Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark one)

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

For the fiscal year ended December 31, 2021

Or

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

For the transition period from to

Commission file number 001-36020

Onconova Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**22-3627252**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
12 Penns Trail, Newtown, PA	**18940**
(Address of principal executive offices)	(Zip Code)

(267) 759-3680
(Registrant's telephone number, including area code)

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $.01 per share	ONTX	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 Section 15(d) of the Act. Yes ☐ No ☒

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

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

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

Large accelerated filer ☐ 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. Yes ☐ No ☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule12b-2 of the Act). Yes ☐ No ☒

As of June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's voting stock held by non-affiliates was approximately $109.0 million, based on the last reported sale price of the registrant's common stock on the Nasdaq Capital Market.

There were 20,895,563 shares of Common Stock outstanding as of March 1, 2022.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for the registrant's 2022 annual meeting of stockholders to be filed within 120 days after the end of the period covered by this annual report on Form 10-K are incorporated by reference into Part III of this annual report on Form 10-K.

ONCONOVA THERAPEUTICS, INC.
INDEX TO REPORT ON FORM 10-K

All common stock, equity, share and per share amounts have been retroactively adjusted to reflect a one-for-fifteen reverse stock split which was effective May 20, 2021.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K ("Annual Report") includes forward-looking statements. We may, in some cases, use terms such as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Forward-looking statements appear in a number of places throughout this Annual Report and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, protection of our intellectual property portfolio, the degree of clinical utility of our products, particularly in specific patient populations, our ability to develop commercial and manufacturing functions, expectations regarding clinical trial data, our results of operations, cash needs, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics and industry change, and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Annual Report.

You should also read carefully the factors described in the "Risk Factors" section of this Annual Report and elsewhere to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements in this report and you should not place undue reliance on any forward-looking statements. These factors include, without limitations, the risks related to:

- our need for additional financing for our future clinical trials and other operations, and our ability to obtain sufficient funds on acceptable terms when needed, and our plans and future needs to scale back operations if adequate financing is not obtained;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing;
- the success and timing of our preclinical studies and clinical trials, including site initiation and patient enrollment, and regulatory approval of protocols for future clinical trials;
- our ability to enter into, maintain and perform collaboration agreements with other pharmaceutical companies, for funding and commercialization of our clinical drug product candidates or preclinical compounds, and our ability to achieve certain milestones under those agreements;
- the difficulties in obtaining and maintaining regulatory approval of our product candidates, and the labeling under any approval we may obtain;
- our plans and ability to develop, manufacture and commercialize our product candidates;
- our failure to recruit or retain key scientific or management personnel or to retain our executive officers;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any of our product candidates;

- obtaining and maintaining intellectual property protection for our product candidates and our proprietary technology;
- the successful development of our commercialization capabilities, including sales and marketing capabilities;
- recently enacted and future legislation and regulation regarding the healthcare system;
- the success of competing therapies and products that are or may become available;
- our ability to maintain the listing of our securities on a national securities exchange;
- the potential for third party disputes and litigation;
- the performance of third parties, including contract research organizations ("CROs") and third-party manufacturers; and
- the impact of the novel coronavirus disease, COVID-19, to global economy and capital markets, and to our business and our financial results.

Any forward-looking statements that we make in this Annual Report speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this Annual Report or to reflect the occurrence of unanticipated events.

PART I

ITEM 1. *BUSINESS*

Overview

Onconova Therapeutics, Inc., sometimes referred to as "we" or the "Company," is a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer. We have proprietary molecularly targeted agents designed to disrupt specific cellular pathways that are important for cancer cell proliferation. We believe that the product candidates in our pipeline have the potential to be efficacious in a variety of cancers with unmet medical need. We have the following two clinical-stage programs: 1. narazaciclib (ON 123300), a multi-targeted kinase inhibitor in solid tumors and hematological malignancies as a single agent or in combination with other anti-cancer therapies; and 2. rigosertib administered alone or in combination for the treatment of solid tumors. We are currently evaluating potential compounds for in-licensing opportunities.

Product Candidates / Compounds

Narazaciclib (ON 123300) — Differentiated Multi-Kinase Inhibitor Targeting CDK4/6

Pursuant to a license agreement with Temple University dated January 1, 1999 as amended March 21, 2013, we licensed compounds including our product candidate narazaciclib from Temple University. Narazaciclib is a multi-targeted kinase inhibitor targeting cyclin-dependent kinases (CDK) 2, 4, 6, and 9, AMPK related protein kinase 5 (ARK5), and colony-stimulating factor 1 receptor (CSF1R) at low nM concentrations as well as other tyrosine kinases believed to drive tumor cell proliferation, survival and metastasis. As an apoptotic and antiproliferative agent, narazaciclib modulates the levels and activities of regulatory proteins of the cell cycle, including cyclin D1 and inhibits retinoblastoma (Rb) protein binding. Narazaciclib inhibits cancer cell growth and suppresses deoxyribonucleic acid (DNA) synthesis by preventing CDK-mediated G1-S phase transition, followed by tumor cell death by induction of mitochondria-mediated apoptosis. We believe, based on data from preclinical studies, that narazaciclib has the potential to overcome the limitations of the current generation of approved cyclin dependent kinase (CDK) 4/6 inhibitors. The below table depicts the half-maximal in vitro inhibitory concentration (IC_{50}) of narazaciclib palbociclib, ribociclib and abemciclib. IC_{50} is a quantitative measure indicating the concentration of each drug needed to inhibit, in vitro, these listed kinases by 50%. We believe our DK inhibitor is differentiated from other agents in the market or in development due to its multi-targeted kinase inhibition profile.

	Narazaciclib	**Palbociclib**	**Ribociclib**	**Abemaciclib**
Sponsor	Onconova	Pfizer	Novartis	Lilly
CDK Family				
CDK4/cyclin D1	2	2	3	0.8
CDK6/cyclin D1	0.6	0.8	6.0	0.6
CDK1/cyclin A	2190	>10,000	>10,000	270
CDK2/cyclin E	69	2300	>10,000	130
CDK9/T1	48	630	390	7
Other Kinases				
CSF1R	0.7	>10,000	>10,000	>10,000
ARK 5/NUAK 1	5	1,400	1,540	773
FLT3	6.0	496	753	72

Source: Reaction Biology 2021

In addition to CDK 4/6, narazaciclib also inhibits ARK5 (NUAK1) with high potency with a 50% inhibitory concentration (IC50) of 4.95 nM (Report EPR-123300-001 and Reddy 2014) while palbociclib, ribociclib, and abemaciclib do not. The equilibrium dissociation constant (Kd) value of narazaciclib binding to ARK5 was found to be 19 nM, while a known NUAK1 specific inhibitor (HTH-015-01) was 790 nM. In addition, using a cellular based assay that measures kinase activity in intact cells, NanoBret technology, it was determined that narazaciclib inhibited ARK5

with an IC50 value of 30 nM, while 2 published inhibitors, HTH-015-01 and WZ4003, had IC50 values of >10,000 nM. ARK5 (also known as NUAK1) is a member of the AMP-activated protein kinase (AMPK) catalytic subunit family and functions as a key regulator of cellular energy homeo-stasis (Lui 2012). ARK5 has been shown to be important in a number of cancer cell regulated survival pathways such as regulating AKT dependent cell survival, cell metabolism through c-MYC activity, tumor cell survival under oxidative stress and tumor cell migration (Faisal, 2020, Lui, 2012, Port, 2018). The combination of CDK and ARK5 inhibitors in the same molecular entity is proposed to have a differentiated effect on cancer cells by simultaneously inhibiting both cell cycle (cytostatic) and cellular metabolism (cytotoxic) pathways through CDK and ARK5, respectively.

Narazaciclib also inhibits CSF1R with IC50 values between 0.7 to 10 nM (Unpublished data and Reddy 2014). The Kd value of narazaciclib binding to CSF1R was determined to be 0.7 nM. In addition, using a cellular based assay that measures kinase activity in intact cells, NanoBret technology, it was determined that narazaciclib inhibited CSF1R with an IC50 value of 0.7 nM. The ability of narazaciclib to bind and inhibit CSF1R at low nanomolar values, in both in vitro and cell-based assays suggests that this compound may have an impact in cancers with a dependence on CSF1R signaling.

We and our partner, HanX Biopharmaceuticals, Inc. (“HanX”), have initiated phase 1 dose escalation clinical studies to begin evaluating the safety, tolerability and PK of narazaciclib in order to establish a recommended phase 2 dose (RP2D). Once we establish the RP2D, we intend to progress clinical development to determine whether the findings from preclinical studies may translate to clinical activity or potential clinical benefit in cancer patients.

In certain in vitro models, the kinase inhibitory profile of narazaciclib had high activity against CDK4, CDK6, ARK5, CSF1R, PDGFRß and PI3K-δ, all of which are associated with the growth, survival and metastasis of human tumor cells (Reddy, 2014). In an in vitro investigation of narazaciclib against a broad spectrum of human tumor cell lines, narazaciclib displayed potent antiproliferative activity, with 50% growth inhibitory concentrations (GI50) ranging from 0.02 µM to 1.5 µM. In these in vitro models, narazaciclib exhibited a broad range of activity against a wide spectrum of cell lines of both hematological origin (lymphoma, leukemia and myeloma) as well as solid tumors derived from multiple organ sites. Studies on drug-resistant human tumor cell lines suggested that narazaciclib is not a multidrug resistance gene (mdr1) substrate and may be active against drug-resistant tumor cell lines (IBv.1 2020; Reddy, 2014). The activity of narazaciclib does not appear to be affected by the overexpression of MDR-1 and induced apoptosis in both ibrutinib-sensitive and ibrutinib-resistant patient derived cells (Divakar, 2016). The ability of narazaciclib to inhibit the CDK4/6/RB1 pathway has also been shown in pre-clinical testing of mantle cell lymphoma (Divakar, 2016), multiple myeloma (Perumal, 2016), various breast cancer subtypes (Reddy 2014) and colorectal cancer (IBv.2 2022).

The effectiveness of first-generation non-selective CDK inhibitors (Selicilib/roscovitine and Alvocidib/ flavopiridol) in early trials was limited due to toxicities (Blachly 2013). Second-generation compounds (palbociclib and ribociclib) specifically inhibit CDK4 and 6, thereby inhibiting retinoblastoma (RB) protein phosphorylation. Abemaciclib is a multi-targeted kinase CDK4/6 inhibitor with low nano molar activity against CDK4/6. The second generation CDK4/6 inhibitors have substantially improved clinical outcomes for patients with hormonal-receptor (HR) positive metastatic breast cancer (Hortobagyi 2018, Sledge 2017, Finn 2016). Several CDK4/6 inhibitors (palbociclib, ribociclib and abemaciclib) have been approved and are now standard of care either alone (abemaciclib) or in combination with anti-estrogen therapy for patients with HR-positive, HER2-negative metastatic breast cancer. Another CDK4/6 inhibitor has recently been approved, trilaciclib, in the supportive care space, for the prevention of myelosuppression following chemotherapy.

In December 2017, we entered into a license and collaboration agreement with HanX, a company focused on development of novel oncology products, for the further development, registration and commercialization in China of narazaciclib. Under the terms of the agreement, we received an upfront payment, and will receive regulatory and commercial milestone payments, as well as royalties on any future Chinese sales if the drug is approved. The key feature of the 2017 collaboration was that HanX provided all funding required for the Chinese Investigational New Drug Application (a “IND”) thereby enabling the studies necessary in order to seek IND approval by the National Medical Products Administration (Chinese FDA). In the fourth quarter of 2019, HanX filed an IND with the Chinese FDA which was approved on January 6, 2020. We and HanX also intended for these studies underlying the Chinese IND approval, to meet the US Food and Drug Administration (“FDA”) standards for IND approval. Accordingly, such studies were used

by us for an IND filing with the US FDA. In September 2020, a Phase 1 Study with narazaciclib in cancer patients was initiated in China. We maintain global rights to the study and study data outside of China.

Our IND submission to the US FDA was submitted in November 2020 and the FDA Study May Proceed letter was issued in December 2020. Enrollment into the US phase 1 study (Study 19-01) commenced in May 2021. Enrollment in the third dose cohort of the Phase 1 solid tumor study of narazaciclib is complete with no dose limiting toxicities (DLT's) observed. The fourth dose cohort is currently ongoing. The study will assess the safety, tolerability and pharmacokinetics of narazaciclib administered orally at increasing doses starting at 40 mg daily for consecutive 28-day cycles in patients (n=36) with relapsed/refractory advanced cancer.

In partnership with HanX, a complementary Phase 1 dose escalation study (Study HX301) for patients with advanced relapsed/refractory cancer has been initiated in China at three sites and the first patient was enrolled on September 15, 2020. In this study HX301 (narazaciclib) is dosed every day for 21 days followed by 7 days off therapy in each 28 -day cycle. In China, the first five dose cohorts have been completed. No dose limiting toxicities have been observed to date.

Collectively, once completed, these two Phase 1 studies are expected to provide preliminary safety data and the recommended Phase 2 dose and schedule for narazaciclib as a single agent.

Retinoblastoma (Rb) protein is a master regulator of cell division and is critical to several cellular processes including senescence, self-renewal, replication and apoptosis (Engel, 2015). It is believed that loss or inactivation of Rb leads to malignant cell formation and occurs in the pathogenesis of some cancers. In a preclinical Retinoblastoma (Rb) positive xenograft model for breast cancer, narazaciclib activity was shown to be similar to palbociclib (Pfizer's Ibrance ®). Moreover, based on the same preclinical model, narazaciclib may have the potential advantage of reduced neutropenia when compared to palbociclib. Whereas both compounds resulted in decreased RBC and platelet counts in this preclinical model system, palbociclib was found to have a more prominent and statistically significant ($P< 0.01$) inhibitory effect on neutrophil counts when compared to narazaciclib. These results would need to be replicated in clinical trials.

In vitro studies compared the growth inhibitory activity of narazaciclib and palbociclib in breast cancer RB null cell lines, which demonstrated resistance to palbociclib while maintaining sensitivity towards narazaciclib (IBv.2 2022). Studies using mantle cell lymphoma cells indicated that narazaciclib was able to induce cell death via induction of apoptosis by inhibiting the AKT/PI3K/mTOR pathway while palbociclib treatment was only able to induce cell cycle arrest due to the inhibition of CDK4/6 (Divakar, 2016). Narazaciclib treatment was associated with the presence of several apoptotic markers (PARP, caspase 3, caspase 7 and caspase 9) and narazaciclib (but not palbociclib) led to the generation of apoptotic cells. Overall, apoptosis following narazaciclib exposure has been observed in the following cell lines: breast cancer (IBv.2 2022, Reddy, 2014), mantle cell lymphoma (Divakar, 2016), multiple myeloma (Perumal, 2016) and colorectal cancer (IBv.2 2022).

