitro medical devices with internationally recognised definitions and changing the classification of medical devices according to levels or risk. The proposals are intended to improve patient and public safety and increase the appeal of the UK market. The new regime is planned to come into force on July 1, 2023, which will align with the date from which the UK is due to stop accepting CE marked medical devices and require UK Conformity Assessed marking. It is envisaged that, in Northern Ireland, the amended regime could run in parallel with any existing or future EU rules in accordance with the Protocol on Ireland and Northern Ireland.

Consequences of Non-Compliance

Failure to comply with applicable requirements may subject us to administrative or judicial sanctions, such as clinical holds, refusal of regulatory authorities to approve or authorize pending product applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, financial penalties and/or criminal prosecution.

Environmental Regulation

In connection with our research and development activities, we are subject to federal, state and local laws, rules, regulations and policies, both internationally and domestically, governing the use, generation, manufacture, storage, air emission, effluent discharge, handling, treatment, transportation and disposal of certain materials, biological specimens and wastes and employee safety and health matters. Although we believe that we have complied with these laws, regulations and policies in all material respects and have not been required to take any significant action to correct any noncompliance, we may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the controlled use of hazardous materials, including, but not limited to, certain hazardous chemicals and radioactive materials. Although we believe that our safety procedures for handling and disposing of such materials comply with applicable law and regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability not covered by insurance could exceed our resources. See the risk factor, "*We may be subject to claims relating to improper handling, storage or disposal of hazardous materials*." in Part I, Item 1A, "Risk Factors" of this Annual Report on Form 10-K for additional information regarding the risks and uncertainties we face due to the use of hazardous materials.

Employees

As of December 31, 2021, we employed 124 individuals, 121 of whom were full-time. Of these employees, 24 were in research and development, 82 were in sales and marketing, and 18 were in business and administrative positions. Our employees do not have a collective bargaining agreement. We believe our relations with our employees are good.

Corporate Information

Our website address is located at www.ctibiopharma.com; however, the information in, or that can be accessed through, our website is not part of or incorporated by reference into this Annual Report on Form 10-K, and any references to our website are intended to be inactive textual references only provided for convenience. We make available free of charge on our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports, and other filings pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after each is electronically filed with, or furnished to, the SEC. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding reports that we file or furnish electronically with them at www.sec.gov.

This Annual Report on Form 10-K includes our trademarks and registered trademarks, including "CTI BioPharma." Each other trademark, trade name or service mark appearing in this Annual Report on Form 10-K belongs to its holder.

Item 1A. Risk Factors

This report contains forward-looking statements that involve risks and uncertainties. The occurrence of any of the risks described below and elsewhere in this document could materially adversely affect our business, financial condition, liquidity, operating results or prospects and the trading price of our securities. Additional risks and uncertainties that we do not presently know or that we currently deem immaterial may also harm our business, financial condition, liquidity, operating results and prospects and the trading price of our securities.

Risks Related to Our Business

We expect to continue to incur net losses, and we may never achieve profitability.

We were incorporated in 1991 and have incurred a net operating loss every year since our formation. As of December 31, 2021, we had an accumulated deficit of $2.4 billion, and we expect to continue to incur net losses. As part of our business plan, we will need to successfully commercialize our one product approved for commercialization, VONJO, continue to conduct research, development, testing and regulatory compliance activities with respect to pacritinib for additional indications and ensure the procurement of manufacturing and drug supply services for our commercial and drug development efforts, the costs of which, together with projected general and administrative expenses, is expected to result in operating losses for the foreseeable future. There can be no assurances that we will ever achieve profitability.

We have not generated any significant revenue from product sales and we may never be profitable.

We have one product approved for commercialization, VONJO, but have not generated any significant revenue from product sales. Our ability to generate significant revenue and achieve profitability depends on our ability, alone or with potential strategic collaboration partners, to successfully commercialize VONJO and to complete the development of, and obtain the regulatory and marketing approvals necessary to commercialize pacritinib for other indications. We do not anticipate generating significant revenue from product sales in the near future.

Obtaining regulatory approval requires substantial time, effort and financial resources, and without additional financing, we lack sufficient resources to pursue the development of pacritinib. Other than our Credit Agreement, we currently have no commitments or arrangements for any significant additional financing to fund the commercial launch of VONJO or the development of pacritinib for additional indications, and we will need to seek additional funding, which may not be available or may not be available on favorable terms. We could also seek another collaborative partnership for the additional development and commercialization of pacritinib, which may not be available on reasonable terms or at all. If we further partner pacritinib, we may have to relinquish valuable economic rights and would potentially forgo additional economic benefits that could be realized if we continued the development and commercialization activities alone.

We anticipate incurring significant costs associated with commercializing VONJO. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies, domestic or foreign, to change our manufacturing processes or assays, or to perform clinical, nonclinical, or other types of post-approval studies in addition to those that we currently anticipate. Our revenue from sales of VONJO will be dependent, in part, upon market size, the accepted price for the product, the approved indication(s), and the ability to obtain reimbursement at any price. If the number of our addressable patients is not as significant as we estimate or the reasonably accepted population for treatment is narrowed by competition, physician choice, or treatment guidelines, we may not generate significant revenue from sales of VONJO.

Our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 global pandemic, in regions where third parties on which we rely, such as Clinical Research Organizations, or CROs, have clinical trial sites or other business operations and may result in significant disruptions to our clinical trials, which could have a material adverse effect on our business.

Our business has been adversely affected and may continue to be adversely affected by the effects of health epidemics, including the ongoing worldwide COVID-19 pandemic, in regions where we are conducting the PACIFICA Phase 3 trial. The spread of this pandemic has caused significant volatility and uncertainty in U.S. and international markets and may disrupt our business and delay our clinical trials and timelines.

Quarantines, shelter-in-place and similar government orders have been enacted in each of the geographies in which we are conducting our clinical trials and such orders, shutdowns or other restrictions on the conduct of business operations could be reinstated, thereby further affecting our clinical trials. The patient populations that are eligible for our clinical trials are immunocompromised and are at higher risk for becoming infected with COVID-19. As COVID-19 affects the parts of the

world where we are conducting our clinical trials, and the patients involved with these clinical trials become infected with COVID-19, we may have more adverse events and deaths in our clinical trials as a result.

We have faced and may continue to face difficulties enrolling patients in our clinical trials as the patient populations that are eligible for our clinical trials are impacted by COVID-19. Patient enrollment may be further delayed due to the diversion of healthcare resources, such as hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, away from the conduct of clinical trials, toward the COVID-19 pandemic.

Additionally, if our clinical trial patients are unable to travel to our clinical trial sites as a result of quarantines or other restrictions resulting from COVID-19, we may experience higher drop-out rates or delays in our clinical trials. Similarly, we may struggle to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19. Any such delays in enrollment hinder our ability to obtain clinical data on the schedule we currently predict.

Travel restrictions continue to be implemented throughout the world in an effort to contain COVID-19, and several countries have expanded screenings of travelers.

We may experience additional disruptions due to the COVID-19 pandemic that could severely impact our business and clinical trials, including:

- delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruption in global shipping that may affect the transport of clinical trial materials;

- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;

- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;

- delays in necessary interactions with local regulators, ethics committees, and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;

- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;

- refusal of the FDA to accept data from clinical trials in affected geographies; and

- interruption or delays to our sourced discovery and clinical activities.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The global pandemic of COVID-19 has been ongoing for two years and continues to rapidly evolve. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, any one or a combination of these events could have an adverse effect on the operation of and results from our clinical trials or our general business operations.

We face direct and intense competition from our competitors in the biotechnology and pharmaceutical industries, and we may not compete successfully against them.

Competition in the oncology market is intense and is accentuated by the rapid pace of technological and product development. We anticipate that we will face increased competition in the future as new companies enter the market. Our

competitors in the United States and elsewhere are numerous and include, among others, major multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions. See “Part I, Item 1, “Competition” in this Annual Report on Form 10-K for information on our specific competitors. In addition to the specific competitive factors discussed above, new anti-cancer drugs or drugs for the treatment of COVID-19 that may be under development or developed and marketed in the future could compete with our various compounds.

Many of our competitors, particularly multinational pharmaceutical companies, either alone or together with their collaborators, have substantially greater financial and technical resources and substantially larger development and marketing teams than us, as well as significantly greater experience than we do in developing, commercializing, manufacturing, marketing and selling products. As a result, products of our competitors might come to market sooner or might prove to be more effective, less expensive, have fewer side effects or be easier to administer than ours. In any such case, sales of any potential future product would likely suffer and we might never recoup the significant investments we have made and will continue to make to develop and market these compounds.

We have limited experience in generating revenue from product sales.

Our ability to generate significant revenue from product sales depends on our ability, alone or with strategic collaboration partners, to successfully commercialize VONJO and obtain the regulatory and marketing approvals necessary to commercialize pacritinib for other indications. We currently have limited commercialization expertise, including sales, marketing, or distribution capabilities, and VONJO may not remain in the market for a number of reasons, including ineffectiveness, harmful side effects, difficulty in scaling manufacturing, political and legislative changes, or competition from existing future alternatives. Our ability to generate substantial future revenue from product sales depends heavily on our success in many areas, including, but not limited to:

- developing a sustainable manufacturing process for VONJO and establishing and maintaining supply and manufacturing relationships with third parties that can conduct the processes and provide adequate (in amount and quality) product supply to support market demand for VONJO;
- launching and commercializing VONJO;
- obtaining market acceptance of VONJO;
- obtaining adequate market share, reimbursement and pricing for VONJO;
- our ability to find patients so they can be diagnosed and begin receiving treatment;
- addressing any competing technological and market developments;
- negotiating favorable terms, including commercial rights, in any collaboration, licensing, or other arrangements into which we may enter, any amendments thereto or extensions thereof;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how; and
- attracting, hiring, and retaining qualified personnel.

If the number of our addressable patients is not as significant as we estimate or the reasonably accepted population for treatment is narrowed by competition, physician choice, or treatment guidelines, we may not generate significant revenue from sales of VONJO.

Failure to comply with regulatory requirements or unanticipated problems with VONJO may result in various adverse actions such as the suspension or withdrawal of VONJO, closure of a facility or enforcement of substantial penalties or fines.

Regulatory agencies will subject any marketed product(s), as well as the manufacturing facilities, to continual review and periodic inspection. If previously unknown problems with a product or with regulatory requirements are discovered, such as adverse events of unanticipated severity or frequency, serious or unexpected side effects or other safety risks, problems with a manufacturing process or laboratory facility, or failure to comply with applicable regulatory approval requirements, a regulatory agency may impose restrictions or penalties on that product or on us. Such restrictions or penalties may include, among other things:

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

We will need to raise additional funds to operate our business, but additional funds may not be available on acceptable terms, or at all. Any inability to raise required capital when needed could harm our liquidity, financial condition, business, operating results and prospects.

We have substantial operating expenses associated with the commercialization of VONJO and the development of pacritinib in other indications, and we have significant contractual payment obligations under the debt and lease arrangements. In addition, we believe that our present financial resources will only be sufficient to fund our operations into the fourth quarter of 2022. This raises substantial doubt about our ability to continue as a going concern and we will need to raise substantial additional capital in the near term in order to fund our operations through and beyond the fourth quarter of 2022 and to continue as a going concern thereafter. See Note 1 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information on our assessment. Uncertainty regarding our ability to continue as a going concern could also have a material and adverse impact on the price of our common stock, which could negatively impact our ability to raise sufficient funds for our operations and continue as a going concern. In addition, cash forecasts and capital requirements are subject to change as a result of a variety of risks and uncertainties. Developments in and expenses associated with our commercialization activities and with our clinical trials and other research and development activities may consume capital resources earlier than planned. Due to these and other factors, forecasts for any periods in which we indicate that we expect to have sufficient resources to fund our operations, as well as any other operational or business projection we have disclosed, or may disclose, may not be achieved.

We will need to acquire additional funds in order to develop our business, continue the commercialization of VONJO and conduct research and development for pacritinib in other indications. We may seek to raise such capital through public or private equity financings, partnerships, collaborations, joint ventures, disposition of assets, debt financings or restructurings, bank borrowings or other sources of financing. However, our ability to raise capital is subject to a number of risks, uncertainties, constraints and consequences. For these and other reasons, additional funding may not be available on favorable terms or at all. If we raise additional funds by issuing equity or equity-linked securities, our stockholders may experience dilution. If we fail to obtain additional capital when needed, we may be required to delay, scale back or eliminate some or all of our research and development programs, reduce our selling, general and administrative expenses, be unable to attract and retain highly qualified personnel, refrain from making our contractually required payments when due (including debt payments) and/or be forced to cease operations, liquidate our assets and possibly seek bankruptcy protection. Any of these consequences could harm our business, financial condition, operating results and prospects.

We are dependent on third-party service providers for a number of critical operational activities. Any failure or delay in these undertakings by third parties could harm our business.

Our business is dependent on the performance by third parties of their responsibilities under contractual relationships. In particular, we rely heavily on third parties for the manufacture and testing of our compounds. We do not have internal analytical laboratory or manufacturing facilities to allow for the testing or production of our compounds in compliance with Good Laboratory Practices, or GLP, and current Good Manufacturing Practices, or cGMP. As a result, we rely on third parties to supply us in a timely manner with manufactured products or product candidates in a manner that is compliant with these standards. We may not be able to adequately manage and oversee the manufacturers we choose, they may not perform as agreed or they may terminate their agreements with us. In particular, we depend on third-party manufacturers to conduct their operations in compliance with GLP and cGMP or similar standards imposed by U.S. and/or applicable foreign regulatory authorities, including the FDA and EMA. Any of these regulatory authorities may take action against a contract manufacturer who violates GLP and cGMP. Failure of our manufacturers to comply with FDA, EMA or other applicable regulations may cause us to curtail or stop the manufacture of such products until we obtain regulatory compliance, and could subject us to penalties.

We may not be able to obtain sufficient quantities of our compounds if we are unable to secure manufacturers when needed, or if our designated manufacturers do not have the capacity or otherwise fail to manufacture compounds according to our schedule and specifications or fail to comply with cGMP regulations. In particular, in connection with the transition of the manufacturing of drug supply to successor vendors, we could face logistical, scaling or other challenges that may adversely affect supply. Furthermore, in order to maintain applicable regulatory approvals, any manufacturers we utilize are required to consistently produce the respective compounds in commercial quantities and of specified quality or execute fill-finish services on a repeated basis and document their ability to do so, which is referred to as process validation. There are no guarantees we will be able to supply the quantities necessary to effect a successful commercial launch of VONJO or satisfy ongoing demand. Any shortage could also impair our ability to deliver contractually required supply quantities to applicable collaborators, as well as to complete any additional planned clinical trials.

We also rely on third-party service providers for certain warehousing, transportation, sales, order processing, distribution and cash collection services. With regard to the distribution of our compounds, we depend on third-party distributors to act in accordance with Good Distribution Practices, or GDP, and the distribution process and facilities are subject to continuing regulation by applicable regulatory authorities with respect to the distribution and storage of products.

In addition, we depend on medical institutions and CROs (together with their respective agents) to conduct clinical trials and associated activities in compliance with GCP, and in accordance with our timelines, expectations and requirements. To the extent any such third parties are delayed in achieving or fail to meet our clinical trial enrollment expectations, fail to conduct our trials in accordance with GCP or study protocol or otherwise take actions outside of our control or without our consent, our business may be harmed. Furthermore, we conduct clinical trials in foreign countries, subjecting us to additional risks and challenges, including as a result of the engagement of foreign medical institutions and foreign CROs, who may be less experienced with regard to regulatory matters applicable to us and may have different standards of medical care.

With regard to certain of the foregoing clinical trial operations and stages in the manufacturing and distribution chain of our compounds, we rely on single vendors. We only have one commercial supplier of VONJO. The use of single vendors for core operational activities, such as clinical trial operations, manufacturing and distribution, and the resulting lack of diversification, exposes us to the risk of a material interruption in service related to these single, outside vendors. As a result, our exposure to this concentration risk could harm our business.

Many of our vendors process personal data on our behalf which is subject to the GDPR, or governed by US State laws regarding data breach (e.g., the New York Shield Act or the California Consumer Protection Act (“CCPA”)). Failure of our vendors to adequately secure that data may result in exposure to us, as controller for that data, under the GDPR or any of the US State laws in the form of legal costs associated with investigation, notification, and reporting of such a breach, and any resulting fines or penalties. Any breach of the security or other significant disruptions to our information technology systems or those of our vendors could have significant implications for our ability to continually operate our business, and may cause reputational harm. While we maintain cybersecurity insurance, such insurance may not cover the full extent of any financial, legal, reputational or business losses associated with any breach or disruption including any vendor systems processing our data.

We are party to a loan and security agreement that contains operating and financial covenants that may restrict our business and financing activities and we may be required to repay the outstanding indebtedness in an event of default, which could have a material adverse effect on our business.

In August 2021, we entered into a credit agreement with Drug Royalty III LP 2 (“DRI”), the proceeds of which were partially used to repay in full all outstanding indebtedness under our prior loan and security agreement with Silicon Valley Bank.

Borrowings under this credit agreement are secured by a first-priority security interest in, subject to certain exceptions, substantially all of our assets. The credit agreement subjects us to customary affirmative and negative covenants that limit our ability to, among other things, grant liens, make investments, incur additional indebtedness, dispose of assets, license certain property, distribute dividends, make certain restricted payments, change the nature of our business, engage in transactions with affiliates and insiders, prepay other indebtedness, or engage in sale and leaseback transactions, subject to certain exceptions. In addition, the credit agreement contains a minimum liquidity covenant requiring us to maintain at all times at least $10 million of unrestricted cash and cash equivalents, subject to certain exceptions. As a result of all of these restrictions, we may be limited in how we conduct our business, unable to raise additional debt or equity financing to operate during general economic or business downturns, unable to compete effectively or to take advantage of new business opportunities or unable to execute our business strategy.

A breach of the covenants under the credit agreement could result in an event of default under the credit agreement. With respect to the audited financial statements as of December 31, 2021, we were unable to satisfy the affirmative covenant in the credit agreement requiring us to deliver to DRI within 120 days after the end of each fiscal year, audited financial statements of the Company accompanied by an unqualified report and opinion of an independent certified public accountant not subject to any "going concern" or like qualification or exception. We have obtained a waiver of breach of such covenant from DRI since the report of independent registered public accounting firm contained within this Annual Report on Form 10-K states that substantial doubt exists about our ability to continue as a going concern.

If any other event of default occurs and is not cured or waived, DRI would be permitted to accelerate the loans under the credit agreement. If we were unable to repay the amounts due and payable under the credit agreement upon acceleration, DRI could proceed against the collateral securing the credit agreement which could adversely impact our ability to conduct our business.

If we are unable to recruit, retain, integrate and motivate senior management, other key personnel and directors, or if such persons are unable to perform effectively, our business could suffer.

Our future success depends, in part, on our ability to continue to attract and retain senior management, other key personnel and directors to enable the execution of our business plan and to identify and pursue new opportunities. Additionally, our productivity and the quality of our operations are dependent on our ability to integrate and train our new personnel quickly and effectively.

If we are unable to continue to provide directors and officers sufficient liability insurance at affordable rates or at all, or if directors and officers perceive our ability to do so in the future to be limited, it may become increasingly more difficult to attract and retain management and qualified directors to serve on our Board of Directors.

The loss of the services of senior management, other key personnel or directors and/or the inability to timely attract or integrate such persons could significantly delay or prevent the achievement of our development and strategic objectives and may adversely affect our business, financial condition and operating results.

We may encounter difficulties in managing our expected growth and in expanding our operations successfully.

Advancing VONJO through the commercialization process has required, and will continue to require us to develop or expand our development, regulatory, manufacturing, medical affairs, marketing and sales capabilities or contract with third parties to provide these capabilities for us. Maintaining additional relationships and managing our future growth will impose significant added responsibilities on members of our management. We must be able to manage our development efforts and clinical trials effectively, hire, train and integrate additional management, development, medical affairs, administrative and sales and marketing personnel, improve our managerial, development, operational and finance systems, and expand our facilities, all of which may impose a strain on our administrative and operational infrastructure. Our future financial performance will depend, in part, on our ability to manage this growth effectively. We may not be able to accomplish these tasks; which failure could prevent us from successfully commercializing VONJO.

If we are unable to in-license or acquire additional product candidates, our future product portfolio and potential profitability could be harmed.

One component of our business strategy is the in-licensing and acquisition of drug compounds developed by other pharmaceutical and biotechnology companies or academic research laboratories, such as pacritinib. Competition for new promising compounds and commercial products can be intense. If we are not able to identify future in-licensing or acquisition opportunities and enter into arrangements on acceptable terms, our future product portfolio and potential profitability could be harmed.

We may owe additional amounts for VAT related to our operations in Europe.

Our European operations are subject to the Value Added Tax, or VAT, which is usually applied to all goods and services purchased and sold throughout Europe. We historically carried out research and development activities in Italy and incurred value added tax, or VAT, from Italian suppliers on the acquisition of goods and services in Italy. This VAT should be considered as an input VAT credit. We treated the majority of our sales made in Italy without output VAT (on the basis that the supplies should be considered outside the scope of Italian VAT). This resulted in the value of input VAT exceeding the value of output VAT, and accordingly we submitted a refund claim for the VAT. The Italian Tax Authority, or the ITA, has challenged

the treatment of the sales transactions and claimed that the sales transactions made by us should have been subject to output VAT.

Further information pertaining to these cases can be found in Part II, Item 8, "Notes to Consolidated Financial Statements, Note 13. Commitments and Contingencies" and is incorporated by reference herein. If the final decision of the Italian Supreme Court is unfavorable to us, or if, in the interim, the ITA were to make a demand for payment and we were to be unsuccessful in suspending collection efforts, we may be requested to pay to the ITA an amount up to €4.4 million, or approximately $4.9 million converted using the currency exchange rate as of December 31, 2021, including interest and penalties for the period lapsed between the date in which the assessments were issued and the date of effective payment.

We are currently subject to certain regulatory and legal proceedings, and may in the future be subject to additional proceedings and/or allegations of wrong-doing, which could harm our financial condition and operating results.

We are currently, and may in the future be, subject to regulatory matters and legal claims, including possible securities, derivative, consumer protection and other types of proceedings pursued by individuals, entities or regulatory bodies. See Part II, Item 8, "Notes to Consolidated Financial Statements - Note 13. Commitments and Contingencies" regarding the regulatory matters and legal claims in which we are currently involved. Litigation and regulatory proceedings are subject to inherent uncertainties, and we have had and may in the future have unfavorable rulings and settlements. Adverse outcomes may result in significant monetary damages and penalties or injunctive relief against us. It is possible that our financial condition and operating results could be harmed in any period in which the effect of an unfavorable final outcome becomes probable and reasonably estimable. If an unfavorable ruling were to occur in any of the legal proceedings we are or may be subject to, our business, financial condition, operating results and prospects could be harmed. The ultimate outcome of litigation and other claims is subject to inherent uncertainties, and our view of these matters may change in the future.

In addition, our insurance is subject to high deductibles and there is no guarantee that the insurance will cover any specific claim that we currently face or may face in the future, or that it will be adequate to cover all potential liabilities and damages. In the event of negative publicity resulting from allegations of wrong-doing and/or an adverse outcome under any currently pending or future lawsuit, our business could be materially harmed.

Our net operating losses may not be available to reduce future income tax liability.

We have substantial tax loss carryforwards for U.S. federal income tax purposes, but our ability to use such carryforwards to offset future income or tax liability is limited under section 382 of the Internal Revenue Code of 1986, as amended, as a result of prior changes in the stock ownership of our company. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards, or other pre-change tax attributes, to offset U.S. federal and state taxable income and taxes may be subject to limitations. Moreover, future changes in the ownership of our stock, including those resulting from issuance of shares of our common stock upon exercise of outstanding warrants, may further limit our ability to use our net operating losses.

We could be subject to additional income tax liabilities.

We are subject to income taxes in the United States and certain foreign jurisdictions. We use significant judgment in evaluating our worldwide income-tax provision. During the ordinary course of business, we conduct many transactions for which the ultimate tax determination is uncertain. We are subject to audit in various jurisdictions, and such jurisdictions may assess additional income tax against us. Although we believe our tax estimates are reasonable, the final determination of tax audits and any related litigation could be materially different from our historical income-tax provisions and accruals. The results of an audit or litigation could have a material effect on our operating results or cash flows in the period or periods for which that determination is made.

We may be subject to claims relating to improper handling, storage or disposal of hazardous materials.

Our research and development activities involve the controlled use of hazardous materials, chemicals and various radioactive compounds. We are subject to federal, state and local laws and regulations, both internationally and domestically, governing the use, manufacture, storage, handlings, treatment, transportation and disposal of such materials and certain waste products and employee safety and health matters. In the event of such an accident, we could be held liable for any damages that result and any such liability not covered by insurance could exceed our resources.

If we or the third parties upon whom we depend are adversely affected by natural disasters or other events, our business continuity and disaster recovery plans may not adequately protect us from such interruptions.

Our headquarters are located in Seattle, Washington. Any unplanned event, such as flood, fire, explosion, earthquake, tsunami, extreme weather condition, power shortage, power outage, telecommunication failure, or other natural or man-made accidents or incidents could disrupt our operations. If a natural disaster or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as 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. We may not carry sufficient business interruption insurance to compensate us for all losses that may occur. The disaster recovery and business continuity plans we have in place may not be adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of a natural disaster or other event, which could have a material adverse effect on our business, and we could potentially lose valuable data and other items. The occurrence of any of the foregoing could have a material adverse effect on our business.

We will incur a variety of costs for, and may never realize the anticipated benefits of, acquisitions, collaborations or other strategic transactions.

We evaluate and undertake acquisitions, collaborations and other strategic transactions from time to time. The process of negotiating these transactions, as well as integrating any acquisitions and implementing any strategic alliances, may result in operating difficulties and expenditures. In addition, these transactions may require significant management attention that would otherwise be available for ongoing development of our business, whether or not any such transaction is ever consummated. These undertakings could also result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities and/or amortization expenses related to intangible assets, and we may never realize the anticipated benefits.

Risks Related to the Development and Commercialization of Our Product Candidates

If the market opportunities for VONJO are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.

Our projections of both the number of patients with myelofibrosis, including patients with myelofibrosis with a platelet count below 50 x 10^9/L who have the potential to benefit from treatment with VONJO are based on our beliefs and estimates. These estimates have been derived from a variety of sources and may prove to be incorrect or new studies may change the estimated incidence or prevalence, and the number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for VONJO may be limited or may not be amenable to treatment with VONJO, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business. Even if we obtain significant market share for VONJO, because the potential target populations are small, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business.

The commercial success of any current or future product will depend upon the degree of market acceptance by physicians, patients, third-party payors, and others in the medical community.

Even with the requisite approvals from the FDA and comparable foreign regulatory authorities, the commercial success of VONJO and any future products will depend in part on the medical community, patients, and payors accepting VONJO and any future products as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, payors, and others in the medical community. The degree of market acceptance of VONJO and any future products will depend on a number of factors, including:

- the efficacy of the product as demonstrated in clinical studies and potential advantages over competing treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product’s approved labeling;
- the clinical indications for which accelerated approval is granted;
- relative convenience and ease of administration;
- the cost of treatment, particularly in relation to competing treatments;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of our field forces and marketing efforts;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in nonclinical and clinical studies, market acceptance of the product will not be fully known until after it is launched. Our efforts to educate the medical community and payors on the benefits of VONJO require significant resources and may never be successful. If VONJO and any future products fail to achieve an adequate level of acceptance by physicians, patients, payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

The insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for VONJO or any future products could limit our ability to market those products and decrease our ability to generate revenue.

Our target patient populations are small, and accordingly the pricing, coverage, and reimbursement of VONJO and other product candidates, if approved, must be adequate to support our commercial infrastructure. Our per-patient prices must be sufficient to recover our development and manufacturing costs and potentially achieve profitability. The cost of a single administration of VONJO is deemed substantial. Accordingly, the availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to afford expensive treatments such as ours. Sales of VONJO will depend substantially, both domestically and abroad, on the extent to which their costs will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other payors. If coverage and reimbursement are not available, are available only to limited levels, or are not available on a timely basis, we may not be able to successfully commercialize VONJO. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to sustain our overall enterprise.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS or private payors will decide with respect to reimbursement for a product such as ours.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries will put pressure on the pricing and usage of VONJO and other product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for VONJO. Accordingly, in markets outside the United States, the reimbursement for VONJO may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for VONJO. We expect to experience pricing pressures in connection with the sale of VONJO due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, additional legislative changes, and statements by elected officials. The downward pressure on healthcare costs in general, and with respect to prescription drugs, surgical procedures, and other treatments in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

We may be required to suspend, repeat or terminate clinical trials if they are not conducted in accordance with regulatory requirements, the results are negative or inconclusive, or the trials are not well-designed.

Regulatory agencies, IRBs or data safety monitoring boards may at any time recommend the temporary or permanent discontinuation of our clinical trials or request that we cease using investigators in the clinical trials if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements, or that they present an unacceptable safety risk to participants. Clinical trials must be conducted in accordance with GCP or other applicable foreign regulatory authority guidelines. In addition, clinical trials must be conducted with product candidates produced in accordance with applicable cGMPs. Clinical trial data may be rejected by the FDA or foreign regulatory authorities or clinical trials may be suspended by the FDA, foreign regulatory authorities, or us for various reasons.

If we elect or are forced to suspend or terminate a clinical trial of any of our current or future product candidates, the commercial prospects for that product will be harmed and our ability to generate product revenue from that product may be delayed or eliminated. Furthermore, any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our product candidates and impair our ability to generate revenue from the commercialization of these products either by us or by our collaboration partners.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for a product candidate and may have to limit its commercialization.

The sale of VONJO and the use of pacritinib in clinical trials expose us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling VONJO, or clinical trial participants. If we cannot successfully defend ourselves against these claims, we may incur substantial liabilities. Regardless of merit or eventual outcomes of such claims, product liability claims may result in:

• decreased demand for VONJO;

• impairment of our business reputation;

• withdrawal of clinical trial participants;

• costs of litigation;

• substantial monetary awards to patients or other claimants; and

• loss of revenues.

Our insurance coverage may not be sufficient to reimburse us for all expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

We are subject to extensive post-approval or authorization regulatory requirements, and any failure to satisfy such ongoing obligations or unanticipated problems with any of our drugs that receive regulatory authorization could negatively affect our business.

We are and will continue to be subject to numerous regulatory requirements, including with respect to development, testing, manufacturing, labeling, marketing, reporting, sales, and reimbursement for VONJO. If we fail to comply with regulatory requirements or if we experience unanticipated problems with any of our drugs that receive regulatory authorization, it may result in, among other things:

- Regulatory authorities may also impose new restrictions on continued product marketing or may require the withdrawal of a product from the market if adverse events of unanticipated severity or frequency are discovered following approval;
- Clinical holds on clinical trials;
- Warning or untitled letters from the FDA;

- Refusal by the FDA, EMA or comparable regulatory authority to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of drug license approvals;

- Drug seizure or detention, or refusal to permit the import or export of drugs; and

- Injunctions or the imposition of civil or criminal penalties.

Any of these events could negatively affect our business, financial condition, operating results or prospects, generate negative publicity, and require us to expend significant time and resources.

We may be subject to fines, penalties, injunctions and other sanctions if we are deemed to be promoting the use of our products for non-FDA-approved, or off-label, uses.

Our business and future growth depend on the development, ultimate sale and use of products that are subject to FDA, EMA and or other regulatory agencies regulation, clearance and approval. Under the FDCA and other laws, we are prohibited from promoting our products for off-label uses, or uses not approved by the FDA. We may also be subject to various federal and state physician payment transparency laws, including the federal Physician Payments Sunshine Act. This means that in the United States, we may not make claims about the safety or effectiveness of our products and may not proactively discuss or provide information on the uses of our products that are not approved by the FDA, unless otherwise allowed by the FDA by policy or other guidance.

If our promotional activities are found to be in violation of applicable law or if we agree to a settlement in connection with an enforcement action, we would likely face significant fines and penalties and would likely be required to substantially change our sales, promotion, grant and educational activities.

We are subject to numerous laws and regulations related to health care fraud and abuse, false claims, anti-bribery and anti-corruption laws, such as the U.S. Anti-Kickback Statute and the FCPA, in which violations of these laws could result in substantial penalties and prosecution.

In the United States, we are subject to various state and federal fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. There are similar laws in other countries. These laws may impact, among other things, the sales, marketing and education programs for our products. Any allegation, investigation, or violation of these domestic health care fraud and abuse laws could result in government or internal investigations, significant diversion of resources, exclusion from government health care reimbursement programs and the curtailment or restructuring of our operations, significant fines, penalties, or other financial consequences, any of which may ultimately have a material adverse effect on our business.

For our sales and operations outside the United States, we are similarly subject to various heavily-enforced anti-bribery and anti-corruption laws, such as the FCPA, as amended, U.K. Bribery Act, and similar laws around the world. We face significant risks if we, which includes our third parties, fail to comply with the FCPA and other anti-corruption and anti-bribery laws.

We leverage various third parties to sell our products and conduct our business abroad. We, our commercial partners and our other third-party intermediaries, including collaborators and licensees, may have direct or indirect interactions with officials and employees of government agencies or state-owned or affiliated entities and may be held liable for the corrupt or other illegal activities of these third-party business partners and intermediaries, our employees, representatives, contractors, partners, collaborators, licensees and agents, even if we do not explicitly authorize such activities.

Any violation of the FCPA, other applicable anti-bribery, anti-corruption laws, and anti-money laundering laws could result in whistleblower complaints, adverse media coverage, investigations, loss of export privileges, severe criminal or civil sanctions and, in the case of the FCPA, suspension or debarment from U.S. government contracts, which could have a material and adverse effect on our reputation, business, operating results and prospects. In addition, responding to any enforcement action or related investigation may result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees.

If development and commercialization collaborations we enter into are not successful, or if we are unable to enter into additional collaborations, we may not be able to effectively develop and/or commercialize our compounds, which could have a material adverse effect on our business.

Historically, we have entered into development and commercialization collaborations to help advance the development of our product candidates. We evaluate collaboration opportunities from time to time and if we enter into such collaborations in the future, our business may become increasingly dependent on the success of such collaborations. Additionally, if we do not successfully enter into additional collaborations when needed, we may be unable to further develop and commercialize the applicable compounds, generate revenues to sustain or grow our business or achieve profitability, which would harm our business, financial condition, operating results and prospects.

Our employees, collaborators and other personnel may engage in misconduct or other improper activities, which could have a material adverse impact on our business.

We are exposed to the risk of fraud or other misconduct by our employees, collaborators, vendors, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA, EMA and other regulators, providing inaccurate or misleading information to the FDA, EMA and other regulators, failure to comply with data privacy and security and healthcare fraud and abuse laws and regulations in the United States and abroad, reporting inaccurate financial information or clinical data or failing to disclose unauthorized activities to us.

Various laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Any misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, officers, directors, agents and representatives, including consultants, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent misconduct 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 and regulations.

Risks Related to Our Intellectual Property

If any of our license agreements for intellectual property underlying our product candidates are terminated, we may lose the right to develop or market that product candidate.

We have acquired or licensed intellectual property from third parties, including patent applications and patents relating to VONJO. Some of our product development programs depend on our ability to maintain rights under license agreements relating to this licensed intellectual property. Each licensor of this intellectual property has the power to terminate its agreement with us if we fail to meet our obligations under that agreement. If we default under any of these agreements, we may lose our right to market and sell any products based on the intellectual property licensed under these agreements and may be forced to cease operations, liquidate our assets and possibly seek bankruptcy protection. Bankruptcy may result in the termination of these agreements.

We hold rights under numerous patents that we have acquired or licensed or that protect inventions originating from our research and development, and the expiration of any of these patents would enable our competitors to use the inventions that are the subject of such patents in competition with us.

We dedicate significant resources to protecting our intellectual property, which is important to our business. We have filed numerous patent applications in the United States and various other countries seeking protection of inventions originating from our research and development, and we have also obtained rights to various patents and patent applications under licenses with third parties and through acquisitions. We have pending patent applications or issued patents in the United States and foreign countries directed to VONJO and other product candidates. Patent coverage for our individual products extends for varying periods according to the date of the patent filing or grant and the legal term of patents in the various countries where we have obtained patent protection.

In addition to our patent rights, we rely, to the extent possible, trade secret and contractual protections for our know-how and other unpatented technology. Ultimately, to the extent any of our product candidates are not protected by patent rights our competitors would be free to use inventions embodied in our product candidates to which they have access to compete with us.

If we fail to adequately protect our intellectual property, our competitive position and the potential for long-term success could be harmed.

Development and protection of our intellectual property are critical to our business. If we do not adequately protect our intellectual property, competitors may be able to practice our technologies, including the inventions embodied in our product candidates.

The U.S. Patent and Trademark Office, or PTO, has not established a consistent policy regarding the breadth of claims that it will allow in pharmaceutical and biotechnology patents. Patent applications in which we have rights may never issue as patents, and the claims of any issued patents may not afford meaningful protection for our product candidates or technologies. In addition, patents issued to us or our licensors may be challenged and subsequently narrowed, invalidated, circumvented or found unenforceable. Litigation, interference or derivation proceedings or other governmental proceedings that we may become involved in with respect to our patent rights or our proprietary technologies or the proprietary technologies of others could result in substantial cost to us.

We also rely upon trade secrets to protect our proprietary know-how and continuing technological innovation to enable us to remain competitive. Third parties may independently develop such know-how or innovations or otherwise obtain access to such know-how or technology. While we require our employees, consultants, corporate partners and other third parties with access to our proprietary information to enter into confidentiality agreements, these agreements may not be honored and may be difficult to enforce.

Patent litigation is widespread in the pharmaceutical and biotechnology industry, and any patent litigation in which we become involved could harm our business.

We may not be able to successfully challenge the validity of third-party patents and could be required to pay substantial damages, possibly including treble damages, for past infringement and attorneys' fees if it is ultimately determined that our products infringe such patents. Further, we may be prohibited from selling our products before we obtain a license, which, if available at all, may require us to pay substantial royalties.

Moreover, third parties may challenge the patents that have been issued or licensed to us. There can be no assurance that our product candidates or technologies will not be found in the future to infringe upon the rights of others or be infringed upon by others. In such a case, others may assert infringement claims against us, and should we be found to infringe upon their patents, or otherwise impermissibly utilize their intellectual property, we might be forced to pay damages, potentially including treble damages. In addition to any damages we might have to pay, we may be required to obtain licenses from the holders of this intellectual property, enter into royalty agreements or redesign our compounds so as not to utilize this intellectual property, each of which may prove to be uneconomical or otherwise impossible. Conversely, we may not always be able to successfully pursue our claims against others that infringe upon our technology and the technology exclusively licensed from any third parties. Thus, the proprietary nature of our technology or technology licensed by us may not provide adequate protection against competitors.

Furthermore, our employees may be subject to claims that we or these employees have used or disclosed trade secrets or other proprietary information of the former employers. If we are unsuccessful in our defense of such claims, in addition to paying monetary damages, we may lose the right to use valuable intellectual property rights relating to our product candidates or technologies. A loss of key research personnel work product could hamper or prevent our ability to commercialize certain potential products, which could severely harm our business. Even if such claims against us are without merit, or if we challenge the validity of issued patents that are asserted against us, lawsuits in which such claims could be asserted or challenges could be made take significant time, may, even if resolved in our favor, be expensive and divert management attention from other business activities requiring attention. Uncertainties resulting from the initiation and continuation of any litigation relating to intellectual property could limit our ability to continue our operations.

We may not be able to protect our intellectual property rights throughout the world.

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

compete with our product and product candidates and our and our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Risks Related to Our Common Stock

The market price of shares of our common stock is extremely volatile, which may affect our ability to raise capital in the future and may subject the value of your investment in our securities to sudden decreases.

The market price for securities of biopharmaceutical and biotechnology companies, including ours, historically has been highly volatile, and the market from time to time has experienced significant price and volume fluctuations that are unrelated to the operating performance of such companies. For example, during the 12-month period ended March 17, 2022, our stock price ranged from a low of $1.43 to a high of $4.87. Fluctuations in the market price or liquidity of our common stock may harm the value of your investment in our common stock. *The Nasdaq Stock Market*, or *the Nasdaq*, and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In addition, broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

We may not be able to maintain our listing on the Nasdaq, or trading on the Nasdaq may otherwise be halted or suspended, which may negatively impact the price of our common stock.

We have in the past and may in the future fail to comply with the Nasdaq requirements. If our common stock ceases to be listed for trading on the Nasdaq for any reason, it may harm our stock price, increase the volatility of our stock price, decrease the level of trading activity and make it more difficult for investors to buy or sell shares of our common stock. Our failure to maintain a listing on the Nasdaq may constitute an event of default under our loan and security agreement and any future indebtedness, which would accelerate the maturity date of such debt or trigger other obligations. In addition, certain institutional investors that are not permitted to own securities of non-listed companies may be required to sell their shares adversely affecting the market price of our common stock. If we are not listed on the Nasdaq, our ability to raise capital will be adversely impacted. Additionally, for so long as our non-affiliate public float does not exceed $75 million, the amount of securities that we may sell pursuant to registration statements on Form S-3 will be limited to the equivalent of one-third of our public float, which will limit our ability to file or use shelf registration statements on Form S-3 and further limit our ability to raise capital. We have relied significantly on shelf registration statements on Form S-3 for most of our financings in recent years, so any such limitations may harm our ability to raise the capital we need.