In addition to CDK4/6 and PI3 Kinase pathways, narazaciclib inhibits several other kinases in vitro including ARK5 (NUAK1) (IC50 of 4.95 nM) (IBv.2 2022, Reddy, 2014) while palbociclib does not. ARK5 is a member of the AMP - activated protein kinase (AMPK) family and is thought to function as a key regulator of cellular energy homeo-stasis (Liu, 2012) and is important in a number of cancer cell survival pathways. Overexpression of ARK5 is associated with poor prognosis in hepatocellular cancer (Cui, 2013), ovarian cancer (Phippen, 2016), colorectal cancer (Port, 2018) and glioblastoma (Lu, 2013). ARK5 is involved in the increased invasiveness, migration and metastatic potential of breast cancer cells (Chang, 2012), colorectal cancer (Kusakai, 2004), gastric cancer (Chen, 2017), and multiple myeloma (Suzuki et al., 2005). Narazaciclib inhibits ARK5 which may result in down regulation of the mTOR/MYC/RB1 pathways leading to cell cycle arrest and apoptosis.

Because ARK5 activity is now recognized as a component in promoting cancer cell migration and invasion (Kusaki, 2004) the effect of narazaciclib treatment may have an impact on cell migration and metastasis. In certain in vitro models, narazaciclib was able to inhibit the percent migration of U87 cells in a concentration- dependent manner. The time and concentrations that were tested did not result in cell death but did inhibit cell division at the higher concentrations (IBv.2 2022). The ability of narazaciclib to inhibit cell migration was compared to palbociclib using a

wound healing model. Triple negative cancer cell migration was inhibited for 72 hours in the presence of narazaciclib but not in the presence of palbociclib (IBv.2 2022).

The pathogenesis and progression of a number of cancers, including breast and multiple myeloma, is linked to C-Myc (Li, 2003) which was dependent on ARK5 activity (Liu, 2012) and calcium dependent metabolism (Monteverde, 2018). The inhibition of ARK5 has been shown to be lethal in MYC overexpressing tumors (Liu, 2012, Perumal, 2016) and targeting ARK5 in the inhibitory profile of narazaciclib has the potential to overcome the emergence of resistance to CDK4/6 inhibitors due to the loss of retinoblastoma function and C-Myc overexpression. Preclinical studies with tumor cell lines suggest that several malignancies including HR-positive breast cancer, colorectal carcinoma, hepatocellular carcinoma, mantle cell lymphoma and multiple myeloma, may be clinically responsive to narazaciclib exposure (Reddy, 2014, Divakar, 2016, Perumal, 2016). Furthermore, narazaciclib has been tested in four murine xenograft models (breast cancer, colorectal cancer, mantle cell lymphoma and multiple myeloma) and was found to have on-target activity and be non-toxic to the animals (Reddy, 2014; Divakar, 2016; Perumal, 2016; and IBv.2 2022).

CSF1R is in the class III kinase receptors that include c-Kit, platelet-derived growth factor receptor (PDGFR) alpha, and FLT3. CSF1R has 2 high affinity binding ligands, colony stimulating factor 1 (CSF-1), also known as macrophage colony stimulation factor (M-CSF) and interleukin 34 (IL-34). CSF-1 is important for the differentiation and proliferation of myeloid progenitor cells into macrophages, monocytes, dendritic cells, and osteoclasts. Macrophages play an important role in the pathogenesis of not only tumor growth but multiple other diseases such as inflammatory diseases and bone metabolism. High levels of CSF-1 are critical for the recruitment of tumor associated macrophages (TAMs), predominantly the immunosuppressive phenotype (M2). They are the main inflammatory immune cells in the tumor microenvironment and are involved in tumor immunosuppression, angiogenesis, invasion, and metastasis.

Overexpression of CSF-1 or CSF1R is associated with tumor aggressiveness and poor prognosis. Inhibiting the signaling pathway of CSF1R provides a method to reduce the number of M2 macrophages/TAMs within the tumor microenvironment and thus improve anti-tumor immunological therapy. Recent studies have found that CSF-1/CSF1R axis blockade can improve the efficiency of immune checkpoint inhibitors, especially programmed death-ligand 1 inhibitors.

Cancer cells can lose RB function through mutation and become resistant or insensitive to palbociclib. Generally, second generation agents have not been shown to be suitable for single agent therapy and must typically be used in combination with hormonal therapy in the treatment of HR+/HER2- mBC. In addition, the rate of disease progression that occurs, especially in patients with visceral disease (Hortobagyi 2018), may benefit from the novel inhibitory effects of narazaciclib. This hypothesis needs to be proven in a clinical trial.

Unfortunately, several mechanisms of acquired resistance are emerging with the approved CDK4/6 inhibitors leading to progression in patients with HR+/HER2- mBC (Spring, 2019; Knudsen, 2020). Therefore, the unmet medical need supports development of the next (third) generation CDK4/6 inhibitors in advanced HR+/HER- mBC. The inhibitory effect of narazaciclib may provide a therapeutic strategy to optimize efficacy of CDK 4/6 inhibition and reduce the emergence of resistance and/or provide clinical benefit for patients with progression on palbociclib, ribociclib and/or abemaciclib.

We believe narazaciclib has a favorable kinase inhibitory profile in comparison to the approved CDK4/6 inhibitors (palbociclib, ribociclib, and abemaciclib) and may result in both tumorigenic and safety benefits (Perumal, 2016, Divakar, 2016).

Based on data from continuous dosing studies in rats and monkeys the safety profile of narazaciclib is anticipated to be better than the approved CDK4/6 inhibitors with myelosuppression and gastrointestinal toxicity being most common. Management of these adverse events is expected to follow that used for the approved CDK 4/6 inhibitors. We believe that the proposed mechanism of action of narazaciclib, the unmet medical need of the advanced cancers potentially targeted by narazaciclib and the anticipated safety profile of narazaciclib as seen in pre-clinical studies, support conducting clinical studies.

Clinical development of narazaciclib for breast cancer as well as other solid tumors and hematological malignancies in clinical trials is warranted based on the preclinical in vitro studies as well as the xenograft models. Onconova plans to advance testing whether narazaciclib will demonstrate activity and/or safety in patients with advanced malignancies.

Oral Rigosertib and PD-1 Combination in KRAS-Mutated Cancers

We are currently supporting investigator-initiated studies (ISS) that are exploring the use of rigosertib for cancers driven by mutated Ras genes including a Phase 1/2a study of rigosertib in combination with a PD-1 inhibitor for patients with progressive K-Ras mutated non-small cell lung cancer (NSCLC). The NSCLC study is open and continues to enroll patients. The objectives of this study are to identify the recommended Phase 2 dose (RP2D) for future studies and characterize the safety profile of the combination treatment. Final results of the Phase 1 portion of the study are expected in late 2022. On June 28, 2021, we announced an update regarding this NSCLC study, with an expansion of the trial underway at the highest dose in the current protocol. To date, one patient with a dose limiting toxicity of hyponatremia has been observed. Continued dose escalation is being considered as we believe the maximum tolerated dose has not been reached. In addition, preliminary efficacy data support the preclinical observation of rigosertib augmenting the response to checkpoint inhibition (CPI) in patients who had previously failed all standard of care treatment, including CPI. Interim data presented at the 3rd Annual RAS Targeted Drug Development Summit (September 21-23, 2021), demonstrated two partial responses and one stable disease out of seven evaluable patients, or a clinical benefit rate of 43% (3/7). The three patients with clinical benefit harbored different KRAS mutations; suggesting that patients with a variety of KRAS mutations may have the potential to respond to the novel combination including rigosertib. We believe this supports further investigation of rigosertib in combination with CPI in KRAS mutated NSCLC.

On June 17, 2021, we announced a publication in Molecular Cancer (Yan, C., Saleh, N., Yang, J. *et al.* Novel induction of CD40 expression by tumor cells with RAS/RAF/PI3K pathway inhibition augments response to checkpoint blockade. *Mol Cancer* **20,** 85; 2021) which demonstrated that rigosertib synergistically combined with CPI improved tumor growth inhibition and survival in a murine melanoma model that did not respond to CPI alone. It was postulated that rigosertib's anti-cancer activity was due to its ability to reverse immunosuppressive tumor microenvironments. We believe this pre-clinical data support the clinical evaluation of rigosertib in combination with a CPI in metastatic melanoma that has progressed on CPI therapy and we expect an ISS for continued development in the area will be open for enrollment in 1H2022.

Rigosertib as Monotherapy

Based on rigosertib's activity against another important cell cycle pathway, PLK-1 (Antanasova, 2019), a Phase 1b/2 ISS with rigosertib monotherapy in patients with advanced squamous cell carcinoma associated with recessive dystrophic epidermolysis bullosa (RDEB-SCC) is enrolling patients. As we disclosed in December 2021 early preliminary data from an investigator-initiated Phase 2 open label trial of rigosertib monotherapy in advanced squamous cell carcinoma complicating recessive dystrophic epidermolysis bullosa (RDEB- SCC) were presented at the Austrian Society of Dermatology and Venerology Annual Conference 2021, which took place from November 25 – 27, 2021.

RDEB is an ultra-rare condition with high unmet medical need caused by a lack of type VII collagen protein expression. Type VII collagen protein is responsible for anchoring the skin's inner layer to its outer layer, and its absence leads to extreme skin fragility and chronic wound formation in RDEB patients. Over time, many of these patients develop squamous cell carcinomas (SCCs) that typically arise in areas of chronic skin wounding and inflammation. Preclinical investigations demonstrated overexpression of polo like kinase 1 (PLK1) in RDEB-associated SCC tumor cells. These tumors show a highly aggressive, early metastasizing course, making them the primary cause of death for these patients, with a cumulative risk of death of 70% and 78.7% by age 45 and 55, respectively (Mellerio, 2016), (Fine, 2016). These neoplasms show limited response rates of mostly short duration to conventional chemo- and radiotherapy as well as targeted therapy with epidermal growth factor and tyrosine kinase inhibitors (Mellerio, 2016), (Stratigos, 2020).

Data from the recent presentation are from a patient with a history of multiple, unresectable SCCs that were unresponsive to prior treatments including cemiplimab. Results showed that intravenously administered rigosertib had an acceptable safety profile and that the patient experienced sustained clinical and histological remission of all target

lesions without signs of metastatic disease following 13 treatment cycles. The patient remains on study and the trial remains ongoing. The enrollment of additional patients is anticipated at sites in Salzburg, Austria; London, UK; and Philadelphia, Pennsylvania.

Though the trial's currently available data are from only a single patient, the investigators believe they represent an encouraging finding that warrants further study. In addition, the investigators and we believe the data generated in preclinical models that suggest rigosertib's activity against PLK1 have now been preliminarily supported in the clinic, and suggest that rigosertib may play a role in other more common cancers driven by PLK1.

Rare Disease Program in "RASopathies"

Based on the mechanism of action data published in the journal Cell in 2016, we initiated a collaborative development program focusing on a group of rare diseases with a well- defined molecular basis in expression or defects involving the Ras effector pathways. Since RASopathies are rare congenital diseases affecting young children, we embarked on a multifaceted collaborative program involving patient advocacy, government and academic organizations. RASopathies are usually caused by germline mutations in genes that alter the RAS subfamily and mitogen-activated protein kinases (MAPK) that control signal transduction and are among the most common genetic syndromes. Together, this group of diseases can impact more than 1 in 1,000 individuals, according to RASopathies.Net.

The NCI has conducted preclinical studies with cell lines from two pediatric solid tumors (rhabdomyosarcoma and neuroblastoma), including xenograft models. For both tumor cell lines, in vitro rigosertib exposure was associated with reduced cell viability associated with destabilization of microtubules, mitotic arrest and apoptosis. In a rhabdomyosarcoma xenograft model, rigosertib treatment delayed time to tumor progression and prolonged survival in the animals treated with rigosertib. (Kowalczyk, 2020)

Programs Discontinued During 2020

Through August 2020, our efforts had been primarily focused on our product candidate, rigosertib, for patients with myelodysplastic syndromes ("MDS"). Rigosertib has been tested in an intravenous formulation as a single agent for patients with relapsed/refractory higher-risk MDS ("HR-MDS"), and an oral formulation as a single agent in lower risk MDS or in combination with azacitidine for patients with newly diagnosed or refractory HR-MDS.

On August 24, 2020, we announced topline results from the INSPIRE trial, which assessed the efficacy and safety of IV rigosertib in HR-MDS patients. The trial did not meet its primary endpoint of improved survival for patients randomized to IV rigosertib compared to the control arm. Based on the results of the INSPIRE trial and the previously conducted ONTIME Phase 3 trial, we currently do not plan to further pursue rigosertib for treating HR-MDS.

Research and Development

Since commencing operations, we have dedicated a significant portion of our resources to the development of our clinical-stage product candidates, particularly rigosertib and more recently narazacicib. We incurred research and development expenses of $7.3 million and $16.9 million during the years ended December 31, 2021 and 2020, respectively. We anticipate that a significant portion of our operating expenses will continue to be related to research and development.

Collaboration and License Agreements

HanX Biopharmaceuticals, Inc. (narazaciclib Agreement)

In December 2017, we entered into a license and collaboration agreement with HanX, a company focused on development of novel oncology products, for the further development, registration and commercialization in Greater China of narazaciclib. We believe narazaciclib has the potential to overcome limitations of current generation CDK 4/6 inhibitors. Under the terms of the agreement, we received an upfront payment, and will receive regulatory and commercial milestone payments, as well as royalties on Chinese sales. The key feature of the collaboration is that HanX

provides all funding required for Chinese IND enabling studies performed for Chinese health authority IND approval. The Chinese IND was approved in January 2020. We and HanX also intended for these studies to comply with the FDA standards. Accordingly, such studies were used by us for an IND filing with the FDA in November 2020. The FDA Study May Proceed letter was received in December 2020. Drug product for the US study was manufactured in North America and stability data was submitted as part of the IND. We maintain global rights to narazaciclib outside of China.