Future financing, strategic and other activities may require us to increase the number of authorized shares in our certificate of incorporation. An inability to secure requisite stockholder approval for such increases could materially and adversely impact our ability to fund our operations.

At our 2021 annual meeting of stockholders, we sought and received approval of an amendment to our certificate of incorporation to increase the total number of authorized shares and the total number of authorized shares of our common stock and we may seek approval to increase the number of authorized shares again in the future. Without future additional increases in the number of authorized shares, we may be constrained in our ability to raise capital when needed, and may lose important business opportunities, which could adversely affect our financial performance, growth and ability to continue our operations. Even if we obtain approval to further increase the number of authorized shares, we are required under the Nasdaq Marketplace Rules to obtain stockholder approval for certain issuances of additional equity securities. However, we might not be successful in obtaining the required stockholder approval for any future issuance that requires stockholder approval pursuant to applicable rules and regulations. If we are unable to obtain financing or our financing options are limited due to stockholder approval difficulties, such failure may harm our ability to continue operations.

Anti-takeover provisions in our charter documents, under Delaware law and in other applicable instruments could make removal of incumbent management or an acquisition of us, which may be beneficial to our stockholders, more difficult.

Provisions of our certificate of incorporation and bylaws may have the effect of deterring or delaying attempts by our stockholders to remove or replace management, to commence proxy contests or to effect changes in control. In addition, as a Delaware corporation, we are subject to Delaware's anti-takeover statute, which imposes restrictions on some transactions between a corporation and certain interested stockholders. Our shareholder rights plan expired pursuant to its terms on December 2, 2018, and was not replaced; however, the Board may, subject to its fiduciary duties under applicable law, choose to implement a similar plan in the future. Likewise, because our principal executive offices are located in Washington, the anti-takeover provisions of the Washington Business Corporation Act may apply to us under certain

circumstances now or in the future. These provisions could also have the effect of delaying or preventing a change in control of our company.

Raising additional capital could cause you to incur dilution and could cause the market price of our common stock to fall.

As of December 31, 2021, options to purchase 20,690,826 shares of our common stock with a weighted-average exercise price of $2.31 per share were outstanding. The exercise of any of these options would result in dilution to current stockholders. Further, because we will need to raise additional capital to fund our operations and clinical development programs, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. Pursuant to our equity incentive plans, our compensation committee is authorized to grant equity-based incentive awards to our employees, directors and consultants. Future option grants and issuances of common stock under our share-based compensation plans may have an adverse effect on the market price of our common stock.

These future issuances of common stock or common stock-related securities, together with the exercise of outstanding options and any additional shares of common stock issued in connection with acquisitions, if any, may result in further dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to those of holders of our common stock.

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

The trading market for our common stock is influenced by the research and reports that securities or industry analysts publish about us or our business. If too few securities or industry analysts cover our company, the market price of our common stock would likely be negatively impacted. If securities and industry analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, the market price of our common stock would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause the market price of our common stock and the trading volume of our common stock to decline.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We currently lease approximately 66,000 square feet of space at 3101 Western Avenue in Seattle, Washington. Beginning May 2022, we will lease approximately 23,000 square feet of space at this address. The lease commenced in May 2012 and expires in April 2025. Approximately 44,000 square feet of space at this address has been subleased commencing December 2017 and ending April 2022. We believe our existing and planned facilities are adequate to meet our present requirements. We anticipate that additional space will be available, when needed, on commercially reasonable terms.

Item 3. Legal Proceedings

Except as set forth in Part II, Item 8, “Financial Statements and Supplementary Data - Notes to Consolidated Financial Statements - Note 13. Commitments and Contingencies,” which is incorporated herein by reference, we are not engaged in any material legal proceedings. From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Except as set forth below, we believe that there are no claims or actions pending against us currently, the ultimate disposition of which would have a material adverse effect on our consolidated results of operation, financial condition or cash flows.

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

Our common stock is currently traded under the symbol "CTIC" on the Nasdaq Capital Market.

As of March 17, 2022, there were 98 stockholders of record of our common stock.

Dividend Policy

We have never declared or paid cash dividends on our common stock and do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance operations. Any future determination relating to our dividend policy will be made at the discretion of our Board of Directors and will depend on a number of factors, including future earnings, capital requirements, financial conditions, future prospects, contractual restrictions and other factors that our Board of Directors may deem relevant.

Recent Sales of Unregistered Securities

None.

Repurchases of Equity Securities

None.

Item 6. Reserved

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business, future financial performance, expense levels and liquidity sources, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the acquisition, development and commercialization of novel targeted therapies for blood-related cancers where there is a significant unmet medical need. Our goal is to build a profitable company by generating income from products we develop and commercialize, either alone or with partners. We have one commercially approved product, VONJO™ (pacritinib), which has received accelerated approval in the United States by the U.S. Food and Drug Administration, or the FDA, for the treatment of adult patients with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 x 10^9/L.

Pacritinib is an oral kinase inhibitor with specificity for JAK2, IRAK1, FLT3 and CSF1R. At clinically relevant concentrations, pacritinib does not inhibit JAK1. The JAK family of enzymes is a central component in signal transduction pathways, which are critical to normal blood cell growth and development, as well as inflammatory cytokine expression and immune responses. Mutations in these kinases have been shown to be directly related to the development of a variety of blood-related cancers, including myeloproliferative neoplasms, leukemia and lymphoma. In addition to myelofibrosis, the kinase profile of pacritinib suggests its potential therapeutic utility in conditions such as AML, MDS, CMML, GvHD, and CLL, due to its inhibition of JAK2, IRAK1, FLT3 and CSF1R. We believe pacritinib has the potential to be delivered as a single agent or in combination therapy regimens.

We have historically funded our operations through the sale of equity securities, debt financing and funding received from our licensees and collaborators. We do not expect to achieve or sustain profitability for the foreseeable future. We had a net loss of $97.9 million for the year ended December 31, 2021 and an accumulated deficit of $2.4 billion as of December 31, 2021, primarily from expenses incurred in connection with our research programs and from selling, general and administrative costs associated with our operations.

We have incurred significant operating losses to date and expect to continue to incur significant expenses and operating losses for at least the next 12 to 24 months. We anticipate that our expenses will increase as we:

- continue our commercialization efforts for VONJO;
- continue our research and clinical development of pacritinib;
- seek regulatory and marketing approvals for pacritinib if we successfully complete the remainder of its anticipated clinical development paths; and
- maintain, protect and expand our intellectual property portfolio.

Factors Affecting Performance

Product Sales

Following FDA approval of VONJO in February 2022, we commenced shipping of VONJO to a limited number of specialty distributor customers and specialty pharmacy customers in the first quarter of 2022. Product sales are recognized upon delivery of our product to our customers and are recorded net of applicable deductions, including trade discounts, distribution service fees, product returns, chargebacks and discounts, government-mandated rebates and other incentives such as co-pay assistance. Our realization of product sales will be dependent, in part, upon our commercialization efforts and the market

acceptance of VONJO among physicians, patients, healthcare payers and the medical community. No product sales have been recognized in the accompanying consolidated financial statements for the year ended December 31, 2021.

Cost of Sales

Cost of sales will primarily consist of shipping and distribution costs of VONJO as well as third-party royalty costs. Cost of sales will reflect only a portion of the costs related to the manufacture of VONJO and related materials, since, prior to FDA approval, these costs were expensed as research and development expenses. We expect to utilize zero cost inventory with respect to VONJO for an extended period of time. No cost of sales has been recognized in the accompanying consolidated financial statements for the year ended December 31, 2021.

Research and Development

We expect to commit significant time and resources to research and development activities relating to our current and any future product candidates. Pacritinib has received accelerated approval for the treatment of adult patients with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 x 10^9/L and is being marketed as VONJO. However, a confirmatory study, PACIFICA, is ongoing and we expect to continue to devote resources to the completion of this study.

Selling, General and Administrative

Selling, general and administrative expenses consist primarily of personnel costs, expenses for outside consulting and professional services, allocated facilities costs and costs required to support the marketing and sales operations of our commercialized product. Following FDA approval of VONJO in February 2022, we anticipate that selling, general and administrative expenses will increase as we expand our commercial activities in support of product launch and further invest in infrastructure to support our expected growth in the United States.

Impact of COVID-19

We continue to evaluate and manage the impact of the global COVID-19 pandemic on our operations and the conduct of our clinical trials, including considerations of the vulnerable nature of the patient population participating in our trials, reduced or halted activities at our clinical trial sites, an increase in fatalities or other adverse events due to medical problems related to the COVID-19 pandemic and the benefits of continued patient access to VONJO.

Financial Summary

Loss from operations was $95.3 million and $47.8 million for the years ended December 31, 2021 and 2020, respectively. Results of operations may vary substantially from year to year and from quarter to quarter and, as a result, you should not rely on them as being indicative of our future performance. As of December 31, 2021, our cash and cash equivalents were $65.4 million.

Results of Operations

Years ended December 31, 2021 and 2020

Operating costs and expenses

Research and development expenses. Our research and development expenses were as follows (in thousands):

	Years ended December 31,	
	2021	**2020**
Compounds under development:		
Pacritinib	$ 31,823	$ 20,463
Operating expenses	7,313	5,480
Total research and development expenses	$ 39,136	$ 25,943

Costs for our compounds include external direct expenses such as principal investigator fees, charges from contract research organizations, or CROs, and contract manufacturing fees incurred for preclinical, clinical, manufacturing and regulatory activities associated with preparing the compounds for submissions of NDAs or similar regulatory filings to the

FDA, the EMA or other regulatory agencies outside the United States and Europe, as well as upfront license fees for acquired technology. Operating expenses include our personnel costs and an allocation of occupancy, depreciation and amortization expenses associated with developing our compounds. Cumulative to date external direct costs incurred by us through December 31, 2021 were $215.2 million for pacritinib (excluding costs for pacritinib prior to our acquisition of certain assets from S*BIO in May 2012 and $29.1 million of in-process research and development expenses associated with the acquisition of certain assets from S*BIO).

Research and development expenses increased to $39.1 million for the year ended December 31, 2021 compared to $25.9 million for the year ended December 31, 2020. The increase between periods was primarily attributable to a $13.7 million increase in professional services, which included regulatory and other costs related to the NDA submission for VONJO, a $1.4 million increase in additional staffing and personnel costs, and a $0.9 million increase in costs related to the PACIFICA Phase 3 trial, offset by a $2.8 million decrease in costs related to the PRE-VENT Phase 3 trial.

Selling, general and administrative expenses. Selling, general and administrative expenses were $56.2 million for the year ended December 31, 2021 compared to $17.6 million for the year ended December 31, 2020. Substantially all of the increase between periods was attributable to activities associated with preparation for the commercialization of VONJO, which consisted of the following: a $23.5 million increase in professional services, a $12.2 million increase in additional staffing and personnel costs, a $2.3 million increase in infrastructure including sales-related service agreements and a $0.6 million increase in travel and other expenses.

Other operating expenses. Other operating expenses of $4.2 million for the year ended December 31, 2020 relate to a full provision for uncollectability of our Italian VAT receivables and deposit. There was no such expense for the year ended December 31, 2021.

Non-operating expense

Interest expense, net. Interest expense, net was as follows (in thousands):

	Years ended December 31,	
	2021	2020
Interest income	$ 38	$ 204
Interest expense	(1,921)	(511)
Amortization of debt discount and issuance costs	(532)	(521)
Interest expense, net	$ (2,415)	$ (828)

Interest income was $38,000 and $0.2 million for the years ended December 31, 2021 and 2020, respectively. Interest income was primarily related to our cash equivalent securities. The change was primarily related to decreases in interest rates and short-term investments between periods.

Interest expense was $1.9 million and $0.5 million for the year ended December 31, 2021 and 2020, respectively. Interest expense was related to our secured term loans. The change between periods was primarily related to an increase in average loan balances outstanding and an increase in interest rate due to the August 2021 $50.0 million loan under the Credit Agreement with DRI.

Amortization of debt discount and issuance costs for the year ended December 31, 2021 was related to the Credit Agreement with DRI and our term loan with Silicon Valley Bank. Amortization of debt discount and issuance costs for the year ended December 31, 2020 was related to our term loan with Silicon Valley Bank.

Other non-operating expenses. Other non-operating expenses were as follows (in thousands):

	Years ended December 31,	
	2021	2020
Foreign exchange loss	$ (23)	$ (80)
Loss on dissolution of majority-owned subsidiary	—	(3,774)
Loss on extinguishment of debt	(138)	—
Other non-operating expense	$ (161)	$ (3,854)

Loss on dissolution of majority-owned subsidiary of $3.8 million for the year ended December 31, 2020 was related to a loss recognized upon dissolution of our majority-owned subsidiary, Aequus Biopharma, Inc., in June 2020.

Loss on extinguishment of debt for the year ended December 31, 2021 was related to a loss recognized upon repayment of our secured term loan with Silicon Valley Bank in August 2021. See "Note 7. Debt Financing Arrangements" for additional information.

Liquidity and Capital Resources

Sources of Liquidity

We have historically funded our operations from proceeds from the sales and the issuance of equity securities, the incurrence of debt and payments received pursuant to license and collaboration agreements. As of December 31, 2021, we had $65.4 million in cash and cash equivalents, which excludes $60.0 million received from DRI following FDA approval of VONJO in February 2022 as discussed below.

Product Sales. We commercially launched VONJO in the first quarter of 2022 following the accelerated approval of VONJO by the FDA in February 2022. We intend to rely on cash flows from product sales as our source of liquidity in the near future as we continue our commercialization efforts with respect to VONJO.

Public Offering of Common Stock and Series X[1] Preferred Stock. In April 2021, we issued 16.4 million shares of our common stock at a $2.50 per share price and 600 shares of our Series X[1] Preferred Stock at a $25,000 per share price, collecting net proceeds of approximately $53.6 million.

Rights Offering. In March 2020, we issued 15.7 million shares of our common stock at a $1.00 per share price and 4,429 shares of our Series X Preferred Stock at a $10,000 per share price, collecting net proceeds of $59.1 million.

At-The-Market Equity Offering. In November 2019, we entered into an Open Market Sale Agreement with Jefferies LLC to sell shares of our common stock, having aggregate sales proceeds of up to $15.0 million, from time to time, through an "at the market" equity offering program under which Jefferies acted as sales agent. In November and December 2020, we sold 2.1 million shares of our common stock for net proceeds of approximately $7.2 million after compensation to Jefferies. In January 2021 we entered into a new Open Market Sale Agreement with Jefferies LLC to sell shares of our common stock having aggregate sales proceeds of up to $50.0 million. We sold 0.9 million shares of our common stock for net proceeds of approximately $2.7 million during the year ended December 31, 2021. Cash received from first quarter 2022 sales under the Open Market Sale Agreement as of the date of this Annual Report on Form 10-K was not material.

Credit Agreement. In August 2021, we entered into a Credit Agreement with Drug Royalty III LP 2, or DRI, as lender and administrative agent, which provided for a loan in the principal amount of $50 million funded by DRI at closing. As of December 31, 2021, we had an outstanding principal balance under the Credit Agreement of $50.0 million. We are required to pay quarterly interest-only payments until August 25, 2026, or the maturity date, with the unpaid principal amount of the outstanding loan due and payable on the maturity date. The loan bears interest at a rate equal to 8.25% per annum, plus the greater of (i) 1.75% and (ii) the three-month LIBOR rate and requires a back-end fee of $1.0 million. These borrowings are secured by a first priority security interest on substantially all of our assets, subject to certain exceptions. In addition, the Credit Agreement requires us to comply with restrictive covenants, including those that limit our operating flexibility and ability to borrow additional funds. A failure to make a required payment or an uncured covenant breach could lead to an event of default, and in such case, all amounts then outstanding may become due and payable immediately.

In connection with the Credit Agreement, we and DRI entered into a Purchase and Sale Agreement, or the Royalty Financing Agreement, pursuant to which we sold to DRI the right to receive certain royalty payments from us for a purchase price of up to $85 million in cash. DRI funded the upfront purchase price of $60 million following FDA approval of VONJO in February 2022 and will be required to provide up to $25 million of additional funding to us if certain minimum VONJO sales thresholds are met in 2023, or sooner. Under the Royalty Financing Agreement, DRI is entitled to receive tiered, sales-based royalties on net product sales of VONJO in the United States.

Historical Cash Flows

Net cash used in operating activities. Net cash used in operating activities was $84.9 million during the year ended December 31, 2021 compared to $42.2 million for the same period in 2020. The increase was primarily due to increases in

payments for research and development and selling, general and administrative expenses associated with continued development and preparation for the commercialization of VONJO.

Net cash provided by (used in) investing activities. Net cash provided by investing activities was $12.0 million during the year ended December 31, 2021, and net cash used in investing activities was $9.6 million during the same period in 2020. The change was due to short-term investments matured and purchased between periods.

Net cash provided by financing activities. Net cash provided by financing activities was $97.9 million and $61.1 million during the year ended December 31, 2021 and 2021, respectively. The change was primarily attributable to net proceeds from the completion of our public offering of common stock and Series X^1 Preferred Stock in April 2021, loan proceeds from the Credit Agreement with Drug Royalty III LP 2 in August 2021, and net proceeds from the completion of our rights offering in March 2020.

Capital Resources

We have prepared our consolidated financial statements assuming that we will continue as a going concern, which contemplates realization of assets and the satisfaction of liabilities in the normal course of business. However, we believe that, as of the date of the filing of this Annual Report on Form 10-K, our present financial resources, combined with $60.0 million received from Drug Royalty III LP 2 following FDA approval of VONJO in February 2022, will be sufficient to fund our operations into the fourth quarter of 2022. This raises substantial doubt about our ability to continue as a going concern and we will need to raise substantial additional capital in the near term in order to fund our operations through and beyond the fourth quarter of 2022 and to continue as a going concern thereafter. See Note 1 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information on our assessment. Further, we have incurred net losses since inception and expect to generate losses for the foreseeable future, primarily due to research and development costs for pacritinib. We have historically funded our operations through equity financings, borrowings and funds obtained under product collaborations, any or all of which may not be available to us in the future. As of December 31, 2021, our available cash and cash equivalents totaled $65.4 million and we had an outstanding principal balance of $50.0 million under our Credit Agreement with DRI.

Financial resource forecasts are subject to change as a result of a variety of risks and uncertainties. Changes in our commercialization efforts, manufacturing, developments in and expenses associated with our clinical trials and the other factors identified under "*Capital Requirements*" below may consume capital resources earlier than planned. Due to these and other factors, the foregoing forecast for the period for which we will have sufficient resources to fund our operations may be inaccurate.

Capital Requirements

We will require additional capital in order to pursue our strategic objectives. We expect to satisfy our capital needs through existing capital balances, revenue from VONJO and a combination of public or private equity financings, partnerships, collaborations, joint ventures, disposition of assets, debt financings or restructurings, bank borrowings or other sources of financing. However, we have a limited number of authorized shares of common stock available for issuance and additional funding may not be available on favorable terms or at all. If additional funds are raised by issuing equity securities, substantial dilution to existing stockholders may result. If we fail to obtain additional capital when needed, our ability to operate as a going concern will be harmed, and we may be required to delay, scale back or eliminate some or all of our research and development programs and commercialization efforts and/or reduce our selling, general and administrative expenses, be unable to attract and retain highly-qualified personnel, be unable to obtain and maintain contracts necessary to continue our operations and at affordable rates with competitive terms, refrain from making our contractually required payments when due (including debt payments) and/or be forced to cease operations, liquidate our assets and possibly seek bankruptcy protection.

Our future capital requirements will depend on many factors, including: our ability to generate sales of VONJO; the cost and timing of establishing our commercial infrastructure and distribution capabilities; our ability to reach milestones triggering payments under certain of our contractual arrangements; the cost of manufacturing VONJO; the cost of manufacturing clinical supplies or of establishing commercial supplies of any products that we may develop in the future; developments in and expenses associated with our research and development activities; our clinical development plans and any changes that we may initiate or that may be requested by the FDA or other regulators as we seek product approval; acquisitions or collaborations with respect to compounds or other assets; competitive market developments; disruptions or other delays to our business and clinical trials resulting from the ongoing worldwide COVID-19 pandemic; and other unplanned business developments.

Critical Accounting Estimates

Management makes certain judgments and uses certain estimates and assumptions when applying accounting principles generally accepted in the United States in the preparation of our consolidated financial statements. We evaluate our estimates and judgments on an ongoing basis and base our estimates on historical experience and on assumptions that we believe to be reasonable under the circumstances. Our experience and assumptions form the basis for our judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Given the global economic climate and additional or unforeseen effects from the ongoing COVID-19 pandemic, these estimates are becoming more challenging. Actual results may vary from what we anticipate and different assumptions or estimates about the future could change our reported results. We believe the following estimates are the most critical to us, in that they are important to the portrayal of our consolidated financial statements and require our subjective or complex judgment in the preparation of our consolidated financial statements:

Research and Development Expenses

We accrue expenses for clinical trial activities performed by CROs based upon the estimated amount of work completed on each trial. The significant factors used in estimating accruals include the number of patients enrolled, the number of active clinical sites, clinical milestones achieved, the duration for which the patients have been enrolled in the trial, and other criteria related to the efforts of our vendors. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, review of contractual terms and correspondence with CROs. We base our estimates on the best information available at the time. However, these estimates will be subject to change as additional information becomes available, which will allow us to make a more accurate estimate in future periods. In that event, we may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain. Amounts ultimately incurred in relation to amounts accrued for these services may be substantially higher or lower than our estimates. Depending on the timing of payments to vendors and estimated services provided, we record net prepaid or accrued expenses related to these costs.

Equity-based Compensation Expense

Equity-based compensation expense for all equity-based payment awards made to employees and directors is recognized and measured based on estimated fair values. For option valuations, we have elected to utilize the Black-Scholes valuation method in order to estimate the fair value of options on the date of grant. The risk-free interest rate is based on the implied yield currently available for United States Treasury securities at maturity with an equivalent term. We have not declared or paid dividends on our common stock and do not currently expect to do so in the future. The expected term of options represents the period that our equity-based awards are expected to be outstanding and was determined based on historical weighted average holding periods and projected holding periods for the remaining unexercised options. Consideration was given to the contractual terms of our equity-based awards, vesting schedules and expectations of future employee behavior. Expected volatility is based on the annualized daily historical volatility, including consideration of the implied volatility and market prices of traded options for comparable entities within our industry. These assumptions underlying the Black-Scholes valuation model involve management’s best estimates.

Generally accepted accounting principles for equity-based compensation also require that we recognize compensation expense for only the portion of awards expected to vest. Therefore, we apply an estimated forfeiture rate that we derive from historical employee termination behavior. If the actual number of forfeitures differs from our estimates, adjustments to compensation expense may be required in future periods. For performance-based awards that do not include market-based conditions, we record share-based compensation expense only when the performance-based milestone is deemed probable of achievement. We utilize both quantitative and qualitative criteria to judge whether milestones are probable of achievement. For awards with market-based performance conditions, we recognize the grant-date fair value of the award over the derived service period regardless of whether the underlying performance condition is met.

Contingencies

On a quarterly basis, we review the status of each significant matter and assess its potential financial exposure. If the potential loss from any claim, asserted or unasserted, or legal proceeding is considered probable and the amount can be reasonably estimated, we accrue a liability for the estimated loss. Significant judgment is required in both the determination of probability and the determination as to whether an exposure is reasonably estimable. Because of uncertainties related to these matters, accruals are based only on the best information available at the time. As additional information becomes available, we reassess the potential liability related to pending claims and litigation and may revise our estimates. These revisions in the estimates of the potential liabilities could have a material impact on our consolidated results of operations and financial position.

Recently Issued and Adopted Accounting Pronouncements

For a description of recently issued and adopted accounting pronouncements, including the expected effects on our results of operations and financial condition, refer to Part II, Item 8, “Financial Statements and Supplementary Data - Notes to Consolidated Financial Statements - Note 1. Description of Business and Summary of Significant Accounting Policies,” which is incorporated herein by reference.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

As a smaller reporting company, we are not required to provide the information requested by this item pursuant to Item 305(e) of Regulation S-K.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

To the Stockholders and the Board of Directors of CTI BioPharma Corp.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of CTI BioPharma Corp. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations, 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.

The Company’s Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company’s ability to continue as a going concern. Management's evaluation of the events and conditions and management’s plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

We conducted our audits 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 consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

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

Accrued Clinical Trial Expenses

Description of the Matter	As of December 31, 2021, the Company recorded $4.1 million for accrued clinical trial expenses. As described in Note 4 to the consolidated financial statements, the Company's expense accruals for clinical trials are based on estimates of contracted services provided by third-party vendors not yet billed. Management is required to make estimates of outstanding obligations to those third-party vendors as of period end regardless of how timely invoices are sent to the Company and whether or not billing terms under vendor contracts coincide with the timing of when services are provided. Accrual estimates are based on a number of factors, including management's knowledge of the research and development programs and clinical activities, invoicing to date, and the provisions in vendor contracts. If possible, the Company obtains information regarding unbilled services directly from its service providers and performs procedures to challenge these estimates based on its internal understanding of the services provided to date. However, the Company may also be required to estimate these services based on information available to its internal clinical or administrative staff if such information is not able to be obtained timely from its service providers. Auditing accrued clinical trial expenses is complex because of the judgments applied by management to determine the commencement and completion date of vendor tasks and the extent of work performed during the reporting period for services not yet billed by contracted third-party vendors.
How We Addressed the Matter in Our Audit	We obtained an understanding of the Company's process for estimating the accrued clinical trial expenses. To test the estimate of accrued clinical trial expenses, we performed audit procedures that included, among others, direct confirmation of billed and unbilled amounts with a sample of the Company's third-party vendors. We confirmed progress of contracted clinical activities with third-party vendors and compared such data to the Company's estimates of progress as reflected in their accrual models. We further tested the accuracy of the calculations; the reliability, completeness and relevance of management's data utilized; and the reasonableness of the assumptions used in management's accrual models by testing actual invoices paid to date, agreeing inputs back to contractual terms and holding discussions with clinical or administrative staff outside of the finance function to corroborate progress and estimated level of expended effort incurred by the Company's third-party vendors.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.

Seattle, Washington
March 31, 2022

CTI BIOPHARMA CORP.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share amounts)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 65,446	$ 40,394
Short-term investments	—	12,057
Prepaid expenses and other current assets	2,933	1,874
Total current assets	68,379	54,325
Property and equipment, net	176	719
Other assets	3,879	3,197
Total assets	$ 72,434	$ 58,241
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 3,891	$ 1,637
Accrued expenses	12,720	7,191
Current portion of long-term debt	47,380	4,455
Other current liabilities	2,660	3,755
Total current liabilities	66,651	17,038
Other liabilities, less current portion	2,016	1,174
Total liabilities	68,667	18,212
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share:		
Authorized shares - 33,333		
Series O Preferred Stock, 12,575 shares issued and outstanding as of December 31, 2021 and 2020 (Aggregate liquidation preference of $25,150 as of December 31, 2021 and 2020)	—	—
Series X Preferred Stock, 3,794 shares and 4,429 shares issued and outstanding as of December 31, 2021 and 2020, respectively (Aggregate liquidation preference of $37,940 and $44,290 as of December 31, 2021 and 2020, respectively)	—	—
Series X[1] Preferred Stock, 600 shares and 0 shares issued and outstanding as of December 31, 2021 and 2020, respectively (Aggregate liquidation preference of $15,000 as of December 31, 2021)	—	—
Common stock, $0.001 par value per share:		
Authorized shares - 266,500,000 and 166,500,000 as of December 31, 2021 and 2020, respectively		
Issued and outstanding shares - 99,763,922 and 75,896,884 as of December 31, 2021 and 2020, respectively	100	76
Additional paid-in capital	2,429,582	2,367,958
Accumulated other comprehensive income	—	2
Accumulated deficit	(2,425,915)	(2,328,007)
Total stockholders' equity	3,767	40,029
Total liabilities and stockholders' equity	$ 72,434	$ 58,241

See accompanying notes.

CTI BIOPHARMA CORP.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except per share amounts)

	Year Ended December 31,	
	2021	2020
Operating costs and expenses:		
Research and development	$ 39,136	$ 25,943
Selling, general and administrative	56,196	17,626
Other operating expense	—	4,200
Total operating costs and expenses	95,332	47,769
Loss from operations	(95,332)	(47,769)
Non-operating expense:		
Interest expense, net	(2,415)	(828)
Other non-operating expenses	(161)	(3,854)
Total non-operating expense	(2,576)	(4,682)
Net loss	$ (97,908)	$ (52,451)
Basic and diluted net loss per common share	$ (1.09)	$ (0.74)
Shares used in calculation of basic and diluted net loss per common share	90,117	71,141

See accompanying notes.

CTI BIOPHARMA CORP.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,	
	2021	2020
Net loss	$ (97,908)	$ (52,451)
Other comprehensive (loss) income:		
Change in unrealized (loss) gain on available-for-sale securities	(2)	2
Other comprehensive (loss) income	(2)	2
Comprehensive loss	$ (97,910)	$ (52,449)

See accompanying notes.

CTI BIOPHARMA CORP.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands)

	Preferred Stock		Common Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Noncontrolling	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Income (Loss)	Deficit	Interest	Equity
Balance at January 1, 2020	13	$ —	57,980	$ 58	$ 2,299,186	$ —	$ (2,275,556)	$ (5,758)	$ 17,930
Issuance of common stock, net (at-the-market equity offering)	—	—	2,071	2	22,607	—	—	—	22,609
Issuance of common stock and Series X preferred stock, net	4	—	15,699	16	43,637	—	—	—	43,653
Conversion of Series X preferred stock to common stock	—	—	3	—	3	—	—	—	3
Dissolution of majority-owned subsidiary	—	—	—	—	(1,949)	—	—	5,758	3,809
Equity-based compensation	—	—	—	—	4,317	—	—	—	4,317
Exercise of stock options and shares issued under employee stock purchase plan	—	—	144	—	157	—	—	—	157
Net loss for the year ended December 31, 2020	—	—	—	—	—	—	(52,451)	—	(52,451)
Other comprehensive income	—	—	—	—	—	2	—	—	2
Balance at December 31, 2020	17	$ —	75,897	$ 76	$ 2,367,958	$ 2	$ (2,328,007)	$ —	$ 40,029
Issuance of common stock, net (at-the-market equity offering)	—	—	858	1	2,961	—	—	—	2,962
Issuance of common stock and Series X[1] Preferred Stock, net	1	—	16,400	16	53,537	—	—	—	53,553
Conversion of Series X preferred stock to common stock	(1)	—	6,350	7	(7)	—	—	—	—
Equity-based compensation	—	—	—	—	4,743	—	—	—	4,743
Exercise of stock options and shares issued under employee stock purchase plan	—	—	263	—	390	—	—	—	390
Cancellation of restricted stock	—	—	(4)	—	—	—	—	—	—
Net loss for the year ended December 31, 2021	—	—	—	—	—	—	(97,908)	—	(97,908)
Other comprehensive loss	—	—	—	—	—	(2)	—	—	(2)
Balance at December 31, 2021	17	$ —	99,764	$ 100	$ 2,429,582	$ —	$ (2,425,915)	$ —	$ 3,767

See accompanying notes.

CTI BIOPHARMA CORP.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,	
	2021	**2020**
Operating activities		
Net loss	$ (97,908)	$ (52,451)
Adjustments to reconcile net loss to net cash used in operating activities:		
Equity-based compensation expense	4,743	4,317
Depreciation and amortization	526	532
Provision for Italian VAT receivables and deposit	—	4,200
Loss on dissolution of majority-owned subsidiary	—	3,774
Other	(113)	(155)
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	2,278	2,274
Accounts payable, accrued expenses and other liabilities	5,585	(4,696)
Net cash used in operating activities	(84,889)	(42,205)
Investing activities		
Purchases of property and equipment	—	(17)
Purchases of short-term investments	—	(12,100)
Proceeds from maturities of short-term investments	12,000	2,500
Net cash provided by (used in) investing activities	12,000	(9,617)
Financing activities		
Gross proceeds from public offering of common stock and Series X[1] preferred stock	56,000	—
Cash paid for offering costs - public offering of common stock and Series X[1] preferred stock	(2,447)	—
Gross proceeds from rights offering	—	59,991
Cash paid for offering costs - rights offering	—	(883)
Gross proceeds from at-the-market equity offering	3,064	7,378
Cash paid for offering costs - at the-market equity offering	(411)	(221)
Gross proceeds from DRI Credit Agreement	50,000	—
Cash paid for issuance costs - DRI Credit Agreement	(1,813)	—
Cash paid for issuance costs - DRI Royalty Financing Agreement	(531)	—
Repayment of Silicon Valley Bank debt	(6,329)	(5,333)
Proceeds from stock option exercises and ESPP stock issuance	408	140
Net cash provided by financing activities	97,941	61,072
Net increase in cash and cash equivalents	25,052	9,250
Cash and cash equivalents at beginning of year	40,394	31,144
Cash and cash equivalents at end of year	$ 65,446	$ 40,394
Supplemental disclosure of cash flow information		
Cash paid during the period for interest	$ 1,950	$ 547
Supplemental disclosure of noncash financing and investing activities		
Conversion of preferred stock to common stock	$ 6,350	$ —

See accompanying notes.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Description of Business and Summary of Significant Accounting Policies

CTI BioPharma Corp. and our subsidiaries, also referred to in this Annual Report on Form 10-K as “we,” “us,” “our,” the “Company” and “CTI,” is a biopharmaceutical company focused on the acquisition, development and commercialization of novel targeted therapies for blood-related cancers where there is a significant unmet medical need. Our goal is to build a profitable company by generating income from products we develop and commercialize, either alone or with partners. We have one commercially approved product, VONJO™ (pacritinib), which received accelerated approval in February 2022 from the the FDA in the United States, for the treatment of adult patients with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 x 10^9/L. We commercially launched VONJO in the first quarter of 2022.

We operate in a highly regulated and competitive environment. The manufacturing and marketing of pharmaceutical products requires approval from, and is subject to, ongoing oversight by the FDA in the United States, the EMA in the EU, and comparable agencies in other countries. Obtaining approval for a new therapeutic product is never certain, may take many years and may involve the expenditure of substantial resources.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of our majority-owned subsidiary, Aequus Biopharma, Inc., or Aequus, until its dissolution in June 2020. We had an approximately 60% interest in Aequus; the remaining interest not held by CTI was reported as *noncontrolling interest* in the consolidated financial statements until its dissolution. All intercompany transactions and balances were eliminated in consolidation through the June 2020 Aequus dissolution. The accompanying consolidated financial statements do not include the accounts of subsidiaries since July 2020.

Liquidity

The accompanying consolidated financial statements have been prepared assuming that we will continue as a going concern, which contemplates realization of assets and the satisfaction of liabilities in the normal course of business within one year after the date the consolidated financial statements are issued. Our management evaluates whether there are conditions or events, considered in aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that the financial statements are issued.

Over the next year and in the normal course of business, we expect to increase our spend on our VONJO commercialization efforts as well as conduct research, development, testing and regulatory compliance activities with respect to other development pathways for pacritinib. While we expect revenues from VONJO to increase after its initial launch, we cannot accurately predict the market acceptance or growth trajectory of VONJO's revenues. Further, we will incur selling, general and administrative expenses. Additional anticipated business activities include procuring clinical drug supplies and establishing commercial supplies of our commercial product, the costs of which, together with our projected selling, general and administrative expenses, when offset against our projected revenues, are expected to result in operating losses for the foreseeable future. We have incurred a net operating loss every year since our formation. As of December 31, 2021, we had an accumulated deficit of $2.4 billion. Our available cash and cash equivalents were $65.4 million as of December 31, 2021. We expect that our present financial resources, combined with $60.0 million received from Drug Royalty III LP 2 following FDA approval of VONJO in February 2022, will be sufficient to meet our obligations as they come due and to fund our operations into the fourth quarter of 2022. Based on our evaluation completed pursuant to Accounting Standard Codification subtopic 205-40 Going Concern, these factors raise substantial doubt about our ability to continue as a going concern within one year after the date that the financial statements are issued, or through the first quarter of 2023.

We will require additional capital in order to pursue our strategic objectives. We expect to satisfy our capital needs through existing capital balances, revenue from VONJO, and some combination of public or private equity financings, partnerships, collaborations, joint ventures, debt financings or restructurings, bank borrowings or other sources of financing. However, we have a limited number of authorized shares of common stock available for issuance and additional funding may not be available on favorable terms or at all. If additional funds are raised by issuing equity securities, substantial dilution to existing stockholders may result. If we fail to obtain additional capital when needed, our ability to operate as a going concern will be harmed, and we may be required to delay, scale back or eliminate some or all of our research and development programs and commercialization efforts and/or reduce our selling, general and administrative expenses, be unable to attract and retain highly-qualified personnel, be unable to obtain and maintain contracts necessary to continue our operations and at affordable rates with competitive terms, refrain from making our contractually required payments when due (including debt payments) and/or be forced to cease operations, liquidate our assets and possibly seek bankruptcy protection.

Our future capital requirements will depend on many factors, including: our ability to generate sales of VONJO; the cost and timing of establishing our commercial infrastructure and distribution capabilities; our ability to reach milestones triggering payments under certain of our contractual arrangements; the cost of manufacturing VONJO; the cost of manufacturing clinical supplies of our product candidates or of establishing commercial supplies of any products that we may develop in the future; developments in and expenses associated with our research and development activities; our clinical development plans and any changes that we may initiate or that may be requested by the FDA or other regulators as we seek product approval; acquisitions or collaborations with respect to compounds or other assets; competitive market developments; disruptions or other delays to our business and clinical trials resulting from the ongoing worldwide COVID-19 pandemic; and other unplanned business developments.

In addition, our ability to comply with covenants under our Credit Agreement with Drug Royalty III LP 2 may be affected by events beyond our control, and we may not be able to meet those covenants. A breach of any of these covenants, including a material adverse change in our business, operations or condition (financial or otherwise), could result in an event of default under the Credit Agreement, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable. See “Note 7. Debt Financing Arrangements” for additional details. The accompanying consolidated financial statements do not include adjustments, if any, that may result from the outcome of this uncertainty.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires estimates and assumptions that affect the reported amounts of assets and liabilities, revenues and expenses, and related disclosures of loss contingencies in the consolidated financial statements and accompanying notes. Estimates are used for, but not limited to, clinical accruals, income taxes, commitments and contingencies, and equity-based compensation forfeiture rates. Given the global economic climate and additional or unforeseen effects from the ongoing COVID-19 pandemic, these estimates are becoming more challenging, and actual results could differ materially from those estimates.

Segment Information

We view our operations and manage our business in a single operating segment focused on the business of acquiring, developing and commercializing novel targeted therapies for blood-related cancers. All of our tangible assets are held in the United States.

Certain Risks, Uncertainties and Concentrations

Cash, cash equivalents and marketable securities are financial instruments which potentially subject us to concentrations of credit risk. We have not experienced any significant credit losses on cash, cash equivalents, or marketable securities to date. We have no off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

We source our drug products for commercial operations and clinical trials from a concentrated group of third-party contractors. If we are unable to obtain sufficient quantities of source materials, manufacture or distribute our products to customers from existing suppliers and service providers, or obtain the materials or services from other suppliers or manufacturers, certain sales and research and development activities may be delayed.

Fair Value of Financial Instruments

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Fair value measurements are based on a three-tier hierarchy that prioritizes the inputs used to measure fair value. There are three levels of inputs used to measure fair value with Level 1 having the highest priority and Level 3 having the lowest:

- Level 1—Valuations based on unadjusted quoted prices for identical assets and liabilities in active markets.
- Level 2—Valuations based on observable inputs other than quoted prices included in Level 1, such as quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets and liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Valuations based on unobservable inputs that are supported by little or no market activity, reflecting our own assumptions. These valuations require significant judgment or estimation.

Our cash equivalents and short-term investments are recorded at fair value. As of December 31, 2021, our cash and cash equivalents consisted of cash and money market funds. As of December 31, 2020, our cash, cash equivalents and short-term investments consisted of cash, money market funds and corporate debt securities.

We measure the fair value of money market funds based on the closing price reported by the fund sponsor from an actively traded exchange. We value all other securities using broker quotes that utilize observable market inputs. We did not hold cash, cash equivalents and short-term investments categorized as Level 3 assets as of December 31, 2021 and 2020. The following table summarizes, by major security type, our cash, cash equivalents and short-term investments that are measured at fair value on a recurring basis and are categorized using the fair value hierarchy (in thousands):

	December 31, 2021			December 31, 2020
	Cost or Amortized Cost	Gross Unrealized Gains / (Losses)	Total Estimated Fair Value	Total Estimated Fair Value
Cash	$ 137	$ —	$ 137	$
Level 1 securities:				
Money market funds	65,309	—	65,309	40,(
Level 2 securities:				
Corporate debt securities	—	—	—	12,(
Total cash, cash equivalents and short-term investments	$ 65,446	$ —	$ 65,446	$ 52,.

We review investments for other-than-temporary impairment whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. Other-than-temporary impairments of investments are recognized in the consolidated statements of operations if we have experienced a credit loss and have the intent to sell the investment or if it is more likely than not that we will be required to sell the investment before recovery of the amortized cost basis.

At December 31, 2021 and 2020, the carrying value of our payables and accruals approximated their fair values due to their short-term maturities. The carrying value of our long-term debt approximated its fair value at December 31, 2021 and
2020 based on borrowing rates for similar loans and maturities.

Cash and Cash Equivalents

We consider all highly liquid instruments with original maturities of three months or less at the time acquired to be cash equivalents. The carrying value of cash and cash equivalents approximates fair value due to the short-term nature of these items.