SymBio Pharmaceuticals Limited

In July 2011, we entered into a license agreement with SymBio Pharmaceuticals Limited ("Symbio"), as subsequently amended, granting SymBio an exclusive, royalty-bearing license for the development and commercialization of rigosertib in Japan and Korea. Under the SymBio license agreement, SymBio is obligated to use commercially reasonable efforts to develop and obtain market approval for rigosertib inside the licensed territory and we have similar obligations outside of the licensed territory. We have also entered into an agreement with SymBio providing for the Company to supply SymBio with development-stage product. Under the SymBio license agreement, we also agreed to supply commercial product to SymBio under specified terms that will be included in a commercial supply agreement to be negotiated prior to the first commercial sale of rigosertib. The supply of development-stage product and the supply of commercial product will be at our cost plus a defined profit margin. We have additionally granted SymBio a right of first negotiation to license or obtain the rights to develop and commercialize compounds having a chemical structure similar to rigosertib in the licensed territory.

Under the terms of the SymBio license agreement, we received an upfront payment of $7,500,000. In addition, we could receive regulatory, development and sales-based milestone payments as well as royalty payments at percentage rates ranging from the mid-teens to 20% based on net sales of rigosertib by SymBio.

Royalties will be payable under the SymBio agreement on a country- by-country basis in the licensed territory, until the later of the expiration of marketing exclusivity in those countries, a specified period of time after first commercial sale of rigosertib in such country, or the expiration of all valid claims of the licensed patents covering rigosertib or the manufacture or use of rigosertib in such country. If no valid claim exists covering the composition of matter of rigosertib or the use of or treatment with rigosertib in a particular country before the expiration of the royalty term, and specified competing products achieve a specified market share percentage in such country, SymBio's obligation to pay us royalties will continue at a reduced royalty rate until the end of the royalty term. In addition, the applicable royalties payable to us may be reduced if SymBio is required to pay royalties to third -parties for licenses to intellectual property rights necessary to develop, use, manufacture or commercialize rigosertib in the licensed territory. The license agreement with SymBio will remain in effect until the expiration of the royalty term. However, the SymBio license agreement may be terminated earlier due to the uncured material breach or bankruptcy of a party, or force majeure. If SymBio terminates the license agreement in these circumstances, its licenses to rigosertib will survive, subject to SymBio's milestone and royalty obligations, which SymBio may elect to defer and offset against any damages that may be determined to be due from us. In addition, we may terminate the license agreement in the event that SymBio brings a challenge against it in relation to the licensed patents, and SymBio may terminate the license agreement without cause by providing us with written notice a specified period of time in advance of termination. The upfront payment is being recognized ratably through December 2037, the expected term of the agreement. We recognize revenues related to the supply agreement with SymBio when control of the product is transferred to Symbio. Revenues related to the supply agreement were $0 and $5,000 for the fiscal years ended December 31, 2021 and 2020, respectively.

SymBio has conducted phase 1 trials with IV and oral rigosertib in Japan at their own expense. SymBio also participated in the INSPIRE trial by enrolling patients in Japan. For all rigosertib trials conducted by SymBio, we supply clinical trial supplies and provide other assistance as requested.

Pint International SA

In March 2018, we entered into a License, Development and Commercialization Agreement (the "Pint License Agreement") with Pint International SA (which, together with its affiliate Pint Pharma GmbH, are collectively referred to as "Pint"). Under the terms of the Pint License Agreement, we granted Pint an exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to develop and commercialize any

pharmaceutical product (the "Pint Licensed Product") containing rigosertib in all uses of rigosertib or the Product in humans in Latin America countries (the "Pint Territory," including Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, El Salvador, French Guiana, British Guiana, Suriname, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay and Venezuela).

Pint agreed to make an upfront equity investment and a subsequent equity investment in our common stock. In addition, we could receive regulatory, development and sales-based milestone payments as well as tiered, double digit royalties based on aggregate net sales in the Pint Territory. Pint and the Company have also agreed to enter into a supply agreement providing for Pint purchasing rigosertib and the Pint Licensed Product from the Company within 90 days of the FDA approval of a New Drug Application ("NDA") for the Pint Licensed Product.

Under the terms of the Pint Securities Purchase Agreement, Pint agreed to make an upfront equity investment in the Company at a specified premium to the Company's share price. Pursuant to the Pint Securities Purchase Agreement, closing of the upfront equity investment occurred on April 4, 2018 and Pint purchased 54,463 shares of common stock for $1,250,000. The total amount of the premium was $319,000 and this amount was allocated to the license.

Pint may terminate the Pint License Agreement in whole (but not in part) at any time upon 45 days' prior written notice. The Pint License Agreement also contains customary provisions for termination by either party in the event of breach of the Pint License Agreement by the other party, subject to a cure period, or bankruptcy of the other party.

Knight Therapeutics, Inc.

In November 2019, we entered into a Distribution, License and Supply Agreement (the "Knight License Agreement") with Knight Therapeutics Inc. ("Knight"). Under the terms of the License Agreement, we granted Knight (i) a non-exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to develop and manufacture any product (the "Knight Licensed Product") containing rigosertib for Canada (and Israel should Knight exercise its option) (the "Knight Territory") and in human uses (the "Knight Licensed Field"), and (ii) an exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to commercialize the Knight Licensed Product in the Knight Territory and in the Knight Licensed Field.

Knight has also agreed to obtain from us all of Knight's requirements of the Knight Licensed Products for the Knight Territory, and we have agreed to supply Knight with all of its requirements of the Knight Licensed Products. We may, at our discretion, use the services of a contract manufacturer to manufacture and package the Knight Licensed Products.

In addition, we have granted Knight an exclusive right of first refusal with respect to all or any part of the Knight Territory, to store, market, promote, sell, offer for sale and/or distribute any ROFR Products. As used in the Knight License Agreement, "ROFR Products" means all products other than the Knight Licensed Product that are owned, licensed, or controlled by us as of the effective date of the Knight License Agreement and all improvements thereto.

We are eligible to receive clinical, regulatory, and sale-based milestone payments as well as tiered, double-digit royalties based on net sales in the Knight Territory.

The License Agreement is for a term of 15 years from the launch on a country by country basis in the Territory and contains customary provisions for termination by either party in the event of breach of the License Agreement by the other party (subject to a cure period), bankruptcy of the other party, or challenges to the patents by any sublicensee or assignee.

Specialised Therapeutics Asia Pte. Ltd.

In December 2019, we entered into a Distribution, License and Supply Agreement (the "STA License Agreement") with Specialised Therapeutics Asia Pte. Ltd. ("STA"). Under the terms of the License Agreement, we granted STA (i) a non-exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to develop and manufacture any product (the "STA Licensed Product") containing rigosertib for Australia and New

Zealand (the "STA Territory") and in human uses (the "STA Licensed Field"), and (ii) an exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to commercialize the STA Licensed Product in the STA Territory and in the STA Licensed Field.

STA has also agreed to obtain from us all of its requirements of the STA Licensed Products for the STA Territory, and we have agreed to supply STA with all of its requirements of the STA Licensed Products. We may, at our discretion, use the services of a contract manufacturer to manufacture and package the STA Licensed Products.

We are eligible to receive clinical, regulatory, and sale-based milestone payments as well as tiered, double-digit royalties based on net sales in the STA Territory.

The STA License Agreement is for a term of 15 years from the launch on a country by country basis in the STA Territory and contains customary provisions for termination by either party in the event of breach of the STA License Agreement by the other party (subject to a cure period), bankruptcy of the other party, or challenges to the patents by any sublicensee or assignee.

HanX Biopharmaceuticals, Inc. (terminated rigosertib agreement)

In May 2019, we entered into a License and Collaboration Agreement (the "HanX rigosertib License Agreement") with HanX . Under the terms of the HanX rigosertib License Agreement, we granted HanX an exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to develop and commercialize any pharmaceutical product (the "HanX Licensed Product") containing rigosertib in all uses of rigosertib or the HanX Licensed Product in humans therapeutics uses in the People's Republic of China, Hong Kong, Macau and Taiwan (the "HanX Territory"). In connection with the HanX rigosertib License Agreement, we also entered into a Securities Purchase Agreement with each of HanX and Abundant New Investments Ltd. ("Abundant"), an affiliate of HanX (each, a "Securities Purchase Agreement" and together, the "HanX Securities Purchase Agreements").

HanX did not fulfill its obligations under the HanX rigosertib License Agreement and effective January 16, 2020, in accordance with the terms of the HanX rigosertib License Agreement, the HanX License Agreement was deemed to be void ab initio. Upon this termination, the rights to HanX Licensed Product in the HanX Territory reverted to us in accordance with the terms of the HanX rigosertib License Agreement.

In addition, the HanX Securities Purchase Agreements terminated automatically effective January 16, 2020 upon the termination of the HanX rigosertib License Agreement in accordance with the HanX Securities Purchase Agreements.

Intellectual Property

Patents and Proprietary Rights

Our intellectual property is derived through our internal research, licensing agreements with Temple University, or Temple, and licensing research agreements with the Mount Sinai School of Medicine, or Mount Sinai.

License Agreement with Temple University

In January 1999, we entered into a license agreement with Temple as subsequently amended, to obtain an exclusive, world-wide license to certain Temple patents and technical information to make, have made, use, sell, offer for sale and import several classes of novel compounds.

Under the terms of the license agreement, we paid Temple a non-refundable up-front payment, and are required to pay annual license maintenance fees, as well as a low single-digit percentage of net sales as a royalty. In addition, we agreed to pay Temple 25% of any consideration received from any sublicensee of the licensed Temple patents and technical information, which does not include any royalties on sales, funds received for research and development or proceeds from any equity or debt investment.

The license agreement with Temple can be terminated by mutual agreement or due to the material breach or bankruptcy of either party. We may terminate the license agreement for any reason by giving Temple prior written notice.

Research Agreement with Mount Sinai School of Medicine

In May 2010, we entered into a research agreement with Mount Sinai. The agreement expired in June 2020 and was not renewed. This agreement is described in more detail under the caption "Certain Relationships and Related Party Transactions — Research Agreement."

Narazaciclib Patents

As of March 2022, we owned or exclusively licensed issued patents and pending patent applications covering composition of matter, formulation and various indications for method-of-use for narazaciclib filed worldwide, including in the United States. The U.S. composition-of-matter patent for narazaciclib expires in 2031. We have recently filed new patent applications covering methods of treatment in target indications that are projected to extend to 2042 before any possible patent term extensions. Patent term extensions may be available, depending on various provisions in the law.

Rigosertib Patents

As of March 2022, we owned or exclusively licensed issued patents and pending patent applications covering composition-of-matter, process, formulation and various indications for method-of-use for rigosertib filed worldwide, including in the United States. The U.S. composition-of-matter patent for rigosertib, which we in-licensed pursuant to the license agreement with Temple, currently expires in 2026. A U.S. method of treatment patent for rigosertib, which we also in-licensed from Temple, expires in 2025. A patent covering the use of rigosertib in combination with anticancer agents including azacitidine is issued and will expire in 2028. The novel formulation patent for rigosertib expires in 2037. We have recently filed new patent applications covering methods of treatment in target indications that are projected to extend to 2042 before any possible patent term extensions. Patent term extensions may be available, depending on various provisions in the law.

General Considerations

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify a proprietary position for our product candidates will depend upon our success in obtaining effective patent claims and enforcing those claims once granted.

Our commercial success will depend in part upon not infringing upon the proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, or our product candidates or processes, obtain licenses or cease certain activities. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. If a third party commences a patent infringement action against us, or our collaborators, it could consume significant financial and management resources, regardless of the merit of the claims or the outcome of the litigation.

The term of a patent that covers an FDA-approved drug may be eligible for additional patent term extension, which provides patent term restoration to account for the patent term lost during product development and the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is determined based upon the time from the IND effective date to the NDA submission date, and the time from NDA submission date and the eventual application approval, as further described below. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products.

Furthermore, we may be able to obtain extension of patent term by adjustment of the said term under the provisions of 35 U.S.C. **§** 154 if the issue of an original patent is delayed due to the failure of the U.S. Patent and Trademark Office. For example, we have received adjustments of 1,139 days extension to the patent term for the rigosertib composition of matter patent (US 7,598,232), 1,155 days extension for the patent covering the process for making rigosertib (US 8,143,453) and 751 days extension for rigosertib formulation patent (US 8,063,109) under the provisions of 35 U.S.C. §154.

In addition to patents, we rely upon unpatented trade secrets, know-how and continuing technological innovation to develop and maintain a competitive position. We seek to protect our proprietary information, in part, through confidentiality agreements with our employees, collaborators, contractors and consultants, and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants and collaborators. The confidentiality agreements are designed to protect our proprietary information and, in the case of agreements or clauses requiring invention assignment, to grant us ownership of technologies that are developed through a relationship with a third party.

Competition

The pharmaceutical industry is highly competitive and subject to rapid and significant technological change. While we believe that our development experience and scientific knowledge provide us with competitive advantages, we face competition from both large and small pharmaceutical and biotechnology companies. There are a number of pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may compete with our products. Many of these companies are multinational pharmaceutical or biotechnology organizations, which are pursuing the development of, or are currently marketing, pharmaceuticals that target the key oncology indications or cellular pathways on which we are focused.

It is probable that the increasing incidence and prevalence of cancer will lead to many more companies seeking to develop products and therapies for the treatment of unmet needs in oncology. Many of our competitors have significantly greater financial, technical and human resources than we have. Many of our competitors also have a significant advantage with respect to experience in the discovery and development of product candidates, as well as obtaining FDA and other regulatory approvals of products and the commercialization of those products. We anticipate intense and increasing competition as new drugs enter the market and as more advanced technologies become available. Our success will be based in part on our ability to identify, develop and manage a portfolio of drugs that are safer and more effective than competing products in the treatment of cancer patients.

There are several ongoing clinical trials aimed at expanding the use of approved chemotherapeutic and immunomodulatory agents in the diseases we are studying, as well as several new clinical programs testing novel technologies. Companies with marketed CDK 4/6 inhibitors in the metastatic breast cancer space include Pfizer (palbociclib), Novartis (ribociclib) and Eli Lilly (abemacicilib).

Manufacturing

Our product candidates are synthetic small molecules. Manufacturing activities must comply with FDA current good manufacturing practices, or cGMP, regulations. We conduct our manufacturing activities under individual purchase orders with third-party contract manufacturers (“CMOs”). We have quality agreements in place with our key CMOs. We have also established an internal quality management organization, which audits and qualifies CMOs in the United States and abroad.

We believe that the manufacturing processes for the active pharmaceutical ingredient and finished drug products for our products are being developed to adequately support future development and commercial demands. If manufacturing challenges occur, they are thoroughly reviewed and, as may be required, reported to health authorities to determine whether the product can be used for clinical trials.

The FDA regulates and inspects equipment, facilities and processes used in manufacturing pharmaceutical products prior to approval. If we or CMOs fail to comply with applicable cGMP requirements and conditions of product approval,

the FDA may seek sanctions, including fines, civil penalties, injunctions, suspension of manufacturing operations, operating restrictions, withdrawal of FDA approval, refusal to approve applications, seizure or recall of products and criminal prosecution. Although we periodically monitor the FDA compliance of our third-party CMOs, we cannot be certain that our present or future third-party CMOs will consistently comply with cGMP and other applicable FDA regulatory requirements.

Commercial Operations

We do not currently have an organization for the sales, marketing and distribution of pharmaceutical products. We may rely on licensing and co-promotion agreements with strategic partners for the commercialization of our products in the United States and other territories. If we choose to build a commercial infrastructure to support marketing in the United States, such commercial infrastructure could be expected to include a targeted, oncology sales force supported by sales management, internal sales support, an internal marketing group and distribution support. To develop the appropriate commercial infrastructure internally, we would have to invest significant financial and management resources.

Government Regulation

As a pharmaceutical company that operates in the United States, 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 the FDC Act, and its implementing regulations set forth, among other things, requirements for the research, testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising, marketing, and promotion of our products. FDA also has issued a growing body of guidance documents that provide the agency's interpretation of regulatory requirements, including a number of guidance documents to assist companies navigating COVID-19, product development, and manufacturing.

Although the discussion below focuses on regulation in the United States, we and/or our partners anticipate seeking approval for, and marketing of, our products in other countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of approval and regulation in Europe are addressed in a centralized way through the EMA, but country-specific regulation remains essential in many respects and enforcement is generally through EU member state authorities. The process of obtaining regulatory marketing approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and may not be successful. In addition, approval in the United States does not automatically result in approval in the European Union or elsewhere.

United States Government Regulation

The FDA is the main regulatory body that controls pharmaceuticals in the United States, and its regulatory authority is based in the FDC Act. Pharmaceutical products are also subject to other federal, state and local statutes. A failure to comply explicitly with any requirements during the product development, approval, or post-approval periods, may lead to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an institutional review board, or IRB, or Independent Ethics Committee (IEC) of a hold on clinical trials, refusal to approve pending marketing applications or supplements, withdrawal of approval, warning letters, untitled letters, cyber letters, product recalls, product seizures or detention, prohibition on importing or exporting, total or partial suspension of production or distribution, injunctions, fines, civil penalties, adverse publicity, disgorgement, restitution, FDA debarment, debarment from government contracting or refusal of future orders under existing contracts, exclusion from Federal healthcare programs, corporate integrity agreements, consent decrees, or criminal prosecution.

The steps required before a new drug may be marketed in the United States generally include:

- Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;

- Submission to the FDA of an IND to support human clinical testing;
- Approval by an IRB at each clinical site or centrally before each trial may be initiated;
- Performance of adequate and well-controlled clinical trials in accordance with federal regulations and with current good clinical practices, or GCPs, to establish the safety and efficacy of the investigational drug product for each targeted indication;
- Submission of a NDA to the FDA;
- Satisfactory completion of an FDA Advisory Committee review, if applicable;
- Satisfactory completion of an FDA inspection of the manufacturing facilities at which the investigational product is produced to assess compliance with cGMP, and to assure that the facilities, methods and controls are adequate, as well as satisfactory completion of FDA inspections of selected clinical trial sites to ensure that clinical trials were conducted in accordance with GCPs; and
- FDA review and approval of the NDA.

Preclinical and Clinical Trials

The testing and approval process of product candidates requires substantial time, effort, and financial resources. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease. Product development typically begins with preclinical studies. Preclinical studies include laboratory evaluation of chemistry, pharmacology, toxicity, and product formulation, as well as animal studies to assess potential safety and efficacy. Such studies must generally be conducted in accordance with the FDA's GLPs.

Prior to commencing the first clinical trial with a product candidate, an IND sponsor must submit the results of the preclinical tests and preclinical literature, together with manufacturing information, analytical data, any available clinical data or literature, and proposed clinical study protocols among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. This authorization is required before interstate shipping and administration of any new drug product to humans that is not the subject of an approved NDA. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational drug to patients under the supervision of qualified investigators following GCPs, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors. Clinical trials are conducted under protocols that detail the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND. The informed written consent of each participating subject is required. The clinical investigation of an investigational drug is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The three phases of an investigation are as follows:

- Phase 1. Phase 1 includes the initial introduction of an investigational drug into humans. Phase 1 clinical trials may be conducted in patients with the target disease or condition or healthy volunteers. These studies are designed to evaluate the safety, metabolism, pharmacokinetics and pharmacologic actions of the investigational drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the investigational product's pharmacokinetics and pharmacological effects may be obtained to permit the design of Phase 2 clinical trials. The total number of participants included in Phase 1 clinical trials varies, but is generally in the range of 20 to 80.

- Phase 2. Phase 2 includes the controlled clinical trials conducted to evaluate the effectiveness of the investigational product for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population, usually involving no more than several hundred participants.

- Phase 3. Phase 3 clinical trials are controlled clinical trials conducted in an expanded patient population at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the investigational product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the product, and to provide an adequate basis for product approval. Phase 3 clinical trials usually involve several hundred to several thousand participants. In most cases, the FDA requires two adequate and well controlled Phase 3 clinical trials to demonstrate the efficacy of the drug.

Additional kinds of data may also help support an NDA, such as patient experience data and real world evidence. Real world evidence may be used to assist in clinical trial design or support an NDA for already approved products.

The decision to terminate development of an investigational drug product may be made by either a health authority body, such as the FDA or IRB/independent ethics committees (“IECs”), or by a company for various reasons. An IRB approves the initiation of a clinical trial and supervises the conduct of the trial to ensure that the risks to human subjects are reasonable in relation to the anticipated benefits and that there are adequate human subject protections in place. The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor. This group provides guidance on whether or not a trial may or should move forward at designated check points. These decisions are based on the limited access to data from the ongoing trial. The suspension or termination of development can occur during any phase of clinical trials if it is determined that the participants or patients are being exposed to an unacceptable health risk, if the product candidate does not show sufficient evidence of efficacy, if the development program does not comply with applicable regulatory requirements, or due to changing sponsor business objectives.

In addition, there are various reporting requirements that clinical trial sponsors and investigators must comply with during the course of a clinical trial. For instance, there are requirements for the registration of ongoing clinical trials of drugs on public registries and the disclosure of certain information pertaining to the trials as well as clinical trial results after completion. Sponsors must also make annual reports to FDA concerning the progress of their clinical trial programs as well as more frequent reports for certain serious adverse events. Sponsors must submit a protocol for each clinical trial, and any subsequent protocol amendments to FDA and the applicable IRBs. IRBs must also receive information concerning unanticipated problems involving risks to subjects. Investigators must further provide certain information to the clinical trial sponsors to allow the sponsors to make certain financial disclosures to the FDA. Moreover, under the 21st Century Cures Act, manufacturers or distributors of investigational drugs for the diagnosis, monitoring, or treatment of one or more serious diseases or conditions must have a publicly available policy concerning expanded access to investigational drugs.

Further, the manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and active pharmaceutical ingredients imported into the United States are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country as well as U.S. export requirements under the FDC Act.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, potency, and purity of the final product.

Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational drug product information is submitted to the FDA in the form of a NDA to request market approval for the product in specified indications.

New Drug Applications

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

In most cases, the NDA must be accompanied by a substantial user fee; there may be some instances in which the user fee is waived. The FDA will initially review the NDA for completeness before it accepts the NDA for filing. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. After the NDA submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. For new molecular entities, or NMEs, FDA has the goal of completing its review within ten months of the application's acceptance for filing. This, however, is just a goal, and the review time may take longer. For instance, the FDA can extend this review by three months to consider certain late-submitted information or information intended to clarify information already provided in the submission. Additionally, this review period may change as the PDUFA statute must be reauthorized by Congress by September 2022.

The FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP. The FDA may refer applications for novel drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. For drugs for which no active ingredient (including any ester or salt of active ingredients) has previously been approved by the FDA, the FDA must refer the drug to an advisory committee or provide in an action letter, a summary of the reasons why the FDA did not refer the product candidate to an advisory committee. Product candidates may also be referred to advisory committees for other reasons. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter indicates that the review cycle of the application is complete and the application is not ready for approval. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application, including additional clinical trials. If a complete response letter is issued, the applicant may either: resubmit the NDA, addressing all of the deficiencies identified in the letter; withdraw the application; or request an opportunity for a hearing. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs, including the imposition of user fees for certain supplements.

Advertising and Promotion

The FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. A product cannot be commercially promoted before it is approved. After approval, product promotion can include only those claims relating to safety and effectiveness that are consistent with the labeling approved by the FDA. Healthcare providers are permitted to prescribe drugs for "off-label" uses — that is, uses not approved by the FDA and therefore not described in the drug's labeling — because the FDA does not regulate the practice of medicine. However, FDA regulations impose stringent restrictions on manufacturers' communications regarding off-label uses. Broadly speaking, a manufacturer may not promote a drug for off-label use, but may engage in non-promotional, balanced communication regarding off-label use under specified conditions. Failure to comply with applicable FDA requirements and restrictions in this area may subject a company to adverse publicity and enforcement action by the FDA, the Department of Justice (the "DOJ"), or the Office of the Inspector General of the Department of Health and Human Services ("HHS"), as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

Post-Approval Regulations

After regulatory approval of a drug is obtained, a company is required to comply with a number of post-approval requirements. For example, as a condition of approval of an NDA, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug. In addition, as a holder of an approved NDA, a company would be required to report adverse reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling for any of its products. Further, under the Drug Quality and Security Act, manufacturers have obligations concerning the tracking and tracing of drug products, as well as the investigation and reporting of suspect and illegitimate products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval to assure and preserve the long-term stability of the drug product. Manufacturing facilities must be registered with FDA and marketed drug products must be listed. Sponsors are also subject to annual program fees, though there may be some exemptions. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural and substantive record keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon a company and any third-party manufacturers that a company may decide to use.

Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing.

Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures, such as risk evaluation and mitigation strategies and phase 4 studies. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development or result in additional post-approval requirements.

After a product is approved for commercial sale, in addition to marketing and promotion restrictions, manufacturers are subject to federal and state laws and regulations requiring them to report certain pricing data, transactions with medical professionals, and similar information. Manufacturers participating in federal health care programs are also required to provide statutorily mandated discounts and rebates.

FDA post-approval requirements are continually evolving. For example, in March 2020, the U.S. Congress passed the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, which includes various provisions regarding FDA drug shortage and manufacturing volume reporting requirements, as well as provisions regarding supply chain security, such as risk management plan requirements, and the promotion of supply chain redundancy and domestic manufacturing. As part of the CARES Act implementation, the FDA recently issued a guidance on the reporting of the volume of drugs produced, which reporting will require additional administrative efforts by drug manufacturers.

The Hatch-Waxman Amendments to the FDC Act

Orange Book Listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant's product or method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA or 505(b)(2) application. In an effort to clarify which patents must be listed in the Orange Book, in January 2021, Congress passed the Orange Book Transparency Act of 2020, which largely codifies FDA's existing practices into the FDCA.

An ANDA provides for marketing of a generic drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug. 505(b)(2) applications provide for marketing of a drug product that may have the same active ingredients as the listed drug and contain the same full safety and effectiveness data as an NDA, but at least some of the information comes from studies not conducted by or for the applicant. 505(b)(2) applicants may rely on published literature or FDA's prior finding of safety and effectiveness for an NDA approved drug product. The ANDA or 505(b)(2) applicant is required to certify to the FDA concerning any patents listed for the approved product referenced in the marketing application in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired;

(iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA or 505(b)(2) applicant may also elect to submit a statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge or carve out the listed patents, the ANDA or 505(b)(2) application approval will not be made effective until all the listed patents claiming the referenced product have expired.

A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from making an approval of the ANDA or 505(b)(2) application effective until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA or 505(b)(2) applicant, or such shorter or longer period as may be determined by a court.

The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity has expired.

Recently, Congress, the Administration, and administrative agencies have taken certain measures to increase drug competition and thus, decrease drug prices. For example, measures have been proposed and implemented to facilitate product importation. Congress also passed a bill requiring sponsors of NDA approved products to provide sufficient quantities of drug product on commercially reasonable market-based terms to entities developing generic and similar drug products. This bill also included provisions on shared and individual REMS for generic drug products.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot receive any ANDA or a 505(b)(2) application for the same active moiety. Certain changes to a drug, such as the addition of a new indication to the package insert, may be associated with a three-year period of exclusivity during which the FDA cannot approve an ANDA for a generic drug or a 505(b)(2) application that includes the change, if the applicant conducted clinical trials essential to the approval of the application, which are not bioavailability or bioequivalence studies. Such exclusivity in the EU under a broadly equivalent regime is ten years.

An ANDA or a 505(b)(2) application may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five year patent extension of a single unexpired patent, that has not previously been extended. The allowable patent term extension is calculated as half of the drug's testing phase — the time between IND application and NDA submission — and all of the review phase — the time between NDA submission and approval up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years from the date of approval. Similar extension rules apply in the EU.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act ("FCPA"), prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and

fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Europe and Other International Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Some countries outside of the United States have a similar process that requires the submission of a clinical trial application, or CTA, much like the IND prior to the commencement of human clinical trials. In Europe, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee (IEC), much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed. With the Clinical Trials Regulation (EC) 536/2014 in force since January 31, 2022, it is now possible to make a single application for a cross-border trial within the EU through an EU clinical trial portal. With the departure of the United Kingdom ("UK") from the EU, trials in the UK have to be approved through the portal and a separate application will need to be made to the UK Medicines and Healthcare products Regulatory Agency. Additionally, in the EU there is an increasing move to transparency of trial summary reports and the above Clinical Trial Regulation will include a publicly accessible database of data and information submitted in accordance with this regulation. Companies' submitting data will need to justify why it should be kept confidential.