Italian Value Added Tax

As disclosed in "Note 13. Commitments and Contingencies," the Italian Tax Authority, or the ITA, assessed us for additional VAT payments for services we provided in Italy, which we do not believe we owe. We have not recorded an amount in the financial statements for this contingent liability as we do not believe the potential payment of up to €4.4 million (or approximately $4.9 million converted using the currency exchange rate as of December 31, 2021) to the ITA is probable at this time.

Leases

Under ASC 842 - *Leases*, we determine if an arrangement is a lease at inception. We recognize a right-of-use asset and lease liability on the balance sheet for all leases with a term longer than 12 months. Leases are classified as operating or finance at lease commencement, which will affect the pattern and classification of expense recognition in our consolidated statements of operations.

Right-of-use assets represent the right to use an underlying asset for the lease term and lease liabilities represent the obligation to make lease payments arising from the lease. Operating lease liabilities are recognized at commencement date based on the present value of lease payments over the lease term. As our leases do not provide a readily determinable implicit rate of return, we derive the present value of lease payments using our incremental borrowing rate, which is the rate of interest that we would have to pay to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment.

An operating lease right-of-use asset is measured at the amount of the lease liability, adjusted for prepaid or accrued lease payments, lease incentives received, unamortized initial direct costs and the impairment of the right-of-use asset. A lease may include options to extend or terminate the lease. When it is reasonably certain that we will exercise such an option, it is considered in the lease term. Right-of-use assets are tested for impairment in the same manner as long-lived assets used in operations.

Lease expense for operating leases is recognized on a straight-line basis over the lease term as part of *Research and development* expenses and *Selling, general and administrative* expenses in our consolidated statements of operations. Right-of-use assets are included in *Other assets*, and the current portion of lease liabilities and the non-current portion of lease liabilities are included in *Other current liabilities* and *Other liabilities*, respectively, in our consolidated balance sheets.

Property and Equipment

Property and equipment are carried at cost, less accumulated depreciation and amortization. Depreciation commences at the time assets are placed in service. We calculate depreciation using the straight-line method over the estimated useful lives of the assets, ranging from three to five years for assets other than leasehold improvements. We capitalize leasehold improvements at cost and amortize them over the lesser of their useful lives of 10 years or the term of the applicable lease.

Impairment of Long-lived Assets

We review our long-lived assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of assets may not be fully recoverable or that the useful lives of these assets are no longer appropriate. If an impairment is indicated, the asset is written down to its estimated fair value.

Contingencies

We record liabilities associated with loss contingencies to the extent that we conclude that the occurrence of the contingency is probable and that the amount of the related loss is reasonably estimable. We record income from gain contingencies only upon the realization of assets resulting from the favorable outcome of the contingent event. See “Note 9. Collaboration, Licensing and Milestone Agreements” and “Note 13. Commitments and Contingencies” for further information regarding our current contingencies.

Research and Development Expenses

Research and development costs are expensed as incurred in accordance with ASC 730, *Research and Development*. Research and development expenses include related salaries and benefits, clinical trial and related manufacturing costs, contract and other outside service fees, and facilities and overhead costs related to our research and development efforts. Research and development expenses also consist of costs incurred for proprietary and collaboration research and development and include activities such as product registries and investigator-sponsored trials. In instances where we enter into agreements with third parties for research and development activities, we may prepay fees for services at the initiation of the contract. We record the prepayment as a prepaid asset and amortize the asset into research and development expense over the period of time the contracted research and development services are performed. Other types of arrangements with third parties may be fixed fee or fee for service, and may include monthly payments or payments upon completion of milestones or receipt of deliverables. We expense upfront license payments related to acquired technologies that have not yet reached technological feasibility and have no alternative future use.

Equity-Based Compensation Expense

Equity-based compensation expense for all equity-based payment awards made to employees and directors is measured based on the grant-date fair value estimated in accordance with U.S. GAAP. We recognize equity-based compensation using the straight-line, single-award method based on the value of the portion of equity-based payment awards that is ultimately expected to vest. We apply estimated forfeiture rates at the time of grant and make revisions, if necessary, in subsequent periods if actual forfeitures differ from those estimates. For performance-based awards that do not include market-based conditions, we record equity-based compensation expense only when the performance-based milestone is deemed probable of achievement. We utilize both quantitative and qualitative criteria to judge whether milestones are probable of achievement. For awards with market-based performance conditions, we recognize the grant-date fair value of the award over the derived service period regardless of whether the underlying performance condition is met.

Income Taxes

The provision for income taxes is computed using the asset and liability method, under which deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial reporting and tax basis of assets and liabilities, and for operating losses and tax credit carryforwards. Deferred tax assets and liabilities are measured using the currently enacted tax rates in effect for the years in which those tax assets and liabilities are expected to be realized or settled. We provide a valuation allowance to reduce deferred tax assets to the amount that is more likely than not to be realized.

Net Loss per Share

Basic net loss per common share is calculated based on net loss divided by the weighted average number of shares outstanding for the period. The calculation of diluted net loss per common share excludes the potential conversion of all dilutive convertible securities, such as convertible preferred stock, using the if-converted method, and the potential exercise or vesting of other dilutive securities, such as options, warrants and restricted stock, using the treasury stock method, as their inclusion would have an anti-dilutive effect.

Recently Adopted Accounting Standards

In August 2020, the FASB issued new accounting guidance for convertible instruments which eliminates two of the three models in ASC 470-20 that require separate accounting for embedded conversion features. Separate accounting is still required in certain cases. For smaller reporting companies, the guidance is effective for fiscal years beginning after December 15, 2023, including interim periods therein. Early adoption is permitted in fiscal years beginning after December 15, 2020. We early adopted this guidance as of January 1, 2021. In April 2021, as discussed in “Note 8. Equity Transactions,” we completed the public offering of our common stock and our Series X^1 Preferred Stock. No beneficial conversion feature was recognized on Series X^1 Preferred Stock upon issuance.

Recently Issued Accounting Standards

In March 2020, the FASB issued new accounting guidance to provide temporary optional expedients to ease the potential burden in accounting for reference rate reform. The guidance includes an optional expedient that simplifies accounting for contract modifications to loans receivable and debt, by prospectively adjusting the effective interest rate. The accounting guidance is effective as of January 7, 2021 through December 31, 2022. As discussed in “Note 7. Debt Financing Arrangements,” in August 2021, we entered into a Credit Agreement, which has an interest rate referenced to the London Interbank Offered Rate, or LIBOR. We plan to elect the optional expedient for our credit facility by prospectively adjusting the effective interest rate if the cessation of the LIBOR occurs. We do not expect the adoption of this guidance to have a material impact on our consolidated financial statements.

Although there were several other new accounting pronouncements issued or proposed by the FASB, we do not believe any of these have had or will have a material impact on our consolidated financial statements.

Reclassifications

Certain prior year items have been reclassified to conform to current year presentation.

2. Property and Equipment

Property and equipment consisted of the following as of December 31, 2021 and 2020 (in thousands):

	2021	2020
Furniture and office equipment	$ 597	$ 663
Leasehold improvements	5,140	5,140
	5,737	5,803
Less: accumulated depreciation and amortization	(5,561)	(5,084)
Property and equipment, net	$ 176	$ 719

Depreciation expense was $0.5 million for each of the years ended December 31, 2021 and 2020.

3. Other Assets

Other assets consisted of the following as of December 31, 2021 and 2020 (in thousands):

	2021	2020
Right-of-use assets	$ 3,109	$ 2,149
Clinical trial deposits	770	770
Refundable security deposit	—	194
Other	—	84
Total other assets	$ 3,879	$ 3,197

4. Accrued Expenses

Accrued expenses consisted of the following as of December 31, 2021 and 2020 (in thousands):

	2021	2020
Clinical trial expenses	$ 4,053	$ 3,512
Employee compensation and related expenses	4,783	2,792
Commercial expenses	3,075	—
Manufacturing expenses	288	238
Other	521	649
Total accrued expenses	$ 12,720	$ 7,191

5. Other Current Liabilities

Other current liabilities consisted of the following as of December 31, 2021 and 2020 (in thousands):

	2021	2020
Operating lease liabilities - current	$ 1,160	$ 2,194
End-of-facility lender fee (1)	1,000	1,440
Other current obligations	500	121
Total other current liabilities	$ 2,660	$ 3,755

(1) The end-of-facility lender fee as of December 31, 2021 represents an amount payable to Drug Royalty III LP 2, or DRI, upon repayment of our secured term loan under the Credit Agreement with DRI. The end-of-facility lender fee as of December 31, 2020 represents an amount payable to Silicon Valley Bank upon repayment of our secured term loan, which was repaid in August 2021. See “Note 7. Debt Financing Arrangements” for additional information.

6. Leases

In January 2012, we entered into an agreement with Selig Holdings Company LLC, or Selig, to lease approximately 66,000 square feet of office space in Seattle, Washington for a term of 10 years, commencing May 2012 and expiring April 2022. We had two five-year options to extend the term of the lease at a market rate determined according to the lease. We also had an option to early terminate the lease after the fifth anniversary from the commencement date. We were provided with a total of $3.9 million for certain tenant improvements and other lease incentives. The options to extend or terminate the lease were not considered in the determination of the right-of-use asset and the lease liability as we did not consider it reasonably certain that we would exercise such options. We also lease parking space under the agreement and had certain office equipment leases until October 2020. We have elected not to separate a non-lease component from a lease component for these leases.

In December 2017, we entered into an agreement to sublease approximately 44,000 square feet of our office space. No payments were due through May 2018, after which monthly rent is due through the sublease termination date in April 2022.

In December 2021, we entered into an amendment to extend the term of the existing lease by 3 years to April 2025 and to reduce the leased office space, beginning May 2022, to approximately 23,000 square feet. We were also provided with

certain tenant improvement costs of up to $50,000. The amendment provides for one five-year option to extend the term of the lease at a market rate at the time of such extension. The option to extend the lease was not considered in the remeasurement of lease liability and the adjustment of the right-of-use asset as we did not consider it reasonably certain that we would exercise such option. The amended lease will continue to be classified as an operating lease. As a result of this amendment, the lease liability balance as well as the right-of-use asset balance increased by $2.4 million as of the effective date.

The operating lease for our office space includes common area maintenance services provided by Selig, which are considered a non-lease component. Since the payments for these services are based on the actual costs incurred by Selig in providing the services, we consider these payments as variable lease expenses.

The components of lease expense, which were included in our consolidated statements of operations, were as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Operating lease expense	$ 1,586	$ 1,653
Variable lease expense	183	230
Sublease income	(1,254)	(1,247)
Total lease expense, net	$ 515	$ 636

The balance sheet classification of operating lease right-of-use assets and operating lease liabilities were as follows (in thousands):

	December 31, 2021
Right-of-use assets (included in *Other Assets*)	$ 3,109
Operating lease liabilities, current (included in *Other current liabilities*)	$ 1,160
Operating lease liabilities, non-current (included in *Other liabilities, less current portion*)	2,016
Total lease liabilities	$ 3,176

As of December 31, 2021, the maturities of operating lease liabilities were as follows (in thousands):

	Operating Lease Payments	Sublease Rental Receipts	Net
2022	$ 1,450	$ (499)	$ 951
2023	976	—	976
2024	1,002	—	1,002
2025	337	—	337
Thereafter	—	—	—
Total payments	3,765	$ (499)	$ 3,266
Less imputed interest	(589)		
Total lease liabilities	$ 3,176		

Supplemental information relating to our operating leases is as follows (in thousands):

	December 31, 2021
Supplemental cash flow information	
Cash paid for amounts included in the measurement of lease liabilities	$ 2,435
Right-of-use assets obtained in exchange for operating lease liabilities due to lease amendment	$ 2,384
Weighted-average remaining lease term of operating leases (years)	3.33
Weighted-average discount rate of operating leases	11.6 %

7. Debt Financing Arrangements

Silicon Valley Bank

In August 2021, in connection with the Credit Agreement we entered into with Drug Royalty III LP 2 as discussed below, we repaid the then-outstanding principal balance of $1.3 million under our loan agreement with Silicon Valley Bank in full, along with the end-of-facility lender fee of $1.4 million and the prepayment premium of $40,000. Accordingly, with respect to the loan agreement with Silicon Valley Bank, among other things, (1) all obligations have been paid, satisfied, released and discharged in full, (2) all unfunded commitments to make credit extensions or financial accommodations to us or any other person under the loan agreement have been automatically and irrevocably terminated, and (3) all related documents have been automatically and irrevocably terminated (other than with respect to customary provisions and agreements that are expressly specified to survive the termination). Upon full repayment of the principal in August 2021, we recorded a loss on debt extinguishment of $0.1 million in *Other non-operating expense* for the year ended December 31, 2021.

Drug Royalty III LP 2

Credit Agreement

In August 2021, we entered into a Credit Agreement with Drug Royalty III LP 2, or DRI, as lender and as administrative agent for the lenders, and received a term loan in the principal amount of $50.0 million under the Credit Agreement, or the Term Loan, with a maturity date of August 25, 2026. The Credit Agreement provides for quarterly interest-only payments until the maturity date, with the unpaid principal amount of the Term Loan due and payable on the maturity date. The Term Loan bears interest at a rate equal to the greater of (i) 1.75% per annum and (ii) the three-month LIBOR rate, plus 8.25% (or, upon the occurrence of and during the continuance of any event of default, plus 10.25% per annum). Our obligations under the Credit Agreement are secured by a first priority security interest in substantially all of our assets, subject to certain exceptions.

We are required to make mandatory prepayments of the Term Loan with the proceeds of certain asset sales, certain VONJO out-licensing or royalty monetization transactions (excluding the Royalty Sale contemplated under the Royalty Purchase Agreement discussed below), extraordinary receipts, debt issuances, or upon a change of control of the Company and specified other events, subject to certain exceptions. We may make voluntary prepayments in whole or in part. Prepayments prior to the fourth anniversary of the closing date are subject to a prepayment premium, which declines over time following the second anniversary of the closing date. Upon the prepayment or repayment, including at maturity, of all or any portion of the Term Loan, we are obligated to pay an exit fee in an amount equal to 2.00% of the principal amount of the Term Loan prepaid or repaid, which is recorded in *Other current liabilities*. See “Note 5. Other Current Liabilities” for additional information. In addition, the Term Loan was subject to a 1.00% commitment fee due and payable on the closing date.

The Credit Agreement contains representations and warranties and affirmative and negative covenants customary for financings of this nature, as well as customary events of default. Certain of the customary negative covenants limit our ability to, among other things, grant liens, make investments, incur additional indebtedness, dispose of assets, license certain property, distribute dividends, make certain restricted payments, change the nature of our business, engage in transactions with affiliates and insiders, prepay other indebtedness, or engage in sale and leaseback transactions, subject to certain exceptions. The Credit Agreement contains a minimum liquidity covenant requiring us to maintain at least $10.0 million of unrestricted cash and cash equivalents, subject to certain exceptions. A failure to comply with the covenants in the Credit Agreement could permit the Lenders under the Credit Agreement to declare the outstanding principal as well as accrued interest and fees to be immediately due and payable.

In addition, the Credit Agreement contains an affirmative covenant requiring us to deliver to DRI, within 120 days after the end of each fiscal year, audited financial statements of the Company accompanied by an unqualified report and opinion of an independent certified public accountant, which report and opinion shall not be subject to any "going concern" or like qualification or exception. We have obtained a waiver of breach of such covenant from DRI since the report of independent registered public accounting firm contained within this Annual Report on Form 10-K states that substantial doubt exists about our ability to continue as a going concern. We may need to obtain similar waivers at future annual reporting dates if substantial doubt continues to exist.

As of December 31, 2021, we had an outstanding Term Loan principal balance of $50.0 million under the Credit Agreement. In connection with the Credit Agreement, we recorded debt discount and debt issuance costs of $1.5 million and $1.3 million, respectively, of which $1.4 million and $1.2 million were unamortized as of December 31, 2021, respectively. The Credit Agreement contains certain settlement provisions which, if deemed probable, would result in the recognition of an embedded feature. However, we do not believe such provisions are probable at this time.

All amounts due under the Credit Agreement have been recorded in *current liabilities* on the consolidated balance sheet as of December 31, 2021 due to the considerations discussed in "Note 1. Description of Business and Summary of Significant Accounting Policies - *Liquidity*" and the assessment that the events of default clause, which includes a material adverse effect provision under the Credit Agreement, is not within our control. We have not been notified of an event of default by DRI as of the date of the filing of this Annual Report on Form 10-K.

As of December 31, 2021, the scheduled principal and interest payments (based on the interest rate of 10.00% as of December 31, 2021) as well as the back-end fee described above are as follows (in thousands):

	Principal	Interest	Back-end fee	Total
2022	$ —	$ 5,069	$ —	$ 5,0
2023	—	5,069	—	5,0
2024	—	5,083	—	5,0
2025	—	5,069	—	5,0
2026 and thereafter	50,000	3,278	1,000	54,2
Total scheduled payments	$ 50,000	$ 23,568	$ 1,000	$ 74,5
Less: debt discount and issuance costs	(2,620)			
Current portion of long-term debt	$ 47,380			

Royalty Financing Agreement

In connection with the Credit Agreement, we entered into a Purchase and Sale Agreement with DRI, or the Royalty Financing Agreement, pursuant to which we sold to DRI the right to receive certain royalty payments from us for a purchase price of up to $85.0 million in cash. Under the Royalty Financing Agreement, DRI is entitled to receive tiered, sales based royalties on net product sales of VONJO in the United States in an amount equal to: (i) 9.60% of annual net sales of VONJO in the United States for annual net sales up to $125 million, (ii) 4.50% of annual net sales of VONJO in the United States for annual net sales between $125 million and $175 million and (iii) 0.50% of annual net sales of VONJO in the United States for annual net sales between $175 million and $400 million. No royalty payments are payable on annual net sales of VONJO in the United States over $400 million.

In March 2022, DRI funded the upfront purchase price of $60.0 million following FDA approval of VONJO in the United States and will be required to provide to us up to $25.0 million of additional funding if certain minimum pacritinib sales thresholds are met in 2023, or sooner.

We are required to make payments of amounts owed to DRI each calendar quarter from and after the first commercial sale of the applicable product in the United States. The transactions contemplated by the Royalty Financing Agreement are referred to herein as the Royalty Sale.

Under the Royalty Financing Agreement, we agreed to specified affirmative and negative covenants, including without limitation covenants regarding periodic reporting of information by us to DRI, obligations to use commercially reasonable efforts to commercialize VONJO in the United States and restrictions on the ability of the Company or any of its subsidiaries to incur certain indebtedness, which restrictions are eliminated after the earliest of: (i) the date on which the trailing twelve months' of VONJO sales equals at least $200 million, (b) the date on which the Company's market capitalization (determined

on an as-converted basis) is at least $1.0 billion for 20 consecutive trading days or (c) DRI receiving royalty payments in an amount equal to 100% of their purchase price. The Royalty Financing Agreement also contains representations and warranties, other covenants, indemnification obligations, settlement and other provisions customary for transactions of this nature.

We have evaluated the terms of the Royalty Financing Agreement and concluded that the features of the funding from DRI are similar to those of a debt instrument. Accordingly, we will account for the transaction as debt and the funding from DRI will be recorded as Royalty Financing Obligation on our consolidated balance sheet. The Royalty Financing Obligation will be amortized over the expected repayment term using an effective interest rate method. The effective interest rate will be calculated based on the rate that would enable the debt to be repaid in full over the anticipated life of the arrangement. The interest rate may vary during the term of the agreement depending on a number of factors, including the amount and timing of forecasted net revenues which affects the repayment timing and ultimate amount of repayment. We will evaluate the effective interest rate quarterly based on our current revenue forecasts utilizing the prospective method.

8. Equity Transactions

At-The-Market Equity Offering

In January 2021, we entered into an Open Market Sale Agreement℠ with Jefferies LLC, or the Sale Agreement, to sell shares of our common stock having aggregate sales proceeds of up to $50.0 million, from time to time, through an “at the market” equity offering program under which Jefferies will act as sales agent.

Under the Sale Agreement, we will set the parameters for the sale of shares, including the number of shares to be issued, the time period during which sales are requested to be made, limitation on the number of shares that may be sold in any one trading day and any minimum price below which sales may not be made. Subject to the terms and conditions of the Sale Agreement, Jefferies may sell the shares by methods deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, including sales made directly on The Nasdaq Capital Market or on any other existing trading market for the common stock. Jefferies will use commercially reasonable efforts in conducting such sales activities consistent with its normal trading and sales practices, applicable state and federal laws, rules and regulations and the rules of The Nasdaq Stock Market LLC.

We and Jefferies may each terminate the Sale Agreement at any time upon ten trading days’ prior notice. We may also sell shares to Jefferies acting as principal for Jefferies’ own account. The compensation to Jefferies for sales of our common stock will be an amount equal to 3% of the gross proceeds of any shares of our common stock sold under the Sale Agreement. We have no obligation to sell any shares under the Sale Agreement, and may at any time suspend solicitation and offers under the Sale Agreement.