To obtain regulatory approval to commercialize a new drug under European Union regulatory systems, we must submit a marketing authorization application, or MAA. The MAA is comparable to the NDA.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Expanded Access

Under certain circumstances, regulators may permit unapproved drugs to be used by patients outside of clinical trials. In the U.S., with FDA approval, manufacturers may provide investigational drugs to patients with serious or immediately life threatening diseases for which there are no comparable or satisfactory alternative therapies. To qualify for U.S. expanded access, the potential benefit must justify the potential risks and the potential risks must not be unreasonable. Providing the investigational drug must also not interfere with product development. There are additional qualifying criteria depending on the number of patients in the expanded access program, and the expanded access sponsor and investigator must comply with FDA's regulations. U.S. law also permits treatment access to certain investigational drugs under the federal Right to Try law, which permits manufacturers to provide investigational drugs to patients with a life-threatening disease or condition, who have exhausted all approved treatment options, who cannot participate in a clinical trial of the drug, and who provides informed consent. Certain reports must be submitted to FDA under the federal Right to Try. There are also state level Right to Try statutes.

In the European Union, early access programs are authorized by EU legislation and, through national laws, EU member states have implemented regulatory requirements related to these programs. National competent authorities may authorize early access program use. In both the EU and U.S. unapproved drug products may not be promoted or marketed.

Compliance

During all phases of development (pre- and post-marketing), failure to comply with applicable regulatory requirements may result in administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an institutional review board, or IRB, of a hold on clinical trials, refusal to approve pending marketing applications or supplements, withdrawal of approval, warning letters, untitled letters, cyber letters, product recalls, product seizures or

detention, prohibition on importing or exporting, total or partial suspension of production or distribution, injunctions, fines, civil penalties, adverse publicity, disgorgement, restitution, FDA debarment, debarment from government contracting or refusal of future orders under existing contracts, exclusion from Federal healthcare programs, corporate integrity agreements, consent decrees, or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

Other Special Regulatory Procedures

Orphan Drug Designation

The FDA may grant Orphan Drug Designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or, if the disease or condition affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the drug would be recovered from sales in the United States. Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain orphan designation if there is a product already approved by the FDA that is intended for the same indication and that is considered by the FDA to be the same as the already approved product. This hypothesis must be demonstrated to obtain orphan exclusivity. In the European Union, the EMA's Committee for Orphan Medicinal Products, or COMP, grants Orphan Drug Designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug.

In the United States, Orphan Drug Designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs for certain kinds of studies, tax credits for certain research and user fee waivers under certain circumstances. Under the 21st Century Cures Act, Congress expanded the potential opportunities for grant funding to include additional kinds of studies. The 2017 Tax Cuts and Jobs Act, however, reduced the available tax credits for orphan products. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to seven years of market exclusivity, which means the FDA may not approve any other application for the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition.

In the European Union, Orphan Drug Designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following drug approval. This period may be reduced to six years if the Orphan Drug Designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity or where the holder of the marketing authorization for the original orphan medicinal product is unable to supply sufficient quantities of the medicinal product. As with the FDA, orphan drug exclusivity does not prevent the EMA from approving a second medicinal product where such the second medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior.

Orphan drug designation must be requested before submission of an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of the regulatory review and approval process.

Priority Review (United States), Accelerated Review (European Union) and other Expedited Programs

The FDA has various programs, including Fast Track designation, accelerated approval, priority review and breakthrough designation, that are intended to expedite or simplify the process for the development and FDA review of certain drug products that are intended for the treatment of serious or life threatening diseases or conditions, and demonstrate the potential to address unmet medical needs or present a significant improvement over existing therapy.

The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a Fast Track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if the product will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy, safety, or public health factors. If Fast Track designation is obtained, drug sponsors may be eligible for more frequent development meetings and correspondence with the FDA. In addition, the FDA may initiate review of sections of an NDA before the application is complete. This "rolling review" is available if the applicant provides and the FDA approves a schedule for the remaining information.

Based on results of one or more Phase 3 clinical trials submitted in an NDA, upon the request of an applicant, a priority review designation may be granted to a product by the FDA, which sets the target date for FDA action on the application at six months from FDA filing, or eight months from the sponsor's submission. Priority review is given to drugs intended to treat serious conditions and which, if approved would provide significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of the serious condition. If criteria are not met for priority review, the standard FDA review period is ten months from FDA filing, or 12 months from sponsor submission. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Moreover, under the provisions of the Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are eligible for the Fast Track designation features as described above, intensive guidance on an efficient drug development program beginning as early as Phase 1 trials, and a commitment from the FDA to involve senior managers and experienced review staff in a proactive collaborative, cross-disciplinary review.

In addition, products for treating serious or life threatening conditions and that provide a meaningful advantage over available therapies may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, FDA will require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoints. The drug may be subject to accelerated withdrawal procedures if such studies do not verify the product's clinical benefit or other evidence shows a lack of safety or efficacy. Promotional materials for products approved via the accelerated approval pathway must be submitted to FDA prior to initial distribution. Such products may also be subject to distribution or use restrictions, if FDA determines that restrictions are needed to assure safe use. Moreover, in recent years, the accelerated approval pathway has come under significant FDA and public scrutiny. Accordingly, depending on the results of our studies, FDA may be more conservative in granting accelerated approval or, if granted, may be more apt to withdrawal approval if clinical benefit is not confirmed.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Under the Centralized Procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the EMA's Committee for Medicinal Products of Human Use, or CHMP). On average, an approval is provided by the European Commission after approximately 15 months.

Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, defined by three cumulative criteria: the seriousness of the disease (e.g., heavy disabling or life-threatening diseases) to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days. There is also a conditional marketing authorization which allows for the early approval of a medicine on the basis of less complete clinical data than normally required, if the medicine addresses an unmet medical need and targets a seriously debilitating or life-threatening disease, a rare disease or is intended for use in emergency situations in response to a public health threat. The benefit to public health must outweigh the risk due to the limited availability of clinical data at the time of marketing authorization.

The EMA has recently been conducting a pilot on 'adaptive pathways' — an iterative process building on existing regulatory processes involving gathering evidence through real-life use to supplement clinical trial data.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, NDAs or certain supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

Also, under the FDA Reauthorization Act of 2017, sponsors submitting applications for product candidates intended for the treatment of adult cancer which are directed at molecular targets that the FDA determines to be substantially relevant to the growth or progression of pediatric cancer must submit, with the application, reports from molecularly targeted pediatric cancer investigations designed to yield clinically meaningful pediatric study data, using appropriate formulations, to inform potential pediatric labeling. The FDA may grant full or partial waivers, or deferrals, for submission of data under PREA and this requirement.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity — Orange Book listed patent or non-patent exclusivity — for a drug if certain conditions are met. Conditions for exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the required timeframe. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. This is not a patent term extension, but it effectively extends the regulatory exclusivity period. Moreover, pediatric exclusivity attaches to all formulations, dosage forms, and indications for products with existing marketing exclusivity or Orange Book listed patent life that contain the same active moiety as that which was studied. Applications under the BPCA for labeling changes receive priority review designation, with all of the benefits that designation confers.

In the European Union all applications for marketing authorization for new medicines have to include the results of studies as described in an agreed pediatric investigation plan, unless the medicine receives a deferral or waiver. Medicines authorized across the EU with the results of studies from a pediatric investigation plan included in the product information are eligible for an extension of their supplementary protection certificate by six months. This is the case even when the studies' results are negative. For orphan medicines, the incentive is an additional two years of market exclusivity.

Healthcare Reform

Enacted in 2010, the President of the United States signed into law the Patient Protection and Affordable Care Act, which we refer to collectively as the Affordable Care Act. The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Affordable Care Act is a sweeping law intended to broaden access to health insurance, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes

and fees on the healthcare industry, and impose additional health policy reforms, all intended to reduce or constrain the growth of healthcare spending.

Among the Affordable Care Act's provisions of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively;

- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- new requirements for applicable manufacturers to report annually specified financial arrangements with physicians, other healthcare professionals and teaching hospitals, as defined in the Affordable Care Act and its implementing regulations, including reporting any "payments or transfers of value" made or distributed to U.S.-licensed physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse midwives, certified registered nurse anesthetists and US teaching hospitals and reporting any ownership and investment interests held by physicians or their immediate family members during the preceding calendar year, with data collection required beginning August 1, 2013 and reporting to the Centers for Medicare and Medicaid Services required by March 31, 2014 and by the 90th day of each subsequent calendar year;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and

- a mandatory nondeductible payment for employers with 50 or more full time employees (or equivalents) who fail to provide certain minimum health insurance coverage for such employees and their dependents, beginning in 2015 (pursuant to relief enacted by the Treasury Department).

There have also been changes to Medicare and Medicaid regulations applicable to pharmaceutical manufacturers. For example, in 2016, CMS finalized a comprehensive rule implementing Affordable Care Act changes to the Medicaid Drug Rebate Program.

In addition, other legislative changes have been adopted since the Affordable Care Act was enacted. For example, under the Budget Control Act of 2011, providers are subject to Medicare payment reductions of 2% per fiscal year, which went into effect on April 1, 2013. While President Biden previously signed legislation to eliminate this reduction through the end of 2021, recent legislation will restart the reductions, which will thereafter remain in effect through 2031 unless additional Congressional action is taken. Such new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. The Bipartisan Budget Act of 2018, effective January 1, 2019, increased manufacturer liability for Medicare Part D covered prescriptions in the period of the coverage gap from 50 percent to 70 percent. The Affordable Care Act was amended by the Tax Cuts and Jobs Act of 2017 to repeal the individual penalty for not purchasing health insurance, and the Affordable Care Act may be further repealed and replaced by Congress. Changes in the law may result in additional downward pressure on coverage and the price that we receive for any approved product, or may require increased manufacturer rebates, and could seriously harm our business.

Pricing, Coverage and Reimbursement

The government is increasingly focused on measures to contain program costs for prescription drugs. Specifically, there have been recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, penalize companies that do not agree to cap prices paid for certain drugs, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. On November 27, 2020, CMS issued an interim final rule implementing a Most Favored Nation payment model under which reimbursement for certain Medicare Part B drugs and biologicals will be based on a price that reflects the lowest per capita Gross Domestic Product-adjusted (GDP-adjusted) price of any non-U.S. member country of the Organisation for Economic Co-operation and Development (OECD) with a GDP per capita that is at least sixty percent of the U.S. GDP per capita. This rule now has been rescinded, but similar programs have been included in current proposed legislation. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. Various state health care programs similarly require reporting of drug pricing information that is used as the basis for their reimbursement of pharmacies and other health care providers and the negotiation of supplemental rebates. Several states, such as California, have also enacted transparency laws that require manufacturers to report price increases and related information, and cap price increases, or require negotiation of supplemental rebates for new drugs entering the market at price points determined to be high. Refusal to negotiate supplemental rebates can negatively affect market access and provider reimbursement. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition, and results of operations.

In the US, many independent third-party payers, as well as the Medicare and state Medicaid programs, reimburse buyers of pharmaceutical products. Medicare is the federal program that provides health care benefits to senior citizens and certain disabled and chronically ill persons. Medicaid is the federal program administered by the states to provide health care benefits to certain indigent persons. In return for including our pharmaceutical commercial products in the Medicare and Medicaid programs, we may need to agree to calculate and report certain price points to the Centers for Medicare and Medicaid Services, and pay a rebate to state Medicaid agencies that provide reimbursement for those products products in an outpatient setting. We will also have to agree to sell our commercial products under contracts with the Department of Veterans Affairs, Department of Defense, Public Health Service, and Indian Health Service, as well as certain hospitals, community health centers, clinics, and other providers that are designated as 340B covered entities (entities designated by federal programs to receive mandatory drug discounts under the 340B program) at prices that are significantly below the price we may charge to commercial pharmaceutical distributors. These programs and contracts are highly regulated and may impose restrictions on our business, including ceiling prices and penalties for price increases that exceed the rate of inflation. These and any additional healthcare reform measures could further constrain our business or limit the amounts that federal and state governments will pay for healthcare products and services, which could result in additional pricing pressures. Failure to comply with these regulations and restrictions could result in a loss of our ability to continue selling our drugs to the federal government or receiving reimbursement for our drugs once approved.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for dug products will allow favorable reimbursement and pricing arrangements of our products.

Other Healthcare Laws and Compliance Requirements

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable in whole or in part under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting some business arrangements from prosecution, the exemptions and safe harbors are drawn narrowly and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. With respect to the safe harbors, HHS recently promulgated a regulation that is effective in two phases. First, the regulation excludes from the definition of “remuneration” limited categories of (a) PBM rebates or other reductions in price to a plan sponsor under Medicare Part D or a Medicaid Managed Care Organization plan reflected in point-of sale reductions in price and (b) PBM service fees. Second, effective January 1, 2023, the regulation expressly provides that rebates to plan sponsors under Medicare Part D either directly to the plan sponsor under Medicare Part D, or indirectly through a pharmacy benefit manager will not be protected under the anti-kickback discount safe harbor. Recent legislation delayed implementation of the second portion of the rule until January 1, 2026, and further proposed legislation would permanently prohibit implementation of the rule beginning in 2026. Our practices may not in all cases meet all of the criteria for safe harbor protection from federal Anti-Kickback Statute liability. The reach of the Anti-Kickback Statute was broadened by the Affordable Care Act, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a per se false or fraudulent claim for purposes of the civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal healthcare 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.

The federal civil False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government or avoiding, decreasing, or concealing an obligation to pay money to the federal government. A claim includes “any request or demand” for money or property presented to the U.S. government. The civil False Claims Act authorizes imposition of treble damages and a civil penalty for each false claim submitted, which, for pharmaceutical products, have frequently resulted in multi-million dollar penalties. Claims under the civil False Claims Act may be brought by the government or private parties on behalf of the government, called “qui tam” actions, which may proceed even if the government does not join as a party.

The civil False Claims Act has been used to assert liability on the basis of kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare provider or supplier numbers when detailing a provider of services, improper promotion of off-label uses not

expressly approved by the FDA in a product's label, and allegations as to misrepresentations with respect to products, contract requirements, and services rendered. In addition, private payers have been filing follow-on lawsuits alleging fraudulent misrepresentation, although establishing liability and damages in these cases is more difficult than under the FCA. Intent to deceive is not required to establish liability under the civil False Claims Act. Rather, a claim may be false for deliberate ignorance of the truth or falsity of the information provided or for acts in reckless disregard of the truth or falsity of that information. If the government decides to intervene in a qui tam action and prevails in the lawsuit, the individual will share in the proceeds from any damages, penalties or settlement funds. If the government declines to intervene, the individual may pursue the case alone. The civil FCA provides for treble damages and a civil penalty for each false claim, such as an invoice or pharmacy claim for reimbursement, which can aggregate into tens and even hundreds of millions of dollars. For these reasons, since 2004, False Claims Act lawsuits against biopharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements, as much as $3.0 billion, regarding certain sales practices and promoting off label uses. Civil False Claims Act liability may further be imposed for known Medicare or Medicaid overpayments, for example, overpayments caused by understated rebate amounts, that are not refunded within 60 days of discovering the overpayment, even if the overpayment was not caused by a false or fraudulent act.

HIPAA created new federal criminal statutes that prohibits, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. The Affordable Care Act amended the intent requirement of certain of these criminal statutes under HIPAA so that a person or entity no longer needs to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation. Further, the government may prosecute conduct constituting a false claim under the criminal False Claims Act. The criminal False Claims Act prohibits the making or presenting of a claim to the government knowing such claim to be false, fictitious, or fraudulent and, unlike the civil False Claims Act, requires proof of intent to submit a false claim. Also, many states have fraud and abuse statutes or regulations that are similar to the federal Anti-Kickback Statute and False Claims Act that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

The Affordable Care Act further created new federal requirements for reporting, by applicable manufacturers of covered drugs, of information related to payments and other transfers of value made to or at the request of covered recipients, such as, but not limited to, physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse midwives and certified registered nurse anesthetists and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family. Payments made to physicians and certain research institutions for clinical trials are included within the ambit of this law.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. The Health Insurance Portability and Accountability Act ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health ("HITECH") Act, and its implementing regulations, imposes requirements relating to the privacy, security, breach notification, and transmission of individually identifiable health information, known as protected health information. Among other things, the HITECH Act makes HIPAA's security and certain privacy standards directly applicable to "business associates" — persons or organizations, other than a member of a covered entity's workforce, that create, receive, maintain, or transmit protected health information on behalf of a covered entity for a function or activity regulated by HIPAA. The HITECH Act also strengthened the civil and criminal penalties that may be imposed against covered entities, business associates and individuals, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. HIPAA also imposes requirements with respect to disclosures of protected health information for research purposes, such as clinical trials. In addition, state laws, such as the California Consumer Privacy Act, govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not be preempted by HIPAA. In 2023, new state privacy laws will become effective in California, Colorado and Virginia, further complicating privacy compliance efforts. In addition, more onerous foreign data privacy provisions may apply. For instance, the EU General Data Protection Regulation imposes stricter rules on the processing of personal

data than apply in the USA and its provisions exclude the export of data relating to identifiable individuals to most countries, including the US, unless certain safeguards are in place.

In the United States, our activities are potentially subject to additional regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of HHS (e.g., the Office of Inspector General), the DOJ and individual U.S. Attorney offices within the DOJ, and state and local governments. If a drug product is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 as well as the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, or the OBRA, and the Veterans Health Care Act of 1992, each as amended. Among other things, the OBRA requires drug manufacturers to calculate and report complex pricing metrics used to determine rebates paid on prescription drugs to state Medicaid programs. Under the Veterans Health Care Act, or VHCA, drug companies are required to offer "covered drugs" (including all drugs approved under an NDA) at no more than a statutory ceiling price, calculated based on a manufacturer's required price calculations, to four federal agencies including the U.S. Department of Veterans Affairs and DoD, the Public Health Service. Also under the VHCA, manufacturers are required to offer drugs for sale at no more than a separate statutory ceiling price calculated by the manufacturer to Public Health Service designated entities in order to participate in other federal funding programs including Medicaid. Legislation subsequent to the VHCA has required that certain discounted prices under the VHCA also be offered for specified DoD purchases for its TRICARE program via a rebate system. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulation.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, private "qui tam" actions brought by individual whistleblowers in the name of the government, suspension or debarment prohibiting us from participating in federal procurement and non-procurement transactions, including government contracts, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in some states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Several states have enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/ or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing specified physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit other specified sales and marketing practices. Additionally, some states have enacted laws that cap increases in prices charged for drugs in that state. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

In Europe, most countries have laws or (more commonly) codes of practice which broadly emulate US 'sunshine laws' and require companies to maintain and publish a record of transfers of value to healthcare professionals. These are in addition to national anti-corruption laws similar to the FCPA — for instance the UK Bribery Act 2010 which has a wider scope than the FCPA in many respects including in that it covers relevant decision makers in both the private and public sectors and applies both domestically and internationally.

Human Capital

We believe that our success is largely dependent upon our ability to attract and retain qualified employees. As of December 31, 2021, we had 15 employees (14 of which were full-time employees), in addition to several consultants or independent contractors working for us. We are not party to any collective bargaining arrangements and consider our relations with our employees to be good. Although we believe that the size of our current workforce is appropriate to achieve our objectives, we may hire additional employees with specialized expertise as we continue to grow our business. We believe that we have been successful to date in attracting skilled and experienced scientific and business professionals.

Corporate Information

We were incorporated in Delaware in December 1998. Our principal executive offices are located at 12 Penns Trail, Newtown, PA 18940 and our telephone number is (267) 759-3680. Our website address is www.onconova.com. The information contained in, or that can be accessed through, our website is not part of this report.

ITEM 1A. *RISK FACTORS*

You should carefully consider the following risk factors together with the other information contained in this Annual Report, including our financial statements and the related notes appearing in this report. We cannot assure you that any of the events discussed in the risk factors below will not occur. If any of the following risks actually occur, they may materially harm our business and our financial condition and results of operations. In this event, the market price of our securities could decline and your investment could be lost. You should understand that it is not possible to predict or identify all such risks. Consequently, you should not consider the following to be a complete discussion of all potential risks or uncertainties.

Risks Related to Our Business and Industry

Our product development efforts may not be successful.

The focus of our development efforts is currently on narazaciclib and oral rigosertib. Although, we believe that there are opportunities for us to develop narazaciclib, our novel multi kinase inhibitor targeting CDK4/6 as well as other tyrosine kinases, in indications such as metastatic breast cancer, mantle cell lymphoma and multiple myeloma, and oral rigosertib in RAS mutated cancers, clinical drug development is expensive, can take many years to complete, and its outcome is inherently uncertain. Even if our clinical development programs are successful, we may not be able to successfully commercialize any product. There can be no assurance that our focus on narazaciclib and oral rigosertib will be successful, and that we will be able to successfully develop a product candidate or, even if we do, that we will be able to successfully commercialize such candidate.

Our future success is dependent primarily on the regulatory approval and commercialization of our product candidates.

Before obtaining regulatory approvals for the commercial sale of any product candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical and well-controlled clinical studies and, with respect to approval in the United States, to the satisfaction of the FDA, that the product candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate. If we are unable to obtain regulatory approval for our product candidates in one or more jurisdictions, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development of our product candidates.

The results of preclinical testing or earlier clinical studies are not necessarily predictive of future results. Any product candidate we advance into clinical trials may not have favorable results in later-stage clinical trials or receive regulatory approval.

Encouraging results in preclinical testing and earlier clinical studies do not ensure that later clinical trials will generate adequate data to demonstrate the efficacy and safety of an investigational drug. Additionally, mechanisms of action, studies in small or single patient populations, and interim study results may not be predictive of later stage studies. The development of a product for one indication may further impact its development for other indications. By example, our phase III study of intravenous rigosertib for HR MDS did not meet its primary endpoints. It is possible that this may impact how regulators or others view the development of rigosertib for alternative indications. If later-stage clinical trials do not produce favorable results, our ability to achieve regulatory approval for any of our product candidates may be adversely impacted.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome.

We may experience delays in our ongoing or future clinical trials and we do not know whether planned clinical trials will begin or enroll subjects on time, need to be redesigned or be completed on schedule, if at all. Regulatory authorities may also find that our development programs do not support product approval. There can be no assurance that the FDA, an IRB, or a comparable foreign regulatory authority will permit our clinical trials to commence and will not put clinical trials of any of our product candidates on clinical hold in the future. Study results may also cause us to discontinue trials. Clinical trials may be delayed, suspended or prematurely terminated and development programs may not be successful for a variety of reasons, including:

- delay or failure in reaching identifying, contracting with, and retaining contract research organizations, or CROs, and clinical trial sites;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial and/or retaining subjects;
- failure to follow the study procedures or applicable regulatory requirements;
- negative or ambiguous study results;
- manufacturing or product quality issues;
- the need to conduct additional development work, including clinical trials;
- changes in governmental laws, regulations, policies, or administrative actions; and
- regulatory authority disagreements regarding the design or implementation of our clinical trials.

If we experience delays in the completion or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. In addition, many of the factors that could cause a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

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

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authority.

As a result of undesirable side effects or safety or toxicity issues that we may experience in our clinical trials, we may not receive approval to market any product candidates, which could prevent us from ever generating revenues or achieving profitability. Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development or deny approval of our product candidates for any or all targeted indications. These side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. They could also result in restrictive labeling for any approved products.

Failure to follow FDA's applicable regulatory requirements may result in enforcement action.

If we or our third party contractors are not able to follow FDA's regulatory requirements, we or they may face enforcement actions that may materially harm our business, including, but not limited to:

- warning letters or untitled letters or otherwise unacceptable inspectional findings;
- injunctions, penalties, fines, or debarment;
- suspension any ongoing clinical studies, clinical holds, or regulatory authority refusal to approve marketing applications;
- restrictions on operations, product seizure or detention, refusal to permit the import or export of products, or product recalls; or
- adverse publicity.

Changes in product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates are developed through preclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. During the course of a development program, sponsors may also change the contract manufacturers used to produce the product candidates. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of clinical trials. Such changes may also require additional testing, FDA notification, or FDA approval. This could delay completion of clinical trials; require the conduct of bridging clinical trials or studies, or the repetition of one or more clinical trials; increase clinical trial costs; delay approval of our product candidates; and jeopardize our ability to commence product sales and generate revenue.

Healthcare legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

The regulations that govern, among other things, marketing approvals, coverage, pricing and reimbursement for new drug products vary widely from country to country and our ability to commercialize any products will depend, in part, on the extent to which coverage and adequate reimbursement for our products is available. In the United States and some foreign jurisdictions, including the European Union, there have been a number of legislative and regulatory

changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities, limit coverage and reimbursement or restrict the prices we may charge including through payments of increased manufacturer rebates, and affect our ability to successfully sell any product candidates for which we obtain marketing approval. Furthermore, in the United States private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates. These and any additional healthcare reform measures in the United States, the European Union and other potentially significant markets could further constrain our business or limit the amounts that governments will pay for healthcare products and services, which could result in additional pricing pressures.

States, in the U.S., have also enacted laws requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, cap price increases, negotiate or pay increased supplemental rebates and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing specified physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit other specified sales and marketing practices.

Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we are able to generate from the sale of the product in that particular country. In the United States, Medicaid and other federal programs impose penalties for increasing prices over the rate of inflation, which can result in penny prices. Federal legislative proposals would create inflation penalties under certain federal government pricing programs that currently do not impose these penalties and alter the caps on the magnitude of inflation penalties paid under these programs. Some states such as California are also regulating price increases. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates even if our product candidates obtain marketing approval. We cannot be sure that timely coverage and adequate reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of coverage and reimbursement will be.

In the event that any of our partners fails to comply with applicable regulatory requirements, FDA or foreign regulatory authorities may not accept the data that they generate in furtherance of our marketing applications, and they or us could be subject to enforcement action. In addition, any decision by our partners to terminate these agreements could also damage our reputation and negatively impact our ability to obtain financing from other sources.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA, Centers for Medicare & Medicaid Services, or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, comply with FDA's laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of certain disease indications for which we are developing our product candidates. For example, large pharmaceutical companies such as Pfizer, Novartis, Eli Lilly successfully market commercialized CDK 4/6 inhibitors palbociclib, ribociclib and abemaciclib and have done so for a number of years. More recently, G1 Therapeutics secured FDA approval of the CDK 4/6 triaciclib for the prevention of myelosuppression following chemotherapy.

The approved CDK 4/6 inhibitor drugs palbociclib, ribociclib and abemaciclib are well established therapies or products and are widely accepted by physicians, patients and third-party payors. By the time narazaciclib possibly is approved in the future, insurers and other third-party payors may also encourage the use of generic products. This may make it difficult for us to achieve market acceptance at desired levels in a timely manner to ensure viability of our business.

More established companies may have a competitive advantage over us due to their greater size, cash flows and institutional experience. Compared to us, many of our competitors may have significantly greater financial, technical and human resources.

If we breach our license agreements or fail to negotiate new agreements pertaining to our product candidates, we could lose the ability to continue the development and potential commercialization of these product candidates.

If we fail to meet our obligations under our current license agreements or if we fail to negotiate future license agreements, our rights under the licenses could be terminated, and upon the effective date of such termination, our right to use the licensed technology would terminate. While we would expect to exercise all rights and remedies available to us, including attempting to cure any breach by us, and otherwise seek to preserve our rights under the patents and other technology licensed to us, we may not be able to do so in a timely manner, at an acceptable cost or at all. Any uncured, material breach under the license agreement could result in our loss of exclusive rights and may lead to a complete termination of our product development and any commercialization efforts for the applicable product candidates.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. Product liability claims may be brought against us by subjects enrolled in our clinical trials, and patients, healthcare providers or others using, administering or selling our products in third party studies, expanded access programs, or commercially, if we receive product approval. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, the clinical development and commercialization of our product candidates could be adversely affected or terminated and we could incur substantial liabilities.

We may engage in future business combinations or collaborations that could disrupt our business, cause dilution to our stockholders and harm our financial condition and operating results.

While we currently have no specific plans to acquire any other specific businesses, we may, in the future, make acquisitions of, or investments in, or otherwise engage in business combinations or collaborations with companies that we believe have products or capabilities that are a strategic or commercial fit with our current product candidates and business or otherwise offer opportunities for our company. In connection with these acquisitions or investments, we may: issue stock that would dilute our existing stockholders' percentage of ownership; incur debt and assume liabilities; and incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We may not be able to complete any future business combination or collaborations on favorable terms, if at all. If we do complete a business combination or collaboration, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future business combinations could pose numerous additional risks to our operations, including: problems integrating the businesses, products or technologies; increases to our expenses; the failure to discover undisclosed liabilities of an acquired asset or transaction partner; diversion of management's attention from their day-to-day responsibilities; and harm to our operating results or financial condition.