For the year ended December 31, 2021, we sold 0.9 million shares of our common stock for net proceeds of approximately $2.7 million under the Sale Agreement. Cash received from first quarter 2022 sales under the Sale Agreement as of the date of this Annual Report on Form 10-K was not material.

Series X Preferred Stock

In March 2020, we completed a rights offering whereby we issued a total of 15.7 million shares of our common stock and 4,429 shares of our Series X Preferred Stock, which shares of Series X Preferred Stock are convertible into 44.3 million shares of our common stock, for aggregate gross proceeds of approximately $60.0 million. See Form 10-K Part II, Item 8, “Notes to Consolidated Financial Statements, Note 8. Equity Transactions” of our Annual Report on Form 10-K for the year ended December 31, 2020 for additional information. During the year ended December 31, 2021, 635 shares of our Series X Preferred Stock were converted into 6.4 million shares of our common stock. There were 3,794 shares of our Series X Preferred Stock outstanding as of December 31, 2021.

Public Offering of Common Stock and Series X^1 Preferred Stock

In April 2021, we completed the public offering of our common stock and our Series X^1 Preferred Stock, or the Offering, whereby we issued 14,260,800 shares of our common stock, par value $0.001 per share, at a public offering price of $2.50 per share, and 600 shares of our Series X^1 Preferred Stock, par value $0.001 per share, at a public offering price of $25,000 per share. In addition, we granted the underwriters a 30-day option to purchase up to additional 2,139,120 shares of our common

stock on the same terms and conditions, which was exercised in full in April 2021. The net proceeds to us from the Offering, after deducting underwriting discounts and offering expenses, were approximately $53.6 million.

At the time of issuance of our Series X^1 Preferred Stock, the carrying amount of our Series X^1 Preferred Stock was initially classified as mezzanine equity in the consolidated balance sheet since we did not have an adequate number of shares of authorized common stock to satisfy the number of required shares under the conversion option of our Series X^1 Preferred Stock. In June 2021, our stockholders approved an increase in the number of shares of authorized common stock, and as such, we can now control settlement of the conversion option's exercise by delivering shares. Accordingly, the carrying amount of our Series X^1 Preferred Stock was reclassified to permanent equity in June 2021.

BVF Partners L.P., or BVF, an existing stockholder of the Company, was one of the investors in the Offering. In connection with the Offering, BVF purchased 2.0 million shares of our common stock and 600 shares of our Series X^1 Preferred Stock. As of December 31, 2021 and 2020, BVF beneficially owned approximately 8.8% and 9.1%, respectively, of our outstanding common stock. Matthew D. Perry, a member of our Board, is the President of BVF and portfolio manager for the underlying funds managed by the firm. No shares of our Series X^1 Preferred Stock were converted into our common stock during the year ended December 31, 2021. There were 600 shares of our Series X^1 Preferred Stock outstanding as of December 31, 2021.

Each share of Series X^1 Preferred Stock is convertible into 10,000 shares of our common stock at a conversion price of $2.50 per share of common stock, at the option of the holder at any time, subject to certain limitations, including that a holder of Series X^1 Preferred Stock is prohibited from converting Series X^1 Preferred Stock into common stock if, as a result of such conversion, such holder, together with its affiliates, would own more than 9.99% of the total number of shares of our common stock issued and outstanding immediately after giving effect to such conversion.

Shares of Series X^1 Preferred Stock generally have no voting rights, except as otherwise expressly provided in the Certificate of Designation of Preferences, Rights and Limitations of Series X^1 Convertible Preferred Stock, or Certificate of Designation, or as otherwise required by law. However, as long as any shares of Series X^1 Preferred Stock are outstanding, we shall not, without the affirmative vote of the holders of a majority of the then outstanding shares of Series X^1 Preferred Stock, (i) alter or change adversely the powers, preferences or rights given to the Series X^1 Preferred Stock or alter or amend this Certificate of Designation, amend or repeal any provision of, or add any provision to, the Certificate of Incorporation or bylaws of the Company, or file any articles of amendment, certificate of designations, preferences, limitations and relative rights of any series of preferred stock, if such action would adversely alter or change the preferences, rights, privileges or powers of, or restrictions provided for the benefit of the Series X^1 Preferred Stock, regardless of whether any of the foregoing actions shall be by means of amendment to the Certificate of Incorporation or by merger, consolidation or otherwise, (ii) issue further shares of Series X^1 Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Series X^1 Preferred Stock, or (iii) enter into any agreement with respect to any of the foregoing.

In the event of our liquidation, dissolution or winding up, holders of Series X^1 Preferred Stock will participate pari passu with any distribution of proceeds to holders of our common stock. Holders of Series X^1 Preferred Stock are entitled to receive dividends on shares of Series X^1 Preferred Stock equal (on an as-converted to common stock basis, without regard to the Beneficial Ownership Limitation (as defined in the Certificate of Designation)) to and in the same form as dividends actually paid on shares of common stock, plus an additional amount equal to any dividends declared but unpaid on such shares, before any payments shall be made or any assets distributed to holders of any class of Junior Securities (as defined in the Certificate of Designation).

Common Stock Authorized

In June 2020, the Company's certificate of incorporation was amended to increase the total number of authorized shares of common stock from 131.5 million to 166.5 million.

In June 2021, the Company's certificate of incorporation was amended to increase the total number of authorized shares of common stock from 166.5 million to 266.5 million.

Common Stock Reserved

As of December 31, 2021, we had 266.5 million authorized shares of common stock, of which 99.8 million shares were issued and outstanding, and 88.2 million shares were available for future issuances. The remaining authorized shares were reserved as follows (in thousands):

Equity incentive plans	21,738
Option agreement with Adam R. Craig per Nasdaq Listing Rule 5635(c)(4)	1,120
New hire stock options granted per Nasdaq Listing Rule 5635(c)(4)	2,382
Employee stock purchase plan	819
Convertible preferred stock	52,323
Common stock purchase warrants	169
Total common stock reserved	78,551

Warrants

A warrant to purchase up to 169,014 shares of our common stock with an exercise price of $2.84 per share, issued in connection with the Loan and Security Agreement with Silicon Valley Bank in 2017, was outstanding as of December 31, 2021. The warrant will expire in November 2027.

9. Collaboration, Licensing and Milestone Agreements

Baxalta

In November 2013, we entered into the Pacritinib License Agreement with Baxter for the development and commercialization of pacritinib for use in oncology and potentially additional therapeutic areas. Baxter assigned its rights and obligations under the Pacritinib License Agreement to Baxalta. Under the Pacritinib License Agreement, we granted to Baxter an exclusive, worldwide (subject to our certain co-promotion rights in the United States), royalty-bearing, non-transferable, and (under certain circumstances outside of the United States) sub-licensable license to our know-how and patents relating to pacritinib.

In October 2016, we entered into the Asset Return and Termination Agreement, or the Baxalta Termination Agreement, with Baxalta, pursuant to which the Pacritinib License Agreement was terminated in its entirety (other than with respect to certain customary provisions that survive termination, including those pertaining to confidentiality and indemnification). The Pacritinib License Agreement has no further force or effect, and all rights and obligations of the Company and Baxalta under the Pacritinib License Agreement were terminated.

Pursuant to the Baxalta Termination Agreement, we are required to make a milestone payment to Takeda in the amount of approximately $10.3 million, upon the first regulatory approval or any pricing and reimbursement approvals of a product containing pacritinib. Baxalta was acquired by Shire plc in 2016, and Shire plc was subsequently acquired by Takeda in 2019. Subsequent to FDA approval of VONJO in February 2022, the $10.3 million milestone payment has become payable to Takeda.

*S*BIO Pte Ltd.*

We acquired the compounds SB1518 (which is referred to as “pacritinib”) and SB1578, which inhibit JAK2 and FLT3, from S*BIO Pte Ltd., or S*BIO, in May 2012. Under our agreement with S*BIO, we are required to make milestone payments to S*BIO up to an aggregate amount of $132.5 million if certain United States, EU and Japanese regulatory approvals are obtained or if certain worldwide net sales thresholds are met in connection with any pharmaceutical product containing or comprising any compound that we acquired from S*BIO for use for specific diseases, infections or other conditions. In addition, S*BIO will also be entitled to receive royalty payments from us at incremental rates in the low single-digits based on certain worldwide net sales thresholds on a product-by-product and country-by-country basis. Subsequent to FDA approval of VONJO in February 2022, a $25.0 million milestone payment has become payable to S*BIO. At our election, we may pay up to 50% of any milestone payments to S*BIO through the issuance of shares of our common stock or shares of our preferred stock automatically convertible into our common stock.

Teva

Pursuant to an acquisition agreement entered into with Cephalon, Inc., or Cephalon, in June 2005, we have the right to receive up to $100.0 million in payments upon achievement of specified sales and development milestones related to TRISENOX. Cephalon was subsequently acquired by Teva Pharmaceutical Industries Ltd., or Teva. As of December 31, 2021, we earned $60.0 million in such potential milestone payments as a result of Teva having achieved certain milestones. We did not earn any milestone revenues during the years ended December 31, 2021 and 2020. The achievement of the remaining milestones is uncertain at this time.

Other Agreements

We have several agreements with contract research organizations, third-party manufacturers and distributors which have durations of greater than one year for the development and distribution of certain of our compounds.

10. Equity-Based Compensation

All of equity-based compensation expense recognized during the years ended December 31, 2021 and 2020 was related to stock options. The following table summarizes equity-based compensation expense for the years ended December 31, 2021 and 2020, which was allocated as follows (in thousands):

	2021	2020
Research and development	$ 758	$ 522
Selling, general and administrative	3,985	3,795
Total equity-based compensation expense	$ 4,743	$ 4,317

Equity-based compensation had a $4.7 million and $4.3 million effect on net loss for the years ended December 31, 2021 and 2020, respectively. It had no effect on cash flows from operating activities for the periods presented.

As of December 31, 2021, unrecognized compensation cost related to unvested stock options amounted to $9.0 million, which will be recognized over the remaining weighted-average requisite service period of 2.03 years.

For the years ended December 31, 2021 and 2020, no tax benefits were attributed to equity-based compensation expense because a valuation allowance was maintained for all net deferred tax assets.

Stock Plans

In May 2017, the Company's 2017 Equity Incentive Plan, or the 2017 Plan, was approved by the Company's shareholders, and no additional awards will be granted under the 2015 Equity Incentive Plan, or the 2015 Plan.

The Company's 2007 Employee Stock Purchase Plan, as amended and restated in August 2009, September 2015 and June 2021, or the Purchase Plan, was amended in June 2021 to increase the maximum number of shares of the Company’s common stock authorized for issuance by 0.8 million shares. Refer to *Employee Stock Purchase Plan* below for further details.

Pursuant to the 2017 Plan, we may grant the following types of incentive awards: (1) stock options, including incentive stock options and non-qualified stock options, (2) stock appreciation rights, (3) restricted stock, (4) restricted stock units and (5) cash awards. The 2017 Plan is administered by the Compensation Committee of our Board, which has the discretion to determine the employees and consultants who shall be granted incentive awards. The Board retained sole authority under the 2017 Plan with respect to non-employee directors’ awards, although the Compensation Committee has authority under its charter to make recommendations to the Board concerning such awards. Options expire 10 years from the date of grant, subject to the recipients' continued service to the Company.

As of December 31, 2021, 24.3 million shares were authorized for issuance under equity incentive plans, of which 4.5 million shares of common stock were available for future grants under the 2017 Plan.

Inducement Grants Outside of Stock Plans

In March 2017, Dr. Adam R. Craig, our President and CEO, was granted stock options to purchase 1.2 million shares of our common stock at an exercise price of $4.24 per share. The stock options have a maximum term of ten years and vest in six equal semi-annual installments over the three-year period beginning March 20, 2017, subject to his continued employment

through the applicable vesting dates and acceleration under certain circumstances. The stock options were granted in connection with his entering into employment with the Company as President and CEO. A portion of the stock options covering 80,000 shares were granted under the 2015 Plan. The balance of such stock options was granted outside of stock plans in accordance with Nasdaq Listing Rule 5635(c)(4). All the options remained outstanding as of December 31, 2021.

As of December 31, 2021, inducement stock options to purchase an aggregate of 2.4 million shares of our common stock at a weighted average exercise price of $2.79 were issued and outstanding. The stock options were granted to our newly-hired employees as an inducement award to each employee entering into employment with the Company. The stock options were granted outside of stock plans in accordance with Nasdaq Listing Rule 5635(c)(4). The stock options have a maximum term of ten years and vest in equal annual installments over a four-year period, subject to the employee's continued employment through the applicable vesting dates.

Stock Options

Fair value for stock options was estimated at the date of grant using the Black-Scholes pricing model, with the following weighted average assumptions:

	Year Ended December 31,	
	2021	2020
Risk-free interest rate	0.8 %	0.5 %
Expected dividend yield	None	None
Expected life (in years)	5.2	4.6
Volatility	101 %	88 %

The risk-free interest rate used in the Black-Scholes valuation method is based on the implied yield currently available for U.S. Treasury securities at maturity with an equivalent term. We have not declared or paid dividends on our common stock and do not currently expect to do so in the future. The expected term of options represents the period that our options are expected to be outstanding and was determined based on historical weighted average holding periods and projected holding periods for the remaining unexercised options. Consideration was given to the contractual terms of our options, vesting schedules and expectations of future employee behavior. Expected volatility is based on both historical and implied volatilities of CTI BioPharma Corp. and our selected peer group of comparable companies within the industry.

Our stock price volatility and option lives, both of which impact the fair value of options calculated under the Black-Scholes methodology and, ultimately, the expense that will be recognized over the life of the option, involve management’s best estimates. As we recognize compensation expense for only the portion of options expected to vest, we apply estimated forfeiture rates that we derive from historical employee termination behavior. If the actual number of forfeitures differs from our estimates, adjustments to compensation expense may be required in future periods.

The following table summarizes stock option activity during the year ended December 31, 2021:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In Thousands)
Outstanding at December 31, 2020 (8,099,000 exercisable)	15,596,000	$ 2.09		
Granted	5,773,000	$ 3.04		
Exercised	(143,000)	$ 0.97		$ 200
Forfeited	(194,000)	$ 2.72		
Cancelled and expired	(341,000)	$ 4.90		
Outstanding at December 31, 2021 (11,776,000 exercisable)	20,691,000	$ 2.31	7.7	$ 15,336
Vested or expected to vest at December 31, 2021	19,781,000	$ 2.29	7.6	$ 15,175
Exercisable at December 31, 2021	11,776,000	$ 2.39	6.9	$ 9,781

The weighted average exercise price of options exercisable at December 31, 2021 and 2020 was $2.39 and $3.01, respectively. The weighted average grant-date fair value of options granted during 2021 and 2020 was $2.07 and $0.76 per option, respectively.

Employee Stock Purchase Plan

Under the Purchase Plan, eligible employees may purchase a limited number of shares of our common stock at 85% of the lower of the subscription date fair market value and the purchase date fair market value. There are two six-month offerings per year. Under the Purchase Plan, we issued approximately 0.1 million shares of our common stock to employees during the year ended December 31, 2021. There are 1.0 million shares of common stock authorized under the Purchase Plan and approximately 0.8 million shares are reserved for future purchases as of December 31, 2021.

11. Employee Benefit Plans

Our employees participate in the CTI BioPharma Corp. 401(k) Plan whereby eligible employees may defer up to 80% of their compensation, up to the annual maximum allowed by the Internal Revenue Service. We may make discretionary matching contributions based on certain plan provisions. We recorded $0.3 million and $0.1 million related to discretionary matching contributions for the years ended December 31, 2021 and 2020, respectively.

12. Net Loss Per Share

Basic net loss per share is calculated based on net loss divided by the weighted average number of shares outstanding for the period. The calculation of diluted net loss per share excludes the potential conversion of all dilutive convertible securities, such as convertible debt and convertible preferred stock, and the potential exercise or vesting of other dilutive securities, such as options, warrants and restricted stock, as their inclusion would have an anti-dilutive effect. Accordingly, diluted net loss per share is the same as basic net loss per share**.**

The computation of net loss per share is as follows (in thousands, except per share amounts):

	Year Ended December 31,	
	2021	2020
Net loss	$ (97,908)	$ (52,451)
Basic and diluted:		
Weighted average shares outstanding	90,117	71,146
Less: weighted average restricted shares outstanding	—	(5)
Shares used in calculation of basic and diluted net loss per common share	90,117	71,141
Net loss per common share: Basic and diluted	$ (1.09)	$ (0.74)

Common shares underlying equity awards, warrants and convertible preferred stock aggregating 74.5 million shares and 56.9 million shares prior to the application of the treasury stock method for the years ended December 31, 2021 and 2020, respectively, have been excluded from the calculation of diluted net loss per share because they were anti-dilutive.

13. Commitments and Contingencies

Commitments

See “Note 6. Leases” and “Note 7. Debt Financing Arrangements” for scheduled lease and debt payments. In addition, certain of our licensing agreements obligate us to make payments upon achievement of milestones and pay a royalty on net sales of products utilizing licensed compounds. See “Note 9. Collaboration, Licensing and Milestone Agreements” for further details. Purchase commitments relating to clinical trial contracts, manufacturing supply, insurance and other obligations also arise in the ordinary course of business. We anticipate the timing of payments under these contracts to range from less than one year to more than three years.

Contingencies

In April 2009, December 2009 and June 2010, the Italian Tax Authority, or the ITA, issued notices of assessment to CTI - Sede Secondaria, or CTI (Europe), based on the ITA’s audit of CTI (Europe)’s value added tax, or VAT, returns for the years

2003, 2005, 2006 and 2007, or, collectively, the VAT Assessments. The ITA audits concluded that CTI (Europe) did not collect and remit VAT on certain invoices issued to non-Italian clients for services performed by CTI (Europe). The assessments, including interest and penalties, for the years 2003, 2006 and 2007 are €0.7 million, €2.8 million and €0.9 million, respectively. We believe that the services invoiced were non-VAT taxable consultancy services and that the VAT returns are correct as originally filed. We have appealed all the assessments and are defending ourselves against the assessments both on procedural grounds and on the merits of the cases, although we can make no assurances regarding the ultimate outcome of these cases.

Following is a summary of the status of the legal proceedings surrounding each respective VAT year return at issue:

2003 VAT Assessment. In June 2013, the Regional Tax Court issued decision no. 119/50/13 in regards to the 2003 VAT Assessment, which accepted the October 2012 appeal of the ITA and reversed a previous decision of the Provincial Tax Court. In January 2014, we appealed such decision to the Italian Supreme Court both on procedural grounds and on the merits of the case. In March 2014, we paid a deposit in respect of the 2013 VAT matter of €0.4 million (or $0.6 million upon conversion from euros as of the date of payment), following the ITA's request for such payment.

2005 VAT Assessment. In January 2018, the Italian Supreme Court issued decision No. 02250/2018 which (i) rejected the April 2013 appeal of the ITA, (ii) confirmed the October 2012 decision of the Regional Tax Court (127/31/2012), which fully accepted the merits of our earlier appeal and confirmed that no penalties could be imposed against us, and (iii) due to the novelty of the arguments at stake, compensated the legal expenses incurred by the parties. The ITA may not use any ordinary means of appeal against the Italian Supreme Court decision, and we have applied for a refund based on the guidance from the ITA.

2006 and 2007 VAT Assessments. In November 2013, the ITA appealed to the Italian Supreme Court an April 2013 decision of the Regional Tax Court (57/35/13), that fully rejected the merits of an earlier ITA appeal, declared that no penalties could be imposed against us and found the ITA liable to pay us approximately €12,000, as a partial refund of legal expenses we incurred.

No hearing dates have been fixed yet for either the 2003 VAT Assessment or consolidated 2006 and 2007 VAT Assessment cases.

If the final decision of the Italian Supreme Court is unfavorable to us, or if, in the interim, the ITA were to make a demand for payment and we were to be unsuccessful in suspending collection efforts, we may be requested to pay the ITA an amount up to €4.4 million, or approximately $4.9 million converted using the currency exchange rate as of December 31, 2021, including interest and penalties for the period lapsed between the date in which the assessments were issued and the date of effective payment. We have not recorded this contingent liability in the consolidated financial statements as we do not believe the potential payment to the ITA is probable at this time.

14. Income Taxes

We file income tax returns in the United States and Germany. A substantial part of our operations takes place in the State of Washington, which does not impose an income tax as that term is defined in ASC 740, *Accounting for Income Taxes*. As such, our state income tax expense or benefit, if recognized, would be immaterial to our operations. We are not currently under examination by an income tax authority, nor have we been notified that an examination is contemplated.