We may not be able to complete any collaboration or business combination or effectively integrate the operations, products or personnel gained through any such business combination.

We depend on information technology and computer systems to operate our business; our business and operations would suffer in the event of any failures or interruptions of our computer system, such as a data breach or cybersecurity incident.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. Cybersecurity attacks are evolving and include, but are not limited to, malicious software, attempts to gain unauthorized access to data and other electronic security breaches that could lead to disruptions in systems, misappropriation of our confidential or otherwise protected information, corruption of data. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability or damage to our reputation, and the further development of our product candidates could be delayed.

Likewise, data privacy or security breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients or other business partners may be exposed to unauthorized persons or to the public. There can be no assurance that our efforts, or the efforts of our partners and vendors, will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The ultimate impact on us, our significant suppliers and our general infrastructure of being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster.

The COVID-19 pandemic could adversely impact our business, including our clinical trials, drug manufacturing and nonclinical activities.

As the COVID-19 pandemic continues around the globe, we may experience disruptions that could severely impact our business, clinical trials, drug manufacturing and nonclinical activities. These potential disruptions may include but

are not limited to delays or difficulties in clinical site initiation and patient recruitment, patient withdrawals, postponement of planned clinical or preclinical studies, redirection of site resources from studies, study modification, suspension, or termination, the introduction of remote study procedures and modified informed consent procedures, study site changes, direct delivery of investigational products to patient homes requiring state licensing, study deviations or noncompliance, diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials, delays in receiving approval from local regulatory authorities to initiate our planned clinical trials, and changes or delays in site monitoring. The foregoing may require that we consult with relevant review and ethics committees, IRBs, and the FDA. The foregoing may also impact the integrity of our study data. The effects of the COVID-19 pandemic may also increase the need for clinical trial patient monitoring and regulatory reporting of adverse effects.

The COVID-19 pandemic may also impact our ability to obtain supplies of our product candidates or other materials that may be necessary for the conduct of our development program. If any of our suppliers are adversely impacted by the COVID-19 pandemic or the restrictions resulting from the outbreak, if they cannot obtain the necessary supplies, or if such third parties need to prioritize other products or customers over us, including under the Defense Production Act, we may experience delays or disruptions in our supply chain, which could have a material and adverse impact on our business. Third party manufacturers may also need to implement measures and changes, or deviate from typical requirements because of the COVID-19 pandemic that may otherwise adversely impact our supply chains or the quality of the resulting products or supplies. Depending on the change, we may need to obtain FDA pre-approval or otherwise provide FDA with a notification of the change.

The pandemic could further impact our ability to interact with the FDA or other regulatory authorities and obtain any necessary inspections. Due to the potential impact of the COVID-19 outbreak on clinical trials, drug development, and manufacturing, FDA issued a number of guidance documents concerning how sponsors and investigators may address these challenges. FDA has also issued guidance on the development of products to treat COVID-19. FDA's guidance is continually evolving.

The COVID-19 pandemic may also result in changes in laws and regulations. By example, in March 2020, the U.S. Congress passed the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, which includes various provisions regarding FDA drug shortage reporting requirements, as well as provisions regarding supply chain security, such as risk management plan requirements, and the promotion of supply chain redundancy and domestic manufacturing. This and any future changes in law may require that we change our internal processes and procedures to ensure continued compliance.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the COVID-19 may impact our business, including our drug manufacturing, nonclinical activities, clinical trials and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the pandemic, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

Our future success depends on our ability to retain our executive officers and to attract, retain and motivate qualified personnel.

We are highly dependent upon Steven Fruchtman, M.D., President and Chief Executive Officer, Mark Guerin, C.P.A., Chief Financial Officer, Abraham Oler, Head of Corporate Development and General Counsel, Mark Gelder, M.D., Chief Medical Officer, and our other executive officers. Although we have employment agreements with the persons named above, these agreements are at-will and do not prevent such persons from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant losses since our inception and anticipate that we will continue to incur losses in the future.

We are a clinical-stage biopharmaceutical company. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that a product candidate could fail to gain regulatory approval or become commercially viable. We do not have any products approved by regulatory authorities for marketing and have not generated any revenue from product sales to date, and we continue to incur significant research, development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in every reporting period since our inception in 1998. For the years ended December 31, 2021, and 2020, we reported net losses of $16.2 million and $25.2 million, respectively, and we had an accumulated deficit of $444.7 million at December 31, 2021.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. These losses may increase as we continue the research and development of, and seek regulatory approvals for, our product candidates, and potentially begin to commercialize any products that may achieve regulatory approval. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

We currently have no source of product revenue and may never become profitable.

To date, we have not generated any revenues from commercial product sales. Our ability to generate revenue from product sales and achieve profitability will depend upon our ability to successfully commercialize products, including any of our current product candidates, or other product candidates that we may in-license or acquire in the future. Even if we are able to successfully achieve regulatory approval for these product candidates, we do not know when any of these products will generate revenue from product sales for us, if at all.

In addition, because of the numerous risks and uncertainties associated with product development, including that our product candidates may not advance through development or achieve the endpoints of applicable clinical trials, we are unable to predict the timing or amount of increased expenses, or when or if we will be able to achieve or maintain profitability. Even if we are able to complete the development and regulatory process for any product candidates, we anticipate incurring significant costs associated with commercializing these products. Even if we are able to generate revenues from the sale of our products, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or suspend our operations.

We need to obtain additional funding to further develop our products in future clinical trials and through regulatory processes; if we are unable to meet our needs for additional funding in the future, we will be required to limit, scale back or cease operations.

Our ability to successfully raise sufficient additional capital, through future financings or through strategic and collaborative arrangements will be necessary to carry out all of our proposed future operating activities. We will need to obtain additional financing in the future in order to fully fund product candidates through the regulatory approval process.

Our future capital requirements will depend on many factors, which could result in variations from our projected operating and liquidity requirements. Additional funds may not be available when needed, or, if available, we may not be able to obtain such funds on terms acceptable to us. If adequate funds are unavailable, we may be required, among other things, to: delay, reduce the scope of or eliminate one or more of our research or development programs; license rights to technologies, product candidates or products at an earlier stage or for indications or territories than otherwise

would be desirable, or on terms that are less favorable to us than might otherwise be available; obtain funds through arrangements that may require us to relinquish rights to product candidates or products that we would otherwise seek to develop or commercialize by ourselves; or further reduce or cease operations.

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

Until we can generate substantial revenue from product sales, if ever, we expect to seek additional capital through a combination of private and public equity offerings, debt financings, strategic collaborations and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt financing, if available, may involve agreements that include restrictive covenants limiting our ability to take important actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic collaborations and alliances or licensing arrangements with third parties, which may include existing collaboration partners, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates or formulations that we would otherwise prefer to develop and market ourselves.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our preclinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We have relied upon and plan to continue to rely upon third-party CROs to monitor and manage data for our ongoing preclinical and clinical programs, as well as clinical trial sites for the conduct of our clinical trials. We rely on these parties for execution of our preclinical and clinical trials, and we control only some aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and sites does not relieve us of our regulatory responsibilities. We also rely on third parties to assist in conducting our preclinical studies in accordance with Good Laboratory Practices, or GLP, and the Animal Welfare Act requirements. We, our clinical trial sites, and our CROs are required to comply with federal regulations and current Good Clinical Practices, or GCP, which are international standards meant to protect the rights and health of patients that are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our sites or CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We or they may also face regulatory enforcement. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under cGMP requirements. Failure to comply with these regulations may require us to repeat preclinical and clinical trials, which would delay the regulatory approval process. We may also face liability and/or regulatory enforcement action should any of the third parties that we rely upon fail to comply with legal and/or regulatory requirements.

Our CROs and the employees at clinical sites are not our employees, and except for remedies available to us under our agreements with such CROs and sites, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, nonclinical and preclinical programs. If CROs or sites do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects

for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Because we have relied on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Though we carefully manage our relationships with our CROs and clinical trial sites, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If we lose our relationships with CROs, our drug development efforts could be delayed.

We rely on third-party vendors and CROs for preclinical studies and clinical trials related to our drug development efforts. Switching or adding additional CROs would involve additional cost and requires management time and focus. Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated. We may also terminate a CRO for a number of reasons. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. In addition, there is a natural transition period when a new CRO commences work and the new CRO may not provide the same type or level of services as the original provider. If any of our relationships with our third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms.

We have limited experience manufacturing our product candidates on a large clinical or commercial scale and have no manufacturing facility. We are dependent on third-party manufacturers for the manufacture of our product candidates for clinical trials as well as on third parties for our supply chain, and if we experience problems with any third parties, the manufacturing of our product candidates or products could be delayed.

We do not own or operate facilities for the manufacture of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. We currently rely on a single source contract manufacturing organization, or CMO, for the chemical manufacture of active pharmaceutical ingredient for each of our product candidates. To meet our projected needs for clinical supplies to support our activities through regulatory approval and commercial manufacturing, the CMOs with whom we currently work will need to increase the scale of production. We may need to identify additional CMOs for continued production of supply for our product candidates. In addition, regulatory authorities enforce cGMP through periodic inspections of active pharmaceutical ingredient, or API and drug product manufacturing sites, quality control contract laboratories and distribution centers. If we or our CMO fail to comply with applicable cGMP, the manufacturing data generated and subsequent API lots and drug product batches in our supply chain may be deemed unreliable. Clinical trials using the product candidate may also be deemed to be unreliable. As such, the FDA or comparable foreign regulatory authorities may require us to perform additional API and drug product manufacturing before continuing clinical trials or approving our marketing applications, may require us to conduct additional studies, and any such deficient product we supply to any collaboration partner may subject us to certain obligations under relevant agreements. We or our contractors may also face enforcement actions. We have not yet qualified alternate suppliers in the event the current CMOs we utilize are unable to scale production, or if we otherwise experience any problems with them. By example, our third party manufacturers may not be able to obtain sufficient quantities of any necessary supplies such as due to changing trade policies or supply shortages. Although alternative third-party suppliers with the necessary manufacturing and regulatory expertise and facilities exist, as we have experienced with respect to our existing CMOs, it could be expensive and take a significant amount of time to arrange for alternative suppliers. If we are unable to arrange for alternative third-party manufacturing sources, or to do so

on commercially reasonable terms or in a timely manner, we may not be able to complete development of our product candidates, or market or distribute them.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates or products ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control, including a failure to synthesize and manufacture our product candidates or any products we may eventually commercialize in accordance with our specifications, and the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or damaging to us. In addition, the FDA and other regulatory authorities require that our product candidates and any products that we may eventually commercialize be manufactured according to cGMP and similar foreign standards. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition, such failure could be the basis for the FDA to issue a warning letter, withdraw approvals for product candidates previously granted to us, or take other regulatory or legal action, including recall or seizure of outside supplies of the product candidate, total or partial suspension of production, suspension of ongoing clinical trials, refusal to approve pending applications or supplemental applications, detention or product, refusal to permit the import or export of products, injunction, or imposing civil and criminal penalties. The manufacturing facilities that we use must also be approved by FDA under a pre-approval inspection. If the facilities cannot pass these inspections, FDA will not approve our marketing application. These manufacturing facilities will further be subject to continuing regulatory oversight and inspection, and, thus, they must continue to expend time and resources to maintain regulatory compliance.

Risks Related to Our Intellectual Property

We could be required to incur significant expenses to perfect our intellectual property rights, and our intellectual property rights may be inadequate to protect our competitive position. If we are unable to protect our intellectual property rights, our competitive position could be harmed.

We depend on our ability to protect our proprietary technology. We rely on trade secret, patent, copyright and trademark laws, and confidentiality, licensing and other agreements with employees and third parties, all of which offer only limited protection. Our commercial success will depend in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. Where we have the right to do so under our license agreements, we seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. The patent positions of biotechnology and pharmaceutical companies generally are highly uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patents, including those patent rights licensed to us by third parties, are highly uncertain.

The steps we have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary information or infringement of our intellectual property rights, both inside and outside the United States. The rights already granted under any of our currently issued patents and those that may be granted under future issued patents may not provide us with the proprietary protection or competitive advantages we are seeking. If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficient, our competitors could develop and commercialize technology and products similar or superior to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

With respect to patent rights, we do not know whether any of the pending patent applications for any of our licensed compounds will result in the issuance of patents that protect our technology or products, or if any of our issued patents will effectively prevent others from commercializing competitive technologies and products. Our pending applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Further, the examination process may require us or our licensor to narrow the claims for our pending patent applications, which may limit the scope of patent protection that may be obtained if these

applications issue. Because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, issued patents that we own or have licensed from third parties may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the loss of patent protection, the narrowing of claims in such patents or the invalidity or unenforceability of such patents, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection for our technology and products. Protecting against the unauthorized use of our patented technology, trademarks and other intellectual property rights is expensive, difficult and may in some cases not be possible. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary in the future to enforce or defend our intellectual property rights, to protect our trade secrets or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. This can be expensive and time consuming. Many of our current and potential competitors have the ability to dedicate substantially greater resources to defend their intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources. In addition, in an infringement proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

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

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates, and to use our proprietary technologies without infringing the proprietary rights of third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and commercializing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, in any such proceeding or litigation, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees, including our senior management, were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have

used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer.

Risks Related to Ownership of Our Common Stock and Common Stock Warrants

If we are unable to maintain compliance with the continued listing requirements of the Nasdaq Capital Market, our Common Stock could be delisted, which could affect our Common Stock's market price and liquidity and reduce our ability to raise capital.

We are required to meet certain qualitative and financial tests to maintain the listing of our securities on the Nasdaq Capital Market. As of December 31, 2021, we were in compliance with the Nasdaq continued listing requirements; however, at certain times during 2021, 2020 and 2019 we were not in compliance with the Nasdaq continued listing requirements related to minimum bid price and at certain times during 2019 and 2018 we were not in compliance with the Nasdaq continued listing requirements related to minimum stockholders' equity.