Loss before income taxes is attributable to the following tax jurisdictions (in thousands):

	Year ended December 31,	
	2021	2020
United States	$ (97,908)	$ (52,451)
Foreign	—	—
Net loss before income taxes	$ (97,908)	$ (52,451)

The reconciliation between the income tax rate and our effective tax rate as of December 31 is as follows:

	2021	2020
Federal income tax rate	21 %	21 %
Research and development tax credits	5	4
Non-deductible compensation	(1)	(2)
Valuation allowance	(24)	20
Receivable impairment	—	(2)
Expired tax attribute carryforwards / Section 382 limitation	—	(29)
Loss on subsidiary liquidation	—	(14)
Unrecognized tax benefits	(1)	2
Net effective tax rate	— %	— %

The principal components of our deferred tax assets and liabilities as of December 31 were as follows (in thousands):

	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 40,061	$ 22,756
Capitalized research and development	35,910	33,280
Research and development tax credit carryforwards	5,386	1,779
Equity-based compensation	3,337	3,176
Intangible assets	7,026	7,251
Depreciation and amortization	785	699
Lease liability	670	629
Other deferred tax assets	231	312
Total deferred tax assets	93,406	69,882
Less: valuation allowance	(92,395)	(69,085)
	1,011	797
Deferred tax liabilities:		
Right-of-use asset	(656)	(451)
Deductions for tax in excess of financial statements	(355)	(346)
Total deferred tax liabilities	(1,011)	(797)
Net deferred tax assets	$ —	$ —

As of December 31, 2021 and 2020, we had U.S. federal net operating loss carryforwards, or the NOL, of approximately $182.7 million and $99.9 million respectively, which are available to reduce future taxable income. The Tax Cuts and Jobs Act enacted in December 2017 altered the carryforward period for federal net operating losses and as a result, all net operating losses generated in 2018 and forward have an indefinite life. Of the net operating losses reported, we have accumulated $170.7 million with an indefinite life as of December 31, 2021. We have accumulated state tax losses of approximately $15.0 million and $12.3 million as of December 31, 2021 and 2020, respectively. We also had U.S. federal tax credits of $5.4 million and $1.8 million as of December 31, 2021 and 2020, respectively, which may be used to offset future tax liabilities. The NOL and tax credit carryforwards, some of which expired in 2021, are subject to annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, or the IRC, of 1986, as amended. This limits the amount of tax attributes that can be utilized annually to offset future taxable income or future tax liabilities. We have undertaken a formal IRC Section 382 study and the attributes disclosed in this footnote reflect the conclusion of that study. However, subsequent ownership changes may further affect the limitation in future years.

We maintain a full valuation allowance on our net deferred tax assets. The assessment regarding whether a valuation allowance is required considers both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable. In making this assessment, significant weight is given to evidence that can be objectively verified. In our valuation, we considered our cumulative loss in recent years and forecasted losses in the near term as significant negative evidence. Based upon a review of the four sources of income identified within ASC 740, we determined that the negative evidence outweighed the positive evidence and that a full valuation allowance on our net deferred tax assets will be

maintained. We will continue to assess the realizability of our deferred tax assets going forward and will adjust the valuation allowance as needed. Our valuation allowance increased by $23.3 million during the year ended December 31, 2021 primarily due to the increase in net operating loss carryforwards and tax credit carryforwards.

We follow the provisions in ASC 740 and the guidance related to accounting for uncertainty in income taxes. We determine our uncertain tax positions based on a determination of whether and how much of a tax benefit taken by us in our tax filings or positions is more likely than not to be sustained upon examination by the relevant income tax authorities. We are subject to U.S. federal and state and U.K. income taxes with varying statutes of limitations. Tax years from 2002 forward remain open to examination due to the carryover of net operating losses or tax credits. Our policy is to recognize interest related to unrecognized tax benefits as interest expense and penalties as operating expenses.

The total balance of unrecognized tax benefits as of December 31 is as follows (in thousands):

	2021	2020
Balance at beginning of period	$ 390	$ 1,268
Gross increases to tax positions in prior periods	—	—
Gross decreases to tax positions in current periods	—	(1,268)
Gross increases to tax positions in current periods	819	390
Balance at end of period	$ 1,209	$ 390

As of December 31, 2021, the total amount of unrecognized tax benefits was $1.2 million, which was recorded as a reduction to the deferred tax asset. We do not anticipate that the amount of existing unrecognized tax benefits will significantly increase or decrease within the next 12 months. We had no accrued interest or penalties as of December 31, 2021.

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

None.

Item 9A. Controls and Procedures

(a) Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in reports filed under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC rules and forms, and that such information is accumulated and communicated to our management to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives.

Our management, under the supervision and with the participation of our President and Chief Executive Officer, or CEO, and Chief Financial Officer, or CFO, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of the end of the period covered by this Annual Report on Form 10-K. Based upon that evaluation, our CEO and CFO have concluded that, as of the end of the period covered by this Annual Report on Form 10-K, our disclosure controls and procedures were effective.

(b) Management’s Annual Report on Internal Controls

Management of the Company, including its consolidated subsidiaries, is responsible for establishing and maintaining adequate internal control over financial reporting. The Company’s internal control over financial reporting is a process designed under the supervision of the Company’s principal executive and principal financial officers to provide reasonable assurance regarding the reliability of financial reporting and the preparation of the Company’s financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles.

As of the end of the Company’s 2021 fiscal year, management conducted an assessment of the effectiveness of the Company’s internal control over financial reporting based on the framework established in “Internal Control—Integrated Framework” (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this

assessment, management has determined that the Company's internal control over financial reporting as of December 31, 2021 was effective.

(c) Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption for "non-accelerated filers."

(d) Changes in Internal Control

There have been no changes to our internal control over financial reporting that occurred during the fourth fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

On December 6, 2021, we entered into a second amendment of our lease with Selig Holdings Company, LLC for our leased property at 3101 Western Avenue in Seattle, Washington, which among other terms, extended the term of the lease until April 30, 2025.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by Item 10 of Form 10-K is incorporated herein by reference to information in our Proxy Statement for the 2022 Annual Meeting of Stockholders, which we expect to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2021.

Our Code of Ethics applies to all of our directors, officers and employees, including our principal executive, principal financial and principal accounting officers, or persons performing similar functions. Our Code of Ethics is posted on our website located at www.ctibiopharma.com. We intend to disclose future amendments, if any, to certain provisions of the Code of Ethics, and waivers of the Code of Ethics granted to executive officers and directors, on the website within four business days following the date of the amendment or waiver.

Item 11. Executive Compensation

The information required by Item 11 of Form 10-K is incorporated herein by reference to information in our Proxy Statement for the 2022 Annual Meeting of Stockholders, which we expect to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2021.

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

The information required by Item 12 of Form 10-K is incorporated herein by reference to information in our Proxy Statement for the 2022 Annual Meeting of Stockholders, which we expect to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2021.

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

The information required by Item 13 of Form 10-K is incorporated herein by reference to information in our Proxy Statement for the 2022 Annual Meeting of Stockholders, which we expect to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2021.

Item 14. Principal Accountant Fees and Services

The information required by Item 14 of Form 10-K is incorporated herein by reference to information in our Proxy Statement for the 2022 Annual Meeting of Stockholders, which we expect to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2021.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) Financial Statements - The financial statements filed as part of this Annual Report on Form 10-K are listed on the Index to Consolidated Financial Statements in Item 8.

(2) Financial Statement Schedules - The financial statement schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or the notes thereto.

(3) Exhibits - The exhibits required by Item 601 of Regulation S-K are listed in paragraph (b) below.

(b) Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference			
		Form	File No.	Exhibit Number	Filing Date
3.1	Amended and Restated Certificate of Incorporation of CTI BioPharma Corp.	S-8	333-257174	4.1	June 17, 2021
3.2	Amended and Restated Bylaws of CTI BioPharma Corp., a Delaware corporation.	8-K	000-28386	3.1	April 13, 2020
4.1	Specimen Common Stock Certificate.	8-K	000-28386	4.1	February 12, 2018
4.2	Warrant to Purchase Stock, dated November 28, 2017, by and between CTI BioPharma Corp. and Silicon Valley Bank.	8-K	000-28386	4.1	November 28, 2017
4.3	Warrant to Purchase Stock, dated November 28, 2017, by and between CTI BioPharma Corp. and Life Science Loans II, LLC.	8-K	000-28386	4.2	November 28, 2017
4.4	Description of Securities.				Filed herewith.
10.1	Office Lease, dated January 27, 2012, by and between CTI BioPharma Corp. and Selig Holdings Company LLC.	10-K	001-12465	10.4	March 8, 2012
10.2†	Sublease agreement by and between CTI BioPharma Corp. and Cascadian Therapeutics, Inc.	8-K	000-28386	10.1	December 5, 2017
10.3*	Offer Letter, dated July 2, 2015, by and between CTI BioPharma Corp. and Bruce J. Seeley.	10-Q	001-12465	10.3	August 6, 2015
10.4*	Employment Agreement, dated February 24, 2017, by and between CTI BioPharma Corp. and Adam Craig.	8-K	000-28386	10.1	February 27, 2017
10.5*	Amendment to Employment Agreement, dated October 31, 2018, by and between CTI BioPharma Corp. and Adam R. Craig.	10-Q	000-28386	10.2	November 1, 2018
10.6*	Form of Severance Agreement for CTI BioPharma Corp.'s Executive Officers (as in effect as of January 6, 2015).	10-K	001-12465	10.6	March 12, 2015
10.7*	Severance Agreement, dated July 27, 2015, by and between CTI BioPharma Corp. and Bruce J. Seeley.	10-K	001-12465	10.11	February 17, 2016
10.8*	Offer Letter, dated August 1, 2017, by and between CTI BioPharma Corp. and David Kirske.	10-Q	000-28386	10.3	August 4, 2017
10.9*	Severance Agreement, dated September 25, 2017, by and between CTI BioPharma Corp. and David Kirske.	8-K	000-28386	10.1	September 26, 2017
10.10*	Form of Indemnity Agreement for CTI BioPharma Corp.'s Executive Officers and Directors.	8-K	000-28386	10.1	January 24, 2018
10.11*	2007 Employee Stock Purchase Plan, as amended and restated.	8-K	000-28386	10.2	June 7, 2021
10.12*	CTI BioPharma Corp. 2015 Equity Incentive Plan, as amended.	8-K	001-12465	10.1	April 29, 2016
10.13*	Global Form of 2015 Equity Incentive Plan Restricted Stock Unit Award Agreement.	10-Q	001-12465	10.3	November 5, 2015

10.14*	Global Form of 2015 Equity Incentive Plan Stock Option Agreement.	10-Q	001-12465	10.4	November 5, 2015
10.15*	Global Form of 2015 Equity Incentive Plan Stock Bonus Award Agreement.	10-Q	001-12465	10.5	November 5, 2015
10.16*	2007 Equity Incentive Plan, as amended and restated.	10-Q	001-12465	10.1	October 31, 2014
10.17*	Form of 2007 Equity Incentive Plan Restricted Stock Award Agreement.	10-K	001-12465	10.14	March 12, 2015
10.18*	Global Form of 2007 Equity Incentive Plan Restricted Stock Unit Award Agreement.	10-K	001-12465	10.15	March 12, 2015
10.19*	Global Form of 2007 Equity Incentive Plan Stock Option Agreement.	10-K	001-12465	10.16	March 12, 2015
10.20*	Form of 2007 Equity Incentive Plan Restricted Stock Award Agreement for Directors (relating to applicable awards granted prior to December 17, 2014).	10-Q	001-12465	10.7	April 26, 2011
10.21*	Form of 2007 Equity Incentive Plan Restricted Stock Award Agreement (relating to applicable awards granted prior to December 17, 2014).	10-Q	001-12465	10.3	October 30, 2013
10.22*	Form of 2007 Equity Incentive Plan Restricted Stock Award Agreement for employees (relating to applicable awards granted prior to December 17, 2014).	10-Q	001-12465	10.6	April 26, 2011
10.23*	Form of 2007 Equity Incentive Plan Stock Option Agreement for Directors and Officers (relating to applicable awards granted prior to December 17, 2014).	10-Q	001-12465	10.1	October 30, 2013
10.24*	Form of Stock Award Agreement for grants of fully vested shares under CTI BioPharma Corp's 2007 Equity Incentive Plan, as amended.	10-Q	001-12465	10.2	October 30, 2013
10.25*	Form of Equity/Long-Term Incentive Award Agreement for Bruce J. Seeley.	10-K	001-12465	10.35	February 17, 2016
10.26*	Form of Amendment to Form of Equity/Long-Term Incentive Award Agreement, dated December 23, 2015, for Bruce J. Seeley.	10-K	001-12465	10.37	February 17, 2016
10.27*	Amended and Restated 2017 Equity Incentive Plan of CTI BioPharma Corp.	8-K	000-28386	10.1	June 7, 2021
10.28*	Form of Stock Option Agreement under the CTI BioPharma Corp. Amended and Restated 2017 Equity Incentive Plan.	10-Q	000-28386	10.1	November 10, 2020
10.29*	CTI BioPharma Corp. Stock Option Agreement (Inducement Form)	10-K	000-28386	10.29	March 17, 2021
10.30	Acquisition Agreement, dated June 10, 2005, by and among CTI BioPharma Corp., CTI Technologies, Inc. and Cephalon, Inc.	8-K	001-12465	10.1	June 14, 2005
10.31†	Asset Purchase Agreement, dated April 18, 2012, by and between CTI BioPharma Corp. and S*BIO Pte Ltd.	8-K	001-12465	10.1	April 24, 2012
10.32	Asset Return and Termination Agreement, dated October 21, 2016, by and between CTI BioPharma Corp. and Baxalta.	8-K	001-12465	10.2	October 24, 2016

10.33	Letter Agreement, dated June 9, 2017, by and between CTI BioPharma Corp. and BVF Partners L.P.	8-K	000-28386	10.1	June 9, 2017
10.34†	Manufacturing and Supply Agreement, dated April 15, 2014, by and between CTI BioPharma Corp. and DSM Fine Chemicals Austria Nfg GmbH & Co KG.	10-Q	001-12465	10.1	August 4, 2014
10.35	Loan and Security Agreement, dated November 28, 2017, by and between CTI BioPharma Corp. and Silicon Valley Bank.	8-K	000-28386	10.1	November 28, 2017
10.36	First Amendment to Loan and Security Agreement, dated May 17, 2018, by and between CTI BioPharma Corp. and Silicon Valley Bank.	10-Q	000-28386	10.3	August 3, 2018
10.37	Waiver Agreement, dated January 19, 2018, by and between CTI BioPharma Corp. and Silicon Valley Bank.	10-K	000-28386	10.58	March 7, 2018
10.38	Letter Agreement, dated December 9, 2015, by and between CTI BioPharma Corp. and BVF Partners L.P.	8-K	001-12465	10.1	December 9, 2015
10.39	Exchange Agreement, dated February 8, 2018, by and between CTI BioPharma Corp. and BVF Partners L.P.	8-K	000-28386	10.1	February 12, 2018
10.40*	CTI BioPharma Corp. Executive Incentive Compensation Plan.	10-K	000-28386	10.45	March 13, 2019
10.41*	CTI BioPharma Corp. Director Compensation Policy.	10-Q	000-28386	10.46	May 6, 2021
10.42	Open Market Sale Agreement℠, dated November 15, 2019, between CTI BioPharma Corp. and Jefferies LLC.	8-K	000-28386	1.1	November 15, 2019
10.43	Open Market Sale Agreement℠, dated January 15, 2021, between CTI BioPharma Corp. and Jefferies LLC.	8-K	000-28386	1.1	January 15, 2021
10.44	Investment Agreement, dated as of January 31, 2020, by and among CTI BioPharma Corp., on the one hand, and the purchasers identified on the signature pages thereto, on the other hand.	8-K	000-28386	10.1	February 3, 2020
10.45††	Purchase and Sale Agreement, dated August 25, 2021, by and between CTI BioPharma Corp. and Drug Royalty III LP 2.	10-Q	000-28386	10.1	November 12, 2021
10.46††	Credit Agreement, dated August 25, 2021, by and between CTI BioPharma Corp. and Drug Royalty III LP 2.	10-Q	000-28386	10.2	November 12, 2021
10.47	Second Amendment to Office Lease, dated December 6, 2021, by and between CTI BioPharma Corp. and Selig Holdings Company, LLC.				Filed herewith.
10.48*	Offer Letter, by and between CTI BioPharma Corp. and James K. Fong, dated as of March 1, 2022	8-K	000-28386	10.1	March 4, 2022
10.49*	Severance Agreement, by and between CTI BioPharma Corp. and James K. Fong, dated as of January 6, 2015	8-K	000-28386	10.2	March 4, 2022
10.50*	Amendment to Severance Agreement, by and between CTI BioPharma Corp. and James K. Fong, dated as of March 1, 2022	8-K	000-28386	10.3	March 4, 2022

23.1	Consent of Independent Registered Public Accounting Firm.	Filed herewith.
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	Filed herewith.
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	Filed herewith.
32	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	Furnished herewith.
101	The following financial statements from the Company's Annual Report on Form 10-K for the year ended December 31, 2021, formatted in Inline XBRL: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Comprehensive Loss, (iv) Consolidated Statements of Stockholders' Equity, (v) Consolidated Statements of Cash Flows, and (vi) Notes to Consolidated Financial Statements, tagged as blocks of text and including detailed tags.	
104	Cover page interactive data file (formatted in Inline XBRL and contained in Exhibit 101).	

* Indicates management contract or compensatory plan or arrangement.

† Portions of these exhibits have been omitted pursuant to a request for confidential treatment.

†† Portions of this Exhibit have been redacted in compliance with Regulation S-K Item 601(b)(10)(iv).

Item 16. Form 10-K Summary

None.

SIGNATURES

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

Dated: March 31, 2022

CTI BioPharma Corp.

By: /s/ Adam R. Craig
Adam R. Craig, M.D., Ph.D.
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Laurent Fischer **Laurent Fischer, M.D.**	Chairman of the Board and Director	March 31, 2022
/s/ Adam R. Craig **Adam R. Craig, M.D., Ph.D.**	President and Chief Executive Officer and Director (Principal Executive Officer)	March 31, 2022
/s/ David H. Kirske **David H. Kirske**	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 31, 2022
/s/ Michael A. Metzger **Michael A. Metzger**	Director	March 31, 2022
/s/ Diane Parks **Diane Parks**	Director	March 31, 2022
/s/ David Parkinson **David Parkinson, M.D.**	Director	March 31, 2022
/s/ Matthew D. Perry **Matthew D. Perry**	Director	March 31, 2022
/s/ Reed V. Tuckson **Reed V. Tuckson, M.D.**	Director	March 31, 2022

Exhibit 4.4

DESCRIPTION OF REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our amended and restated certificate of incorporation ("certificate of incorporation"), our amended and restated by-laws ("bylaws") and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and by-laws, which are filed as exhibits to our Annual Report on Form 10-K, to which this exhibit is also appended.

Our authorized capital stock consists of 266,500,000 shares of common stock, par value $0.001 per share, and 33,333 shares of preferred stock, par value $0.001 per share, of which 12,575 are designated as the Series O Preferred Stock, 4,500 are designated as the Series X Convertible Preferred Stock, and 600 are designated as the Series X^1 Preferred Stock.

Common Stock

General

Each holder of common stock is generally entitled to one vote for each share held on all matters to be voted upon by the shareholders and there are no cumulative voting rights. All matters put to a shareholder vote generally require the approval of a majority of shares entitled to vote, except as otherwise provided by our certificate of incorporation or bylaws or required by law. Subject to preferences that may be applicable to any outstanding preferred stock, holders of common stock are entitled to receive ratably the dividends, if any, that are declared from time to time by the board of directors out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, the holders of common stock are entitled to share in our assets remaining after the payment of liabilities and the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are validly issued, fully paid and non-assessable, and any issued shares of common stock will be validly issued, fully paid and non-assessable. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Bylaw Amendments

The Board is expressly authorized to make, alter or repeal any provision of our bylaws.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Listing

Our shares of common stock trade on The Nasdaq Capital Market under the symbol "CTIC."

Preferred Stock

Under our certificate of incorporation, our board of directors has the authority, without further action by stockholders, to designate up to 33,333 shares of preferred stock, par value $0.001 per share, in one or more series and to fix the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon the preferred stock, including but not limited to dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of our common stock.

Certain Anti-Takeover Matters

Delaware corporate law contains certain provisions that may have the effect of delaying, deterring or preventing a change in control of the company. Section 203 of the Delaware General Corporation Law ("DGCL") prohibits us, with certain exceptions, from engaging in certain business combinations with an "interested shareholder" (defined generally as a person who owns 15% or more of our voting stock or is an affiliate of the Company and the owner of 15% of our voting stock within a 3 year period) for a period of three years following date that such shareholder becomes an interested shareholder. The prohibited

transactions include, among others, a merger or consolidation with, disposition of assets to, or issuance or redemption of stock to or from, the interested shareholder, or any other receipt by the interested shareholder of a disproportionate benefit as a shareholder. Exceptions to this statutory prohibition include approval of the business combination or transaction which resulted in the shareholder becoming an interested shareholder by the board of directors, ownership of at least 85% of the voting stock of the company outstanding at the time of the transaction or approval of the business combination and approval by the board of directors and holders of not less than two-thirds of the outstanding shares entitled to vote on the business combination which is not owned by the interested shareholder on or subsequent to the date of the business combination. Our certificate of incorporation does not exclude us from the restrictions imposed under Section 203 of the DGCL. These statutory provisions may have the effect of delaying, deterring or preventing a change in control of the company.

Directors are elected annually, for terms of one year and until their successors are elected and qualified. Our bylaws provide that, in any election of directors, those candidates receiving the largest number of votes cast by the shares entitled to vote in the election, up to the number of directors to be elected by such shares, will be elected to our board of directors. Our bylaws also provide that any vacancy in our board of directors may be filled only by the affirmative vote of a majority of directors then in office, though less than a quorum. Further, our bylaws require a shareholder to provide notice to us of such shareholder's intention to nominate a person or persons for election as directors not later than 90 days prior to the first anniversary of the previous year's annual meeting or, in the case of an election to be held at a special meeting of the shareholders for the election of directors, the close of business on the tenth day following the date on which notice of such meeting is first given to shareholders. A shareholder must also provide us with notice of such shareholder's intent to make any proposal at an annual meeting of shareholders not later than 90 days prior to the first anniversary of the previous year's annual meeting of shareholders. These provisions may have the effect of deterring hostile takeovers or delaying a change in control of our management.

SECOND AMENDMENT TO LEASE

THIS SECOND AMENDMENT TO LEASE (this "**Amendment**") is made as of the 10th day of ~~November~~ December, 2021, by and between **SELIG HOLDINGS COMPANY, LLC**, a Delaware limited liability company ("**Selig**" or "**Lessor**"), and **CTI BIOPHARMA CORP.**, a Delaware corporation ("**CTI**" or "**Lessee**").

W I T N E S S E T H:

WHEREAS, Lessor and Cell Therapeutics, Inc. ("**Original Tenant**"), predecessor in interest to Lessee, entered into that certain Lease titled "3101 Western Avenue Office Lease" dated January 27, 2012 (the "**Original Lease**"), as amended by that certain letter agreement by and between Lessor and Original Tenant, dated June 7, 2012 (the "**First Amendment**" together with the Original Lease, the "**Lease**" or "**Existing Lease**"), pertaining to certain premises more particularly described in the Lease in the building commonly known as 3101 Western Avenue (the "**Building**"), located at 3101 Western Avenue, Seattle, Washington 98121;

WHEREAS, the term of the Lease is currently scheduled to expire on April 30, 2022; *and*

WHEREAS, Lessor and Lessee now desire to extend the Lease term, reduce the Premises, and to further amend the Lease subject to the terms and conditions set forth below.

NOW, THEREFORE, we hereby agree that, in consideration of the foregoing and other consideration, the receipt of sufficiency of which are hereby acknowledged, upon full execution of this Second Amendment (the "**Second Amendment Date**") Lessor and Lessee agree the Existing Lease will be modified as follows (and from and after such execution, all references in the Existing Lease to the "Lease" or words of similar effect shall mean "the Existing Lease as modified by the Second Amendment"):

1. **Defined Terms**. Unless otherwise defined in this Amendment, any capitalized or defined term used herein shall have its respective meaning as set forth in the Lease. As used in this Amendment, the following terms shall have the respective meanings indicated below:

(a) "**Extension Commencement Date**" shall mean May 1, 2022;

(b) "**Existing Premises**" shall mean the existing premises demised pursuant to the Lease, namely those certain premises containing approximately 66,045 rentable square feet on the sixth, seventh, and eighth floors of the Building;

(c) "**First Extension Premises**" shall mean the Premises existing as of the Extension Commencement Date.

2. **Term**. The lease term ("**Term**") is hereby extended, by three (3) years, bringing forth a new expiration date of April 30, 2025 (such additional period, the "**First Extension Term**"). From and after the Second Amendment Date, all references in the Lease to the "Term", the "term of the Lease", and/or the "Lease term" shall be deemed to mean "the original term of the Existing Lease, as extended by the First Extension Term."

3. **Reduction of Premises**. On April 30, 2022 (at 11:59 p.m. local time):

(a) CTI shall relinquish all rights and responsibilities associated with the 6th and 7th floors of the Building (the "**First Reduction Premises**");

(b) CTI shall return the First Reduction Premises to Selig in a broom clean condition, normal wear and tear excepted, and otherwise in accordance with Section 7 of the Existing Lease; *and*

(c) Notwithstanding anything to the contrary contained herein, CTI shall continue to pay Selig as and when due for rent and all other amounts due under the Existing Lease that may accrue through April 30, 2022, as to the First Reduction Premises.

4. **Existing Lease Terms**. Upon the Extension Commencement Date:

(a) The Premises shall mean the Existing Premises, less the First Reduction Premises. The "Premises" will consist of 23,147 rentable square feet measured in accordance with BOMA's 2017 Standard Method of Measurement and "Lessee proportionate share" shall be equal to 11.959% CTI and Selig acknowledge and agree that the number of rentable square feet in the Building in which the leased Premises are located is 193,552 square feet;

(b) Notwithstanding anything to the contrary set forth in Section 19 of the Existing Lease, for purposes of determining Lessee's proportionate share of Operating Services and Real Estate Taxes, the "Base Year" shall be reset to 2022, and only actual increases from these Base Year Costs (determined using a 2022 Base Year), if any, will be passed on to Lessee on a proportionate basis pursuant to the method set forth in the Existing Lease provided increases in Controllable Expenses shall not exceed five percent (5%) annually on a cumulative, compounding basis. The Monthly Rent described below includes CTI's proportionate share of Operating Services and Real Estate Taxes for the first twelve months of the First Extension Term, "Base Year Costs", and CTI shall not be responsible for the payment of Lessee's proportionate share of increases in Operating Services and Real Estate Taxes until the commencement of the 13th month of the First Extension Term (i.e., May 1, 2023, and so Lessee's proportionate share of any increases in Operating Services and Real Estate Taxes in calendar year 2023 shall be pro-rated based on the number of days in 2023 after the commencement of such 13th month of the First Extension Term); *and*

(c) The first four sentences of the defined term "Computation of Adjustments to Base Year Costs" is hereby deleted and replaced as follows:

"Commencing with calendar year 2023, Lessor will provide Lessee with its estimate of Lessee's proportionate share of any increases in Base Year Costs for such calendar year based on a review of historical data. Commencing with the 13th month of the First Extension Term, and the 1st month of any calendar year thereafter, Lessee will pay with its Monthly Rent such monthly estimated amount of Lessee's proportionate share of any increases in Base Year Costs for such calendar year. If Lessor has not provided an updated estimate of Lessee's proportionate share of increases in Base Year Costs at the time any calendar year commences, Lessee shall continue to make estimated payments at the same rate as the prior year until Lessor provides a new estimated amount to Lessee. Lessee shall be responsible for any increase between Lessee's proportionate share of Base Year Costs and Lessee's proportionate share of each respective Comparison Year(s) Costs, subject to the proration of such increases in 2023 as provided above."

5. **Landlord Work**. Selig shall, at Selig's sole cost and expense pay for and complete the following improvements, in each case no later than the Extension Commencement Date:

(a) professionally shampoo and clean the carpets throughout the First Extension Premises (as defined below);

(b) repaint the walls throughout the First Extension Premises using one (1) base color and at least one (1) accent color, such colors to be acceptable to CTI;

(c) demolish the conference room walls as shown in the floor plans attached as Exhibit A attached hereto and replace such walls with folding or stacking walls and doors so that the applicable portion of the Premises can be opened for large gatherings, such walls and doors to be acceptable to CTI. The cost to provide and install such walls shall not exceed $50,000.00 unless such excess is consented to in advance by CTI. CTI shall pay any such approved excess amount. Upon completion of installation of the new walls and doors, Selig shall, no later than the Extension Commencement Date and at Selig's sole cost and expense, also modify all building and Premises mechanical, electrical, and plumbing systems affected and to recalibrate same so they are in good working order for within the Premises. CTI shall, at CTI's sole cost and expense, be responsible for modification of any data/telephone lines affected; provided, no modifications of data/telephone lines shall be made without CTI's prior written approval. In connection with the work described in this paragraph, Selig shall, or shall cause to be done:

i. conduct and complete all work in good and workmanlike fashion using no lesser quality materials than building-standard;
ii. use commercially reasonable efforts not to disrupt the operations of CTI (including conducting work during nights and weekends to the extent reasonably practicable);
iii. provide CTI with at least (x) seven (7) days prior notice before commencing such work, (y) fourteen (14) days prior notice before commencing any work during business hours and (z) with regard to the work described in item (c) of this paragraph, the timing for such work shall be determined in CTI's sole discretion, but shall not extend beyond reasonably practicable times; *and*
iv. upon completion of such work, leave any affected areas in broom-clean condition, and free from all trash and debris.

6. **Amendment to Section 42**. Effective as of the Second Amendment Date and continuing throughout the term of the Lease (as amended hereby), Section 42 of the Existing Lease is hereby deleted in its entirety and replaced as follows:

"42. RIGHT OF FIRST REFUSAL. Without limiting Lessee's rights pursuant to Paragraph 38, Lessor hereby grants Lessee a continuing right of first refusal to lease the entirety of any space available on the seventh (7th) floor of the Building (the "ROFR Space") which is currently available or later becomes available during the Term and any extension thereof (the "Right of First Refusal"). If Lessor receives a bona-fide good-faith offer from a prospective tenant (a "Prospective Tenant") to lease the ROFR Space, Lessor shall give written notice to Lessee (the "ROFR Notice") within five (5) days of the third-party offer. Lessee shall have ten (10) business days from the receipt of the ROFR Notice to exercise, in writing to the Lessor, the Right of First Refusal. If Lessee fails to notify Lessor of its intent to exercise the Right of First Refusal within the time frame described herein, Lessee shall be deemed to have waived the Right of First Refusal with respect to that prospective tenant's offer. If Lessee exercises the Right of First Refusal, Lessee shall be required to lease the ROFR Space. If Lessee exercises its Right of First Refusal for any ROFR Space during the first twenty-four (24) months of the Lease term following the Second Amendment Date, the lease of the ROFR Space shall be on the same terms and conditions as set forth in this Lease. If Lessee exercises its Right of First Refusal for any ROFR Space after the first twenty-four (24) months of the Lease term, the Monthly Rent and allowances for the ROFR Space shall be the Market Rent.

"Lessee's rent for the ROFR Space shall commence when such space is available for occupancy or upon the substantial completion of the mutually agreed-upon improvements of such space (excepting any minor punch-list items), subject to a reasonable and mutually agreed upon schedule for completion of such improvements. The costs for the improvements to the ROFR Space shall be mutually agreed upon by the parties hereto.

"In the event the parties cannot agree on the Monthly Rent and allowances fair market value described in this Section, and Lessee still desires to exercise the Right of First Refusal, they shall agree to establish such rent by the method of arbitration described in Section 41.

"Lessee shall not have the right to exercise the Right of First Refusal at any time that it is in default under the terms and conditions of this Lease.

"Notwithstanding the foregoing limitations, Lessor shall be free to offer renewal options for ROFR Space to Prospective Tenants, provided such offers are subordinate to the Right of First Refusal."

7. **Amendment to Section 41**. Effective as of the Second Amendment Date and continuing throughout the term of the Lease (as amended hereby), the first two sentences of Section 41 of the Existing Lease are hereby deleted in their entirety and replaced as follows:

"41. RENEWAL OPTION. Lessee shall have one (1) five (5)-year option to extend the Term of this Lease for a portion of or the entire Premises upon the terms and conditions of this Lease (the "Renewal Term"). In such event, Lessor will provide a refurbishment allowance of $5.00 per rentable square foot of the Premises (the "TI Allowance") at the beginning of the Renewal Term. The Monthly Rent for a Renewal Term will be the fair market value (the "Market Rent") for comparable space in comparable buildings in the surrounding area (the "Market Area"), which Market Rent shall be further described as one-hundred percent (100%) of prevailing rates for the most recently negotiated leases and lease amendments taking into account all relevant factors, but without any increase in rental value attributable to the improvements in the Premises or the TI Allowance, in the Market Area and shall not require a minimum subject to Lessee's previous rental rates. The determination of the Market Rent shall take into account all concessions granted to tenants in the Market Area including, but not limited to, free rent, free parking, leasing commissions paid to Lessee's agent, if any, and moving or other allowances."

8. **Amendment to Section 39**. Section 39 of the Existing Lease is hereby modified such that CTI shall have the right but, not the obligation, to rent, up to a total of 41 parking stalls of which up to 4 stalls inside are reserved and up to 4 stalls outside are reserved in each case in CTI's sole discretion. The balance are non-reserved inside stalls. The monthly rate of parking shall be consistent with market rates (provided increases shall not exceed three percent (3%) annually on a non-cumulative basis). The parking rental rates, as of the Second Amendment Date are as follows: (a) Inside non-reserved: $210 plus taxes; (b) Inside reserved: $420.00 and is not subject to tax; (c) outside non-reserved: $185.00 plus taxes; and (d) outside reserved: $370.00 and is not subject to tax.

9. **First Extension Term Monthly Rent**. The rate of Monthly Rent during the First Extension Term shall be as follows:

Extension Commencement Date – April 30, 2023:	$70,966.57 per month
May 1, 2023 – April 30, 2024:	$73,095.57 per month
May 1, 2024 – April 30, 2025:	$75,288.43 per month

10. **Prepaid Rent**. Selig acknowledges that it is currently holding pre-paid rent in the original deposited amount of One Hundred Ninety-Three Thousand Eight Hundred Ninety-One and 00/100 Dollars ($193,891.00). Within five (5) business days after the Second Amendment Date, Selig shall return such amount, together with any interest thereupon, to CTI. From and after the return of the foregoing amounts, Section 4 of the Existing Lease shall be deleted in its entirety and replaced as follows: "4. Reserved"

11. **Brokers**. CTI hereby represents to Selig that CTI has dealt with no broker in connection with this Second Amendment other than Flinn Ferguson Cresa ("Tenant's Broker"). CTI agrees to defend, indemnify, and hold Selig harmless from all claims of any brokers (other than Tenant's Broker) claiming to have represented CTI in connection with this Second Amendment. Selig hereby represents to CTI that Selig has dealt with no broker in connection with this Second Amendment. Selig agrees to indemnify and hold CTI harmless from all claims of Tenant's Broker and any brokers claiming to have represented Selig in connection with this Second Amendment.

12. **Landlord Representations**. Selig hereby represents that: (a) the Existing Lease is in full force and effect and has not been modified or amended except as described herein and modified hereby; (b) Selig is the owner of the Building and has not assigned or otherwise transferred its interest in the Lease; (c) neither Selig nor CTI is in default of its respective obligations under the Lease, nor do any facts, circumstances or occurrences exist that, but for the passage of time or the delivery of notice, would result in a default under the Lease; and (d) the execution, delivery and compliance with, and performance of the terms and provisions of, this Amendment will not conflict with or result in any violation of any provision of any bond, note or other instrument of indebtedness, contract, indenture, mortgage, deed of trust, loan agreement, lease or other agreement or instrument to which Lessor or any affiliate thereof is a party.

13. **Incorporation**. Except as modified herein, all other terms and conditions of the Existing Lease shall remain unchanged. The Existing Lease, as amended herein, constitutes the entire understanding and agreement of the parties with respect to the subject matter hereof, and all prior agreements, representations, and understandings between the parties with respect to the subject matter hereof, whether oral or written, are or should be deemed to be null and void, all of the foregoing having been merged into this Second Amendment. This Second Amendment may be executed in multiple counterparts each of which is deemed an original but together constitute one and the same instrument. This Second Amendment may be executed in so-called "pdf" format and each party has the right to rely upon a pdf counterpart of this Second Amendment signed by the other party to the

same extent as if such party had received an original counterpart. The provisions of this Second Amendment shall bind and inure to the benefit of the parties hereto and their respective heirs, representatives, successors, and assigns to the same extent as set forth in the Existing Lease. Each signatory of this Second Amendment represents hereby that he or she has the authority to execute and deliver the same on behalf of the party hereto for which such signatory is acting without the need for any consent that has not already been secured.

SIGNATURE PAGES FOLLOW

AGREED AND ACCEPTED:

SELIG HOLDINGS COMPANY, LLC		CTI BioPharma Corp.	
By:	Martin Selig	By:	Adam Craig
Its:	Manager	Its:	CEO
Dated:	December 6, 2021	Dated:	December 6, 2021

LESSOR ACKNOWLEDGMENT

STATE OF WASHINGTON)
) ss.
COUNTY OF KING)

On this the 6th day of December, 2021, before me a Notary Public duly authorized in and for the said County in the State aforesaid to take acknowledgments personally appeared Martin Selig, personally known to me to be the Manager of the Selig Holdings Company, LLC's the Lessor that executed the foregoing instrument and acknowledge the said instrument to be the free and voluntary act and deed of said governmental agency for the uses and purposes therein mentioned, and on oath stated that (s)he was authorized to execute said instrument.

In Witness Whereof I have hereunder set my hand and affixed my official seal the day and year first above written.

MELANIE JOBE 163482 NOTARY PUBLIC COMMISSION EXPIRES 09-30-25 STATE OF WASHINGTON

Melanie Jobe
Name Printed:
Melanie Jobe
Notary Public in and for the State of
Washington
residing at
Renton
My commission expires: 09-30-25.

LESSEE ACKNOWLEDGMENT

STATE OF WASHINGTON)
) ss.
COUNTY OF KING)

On this the 6 day of December, 2021, before me a Notary Public duly authorized in and for the said County in the State aforesaid to take acknowledgments personally appeared Adam Craig, personally known to me to be the CEO + President of the CTI BioPharma Corp. the Lessee that executed the foregoing instrument and acknowledge the said instrument to be the free and voluntary act and deed of said governmental agency for the uses and purposes therein mentioned, and on oath stated that (s)he was authorized to execute said instrument.

In Witness Whereof I have hereunder set my hand and affixed my official seal the day and year first above written.

SUSAN R VAN DEN AMEELE
Commission Expires 09-21-2023
NOTARY PUBLIC
License Number 130745
STATE OF WASHINGTON

Name Printed:
Susie Van Den Ameele
Notary Public in and for the State of
WA,
residing at
Seattle
My commission expires: 9-21-2023

EXHIBIT A
DEPICTION OF CONFERENCE ROOM WALL

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Form S-3 Nos. 333-251161, 333-200453, 333-192749, 333-192748, 333-182330, 333-163479, 333-157376, 333-152171, 333-149981, 333-149980, 333-134126, and 333-108926 of CTI BioPharma Corp., and

(2) Form S-8 Nos. 333-239311, 333-231708, 333-225116, 333-218947, 333-218946, 333-211006, 333-207177, 333-207176, 333-196510, 333-189611, 333-184004, 333-178158, 333-170044, 333-162955, 333-158260, 333-152168, 333-146624 and 333-257174 pertaining to equity and option plans of CTI BioPharma Corp.

of our report dated March 31, 2022, with respect to the consolidated financial statements of CTI BioPharma Corp. included in this Annual Report (Form 10-K) of CTI BioPharma Corp. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Seattle, Washington
March 31, 2022

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO
SECURITIES EXCHANGE ACT OF 1934 RULES 13a-14(a) AND 15d-14(a)
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Adam R. Craig, certify that:

1. I have reviewed this Annual Report on Form 10-K of CTI BioPharma Corp.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and we have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions) of internal control over financial reporting:

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 31, 2022

By: /s/ Adam R. Craig
Adam R. Craig
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO
SECURITIES EXCHANGE ACT OF 1934 RULES 13a-14(a) AND 15d-14(a)
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David H. Kirske, certify that:

1. I have reviewed this Annual Report on Form 10-K of CTI BioPharma Corp.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and we have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 31, 2022

By: /s/ David H. Kirske
David H. Kirske
Chief Financial Officer

Exhibit 32

CERTIFICATION OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Adam R. Craig, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of CTI BioPharma Corp. on Form 10-K for the fiscal year ended December 31, 2021 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and that information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition and results of operations of CTI BioPharma Corp.

A signed original of this written statement required by Section 906 has been provided to CTI BioPharma Corp. and will be retained by CTI BioPharma Corp. and furnished to the Securities and Exchange Commission or its staff upon request.

Dated: March 31, 2022

By: /s/ Adam R. Craig
Adam R. Craig
President and Chief Executive Officer

I, David H. Kirske, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of CTI BioPharma Corp. on Form 10-K for the fiscal year ended December 31, 2021 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and that information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition and results of operations of CTI BioPharma Corp.

A signed original of this written statement required by Section 906 has been provided to CTI BioPharma Corp. and will be retained by CTI BioPharma Corp. and furnished to the Securities and Exchange Commission or its staff upon request.

Dated: March 31, 2022

By: /s/ David H. Kirske
David H. Kirske
Chief Financial Officer