There can be no assurance that we will be able to maintain compliance with the Nasdaq Capital Market listing criteria. If we are unable to maintain compliance with the continued listing requirements of the Nasdaq Capital Market, our common stock could be delisted, making it more difficult to buy or sell our securities and to obtain accurate quotations, and the price of our securities could suffer a material decline. Delisting could also impair our ability to raise capital.

Our share price and the liquidity of our stock may be volatile and result in substantial losses to our stockholders.

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition, the stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of these risks or any of a broad range of other risks could have a dramatic and material adverse impact on the market price of our common stock.

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

In the past companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our Tenth Amended and Restated Certificate of Incorporation, as amended, or Certificate of Incorporation, and Amended and Restated Bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management. These include provisions that will:

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (as of February 28, 2022, we had no shares of preferred stock issued and outstanding);

- provide that all vacancies on our board of directors, including as a result of newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;

- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;

- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;

- not provide for cumulative voting rights, thereby allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election; and

- provide that special meetings of our stockholders may be called only by the board of directors or by such person or persons requested by a majority of the board of directors to call such meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. Under Delaware law, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

ITEM 1B. ***UNRESOLVED STAFF COMMENTS***

None.

ITEM 2. ***PROPERTIES***

Our corporate headquarters is located in Newtown, Pennsylvania, where we lease short-term flexible office space. We believe that suitable additional or alternative space would be available on commercially reasonable terms if required in the future.

ITEM 3. ***LEGAL PROCEEDINGS***

We are not a party to any legal proceedings and we are not aware of any such proceedings contemplated by government authorities.

ITEM 4. ***MINE SAFETY DISCLOSURES***

Not applicable.

PART II

ITEM 5. *MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES*

Market Information

Our common stock is listed under the symbol "ONTX" on the Nasdaq Capital Market.

Stockholders

As of February 28, 2022, there were approximately 98 holders of record for shares of our common stock. This does not reflect beneficial stockholders who held their common stock in "street" or nominee name through brokerage firms.

Securities Authorized for Issuance Under Equity Compensation Plans

Information regarding securities authorized for issuance under the Company's equity compensation plans is contained in Part III, Item 11 of this Annual Report.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future.

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 and other financial information included elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" section of this Annual 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 clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer. We have proprietary targeted anti-cancer agents designed to disrupt specific cellular pathways that are important for cancer cell proliferation. We believe that the product candidates in our pipeline have the potential to be efficacious in a variety of cancers with unmet medical need. We have the following two clinical-stage programs: 1. narazaciclib (ON 123300), a multi-kinase inhibitor in solid tumors; and 2. rigosertib administered alone or in combination with PD-1 inhibitors for treatment of solid tumors. We are currently evaluating potential compounds for in-licensing opportunities.

We were incorporated in Delaware in December 1998 and commenced operations in January 1999. Our operations to date have included our organization and staffing, business planning, raising capital, in-licensing technology from research institutions, identifying potential product candidates, developing product candidates and building strategic alliances, as well as undertaking preclinical studies and clinical trials of our product candidates.

Since commencing operations, we have dedicated a significant portion of our resources to the development of our clinical-stage product candidates, particularly rigosertib. We incurred research and development expenses of $7.3 million and $16.9 million during the years ended December 31, 2021 and 2020, respectively. We anticipate that a significant portion of our operating expenses will continue to be related to research and development as we continue to advance narazaciclib and our other programs.

In January 2020, we closed on an offering of common stock. We issued 1,844,168 shares of common stock and net proceeds were approximately $9.0 million. Also, during 2020, common warrants were exercised for 3,057,560 shares of common stock and net proceeds were approximately $10.3 million.

In January 2021, we closed on an offering of common stock. We issued 1,303,408 shares of common stock and net proceeds were approximately $8.5 million. In February 2021, we closed on an offering of common stock. We issued 1,916,667 shares of common stock and net proceeds were approximately $26.7 million. In September 2021, we closed on an offering of common stock. We issued 5,000,000 shares of common stock and net proceeds were approximately $19.5 million.

Our net losses were $16.2 million and $25.2 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $444.7 million. We expect to incur significant expenses and operating losses for the foreseeable future as we continue the development and clinical trials of, and seek regulatory approval for, our product candidates, even if milestones under our license and collaboration agreements may be met.

As of December 31, 2021 we had $55.1 million in cash and cash equivalents.

Financial Overview

Revenue

During the years ended December 31, 2021 and 2020, our revenues were derived exclusively from activities conducted in accordance with our collaboration arrangement with SymBio.

We have not generated any revenue from commercial product sales. In the future, if any of our product candidates currently under development are approved for commercial sale in the United States or other territories where we have retained commercialization rights, we may generate revenue from product sales, or alternatively, we may choose to select a collaborator to commercialize our product candidates in these markets.

We are recognizing the $7.5 million upfront payment received in 2011 under the SymBio collaboration agreement as revenue on a straight-line basis through December 2037, reflecting our estimate of when we will complete our obligations under the agreement. For the years ended December 31, 2021 and 2020, we recognized revenues of $226,000 and $226,000, respectively, under the SymBio collaboration agreement. In addition, we recognized revenues of $0 and $5,000 for the years ended December 31, 2021 and 2020, respectively, related to the supply agreement.

Operating Expenses

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

	2021	2020
General and administrative	$ 9,425,000	$ 8,326,000
Research and development	7,297,000	16,898,000
Total operating expenses	$16,722,000	$25,224,000

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for executive and other administrative personnel, including stock-based compensation and travel expenses. Other general and administrative

expenses include facility-related costs, communication expenses, insurance, board of directors expenses and professional fees for legal, patent review, consulting and accounting services.

We anticipate that our general and administrative expenses will remain consistent in the short-term, but would increase in the future with the continued research and development and potential commercialization of our product candidates. These increases will likely include increased costs for insurance, costs related to the hiring of additional personnel and payments to outside consultants among other expenses. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and expense as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

Research and Development Expenses

Our research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- expenses incurred under agreements with CROs and investigative sites that conduct our clinical trials and preclinical studies;
- the cost of acquiring, developing and manufacturing clinical trial materials;
- direct expenses for maintenance of research equipment, clinical trial insurance and other supplies; and
- costs associated with preclinical activities and regulatory operations.

Research and development costs are expensed as incurred. License fees and milestone payments we make related to in-licensed products and technology are expensed if it is determined that they have no alternative future use. We record costs for some development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

Through the year ended December 31, 2020, our research and development expenses related primarily to the development of rigosertib and the related INSPIRE trial in HR-MDS patients. The INSPIRE trial failed to meet its primary endpoint and was discontinued in August 2020. For 2021 and in the future, research and development expenses will be related to narazaciclib, other candidates in our pipeline, and potentially in-licensed products. We do not currently utilize a formal time allocation system to capture expenses on a project-by-project basis because we are organized and record expense by functional department and our employees may allocate time to more than one development project. Accordingly, we do not allocate expenses to individual projects or product candidates, although we do allocate some portion of our research and development expenses by functional area and by compound.

It is difficult to determine with certainty the duration and completion costs of our current or future preclinical programs and clinical trials of our product candidates, or if, when or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of future clinical and preclinical studies, uncertainties in clinical trial enrollment rate and significant and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. We will determine which programs to pursue and how

much to fund each program in response to the scientific and clinical success of each product candidate, an assessment of each product candidate's commercial potential and our available funds.

Interest Expense and Other Income, Net

Other income, net consists principally of interest income earned on cash and cash equivalent balances and foreign exchange gains and losses.

Critical Accounting Policies and Estimates

This management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

We believe the following accounting policies may involve a higher degree of judgment and complexity in their application than our other accounting policies and represent the most critical judgments and estimates used in the preparation of our consolidated financial statements. Our significant accounting policies are presented within Note 2 to our Financial Statements.

Clinical Trial Expense

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses. Our clinical trial accrual process is designed to account for expenses resulting from our obligations under contracts with vendors, consultants and CROs and clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts. Our objective is to reflect the appropriate clinical trial expenses in our consolidated financial statements by matching the appropriate expenses with the period in which services are provided and efforts are expended. We account for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. We determine accrual estimates through financial models that take into account discussion with applicable personnel and outside service providers as to the progress or state of completion of trials, or the services completed. During the course of a clinical trial, we adjust our clinical expense recognition if actual results differ from our estimates. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on the facts and circumstances known to us at that time. Our clinical trial accrual and prepaid assets are dependent, in part, upon the receipt of timely and accurate reporting from CROs and other third-party vendors. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low for any particular period.

Stock-Based Compensation

We account for stock-based payments to employees and non-employees using an option pricing model for estimating fair value. Accordingly, stock-based compensation expense is measured based on the estimated fair value of the awards on the date of grant, net of forfeitures. Compensation expense is recognized for the portion that is ultimately expected to vest over the period during which the recipient renders the required services, using the straight-line single option method.

We record stock-based compensation expense as a component of research and development expenses or general and administrative expenses, depending on the function performed by the optionee. For the years ended December 31, 2021 and 2020, we allocated stock-based compensation as follows:

	Year ended December 31,	
	2021	2020
General and administrative	$ 490,000	$ 160,000
Research and development	86,000	209,000
	$ 576,000	$ 369,000

Fair Value Estimates

We estimate the fair value of share-based awards to employees and non-employees using the Black-Scholes option pricing model. The Black-Scholes model requires the input of highly complex and subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of the expected term of the award, (c) the risk free interest rate and (d) expected dividends. Expected volatility is based on the historical volatility of the Company's common stock. We estimate the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the arithmetic average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted. We have never paid, and do not expect to pay dividends in the foreseeable future.

Income Taxes

We recorded deferred tax assets of $173.9 million as of December 31, 2021, which have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. The deferred tax assets are primarily composed of federal and state tax net operating loss ("NOL"), carry forwards and research and development tax credit carry forwards. As of December 31, 2021, we had federal NOL carry forwards of $293.7 million, state NOL carry forwards of $251.3 million, federal research and development tax credit carry forwards of $87.9 million and state research and development tax credit carry forwards of $1.1 million available to reduce future taxable income, if any. Federal NOL carry forwards generated before 2018 will begin to expire at various dates starting in 2022. The state NOL carry forwards will begin to expire at various dates starting in 2025. In general, if we experience a greater than 50 percentage point aggregate change in ownership of specified significant stockholders over a three-year period, utilization of our pre-change US NOL, tax credit and other tax attribute carry forwards may be subject to an annual limitations under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended (the "Code") and similar state laws. Such limitations may result in expiration of a portion of the NOL carry forwards before utilization and may be substantial. The amount of the annual limitation, if any, will be determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company believes such a change occurred and may impact available net operating losses and carry over research credits generated. The Company has not performed any detailed analysis as it expects these to expire before utilization and has provided for a full valuation allowance but will perform a Section 382 and 383 study if any tax attributes are to be utilized in a given year.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

	Year Ended December 31,		
	2021	2020	Change
Revenue	$ 226,000	$ 231,000	$ (5,000)
Operating expenses:			
General and administrative	9,425,000	8,326,000	(1,099,000)
Research and development	7,297,000	16,898,000	9,601,000
Total operating expenses	16,722,000	25,224,000	8,502,000
Loss from operations	(16,496,000)	(24,993,000)	8,497,000
Change in fair value of warrant liability	321,000	(208,000)	529,000
Other income, net	12,000	48,000	(36,000)
Net loss before income taxes	(16,163,000)	(25,153,000)	8,990,000
Income taxes	—	4,000	4,000
Net loss	$ (16,163,000)	$ (25,157,000)	$ 8,994,000

Revenues

Revenues decreased by $5,000 for the year ended December 31, 2021 when compared to the same period in 2020 due to lower clinical supply revenue from SymBio in 2021.

General and administrative expenses

General and administrative expenses increased by $1.1 million or 13.2%, to $9.4 million for the year ended December 31, 2021 from $8.3 million for the year ended December 31, 2020. The increase was attributable primarily to $1.5 million higher expenses for investor relations, proxy solicitation, and fees related to our special meeting by proxy in the 2021 period, to $0.3 million higher personnel related costs, to $0.3 million higher stock compensation expenses in the 2021 period, and to $0.2 million higher insurance costs. These increases were partially offset by $0.4 million lower professional and consulting fees, and $0.8 million lower commercial expenses during the 2021 period.

Research and development expenses

Research and development expenses decreased by $9.6 million, or 56.8%, to $7.3 million for the year ended December 31, 2021 from $16.9 million for the year ended December 31, 2020. This decrease was caused primarily by $6.9 million lower clinical development and consulting expenses on the INSPIRE program and the oral rigosertib combination program in the 2021 period, by $0.1 million lower manufacturing costs, and also by $2.6 million lower personnel and stock compensation expense during the 2021 period, following reductions in our workforce completed in the third and fourth quarter of 2020.

The details of our research and development expenses are:

	Year Ended December 31,	
	2021	2020
Preclinical & clinical development	$ 2,242,000	$ 7,948,000
Personnel related	1,955,000	4,444,000
Manufacturing, formulation & development	1,336,000	1,411,000
Stock based compensation	86,000	209,000
Consulting fees	1,678,000	2,886,000
	$ 7,297,000	$ 16,898,000

Change in fair value of warrant liability

The fair value of the warrant liability decreased $321,000 for the year ended December 31, 2021, compared to an increase of $208,000 for the year ended December 31, 2020. This change was caused by the elimination of the warrant liability during the third quarter of 2021 due to the expiration of the tradable warrants in July, 2021.

Other income, net

Other income, net, decreased by $36,000 for the year ended December 31, 2021 compared to the year ended December 31, 2020 due primarily to $45,000 lower foreign exchange expense and $81,000 lower net interest income in the 2020 period.

Liquidity and Capital Resources

Since our inception, we have incurred net losses and experienced negative cash flows from our operations. We incurred net losses of $16.2 million and $25.2 million for the year ended December 31, 2021 and 2020, respectively. Our operating activities used $19.5 million and $23.1 million of net cash during the year ended December 31, 2021 and 2020, respectively. At December 31, 2021, we had an accumulated deficit of $444.7 million, working capital of $49.3 million, and cash and cash equivalents of $55.1 million. We believe that our cash and cash equivalents will be sufficient to fund our ongoing trials and business operations for at least two years.

Cash Flows

The following table summarizes our cash flows for the year ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
Net cash (used in) provided by:		
Operating activities	$(19,487,000)	$(23,075,000)
Investing activities	—	(15,000)
Financing activities	55,560,000	19,357,000
Effect of foreign currency translation	(28,000)	32,000
Net increase (decrease) in cash and cash equivalents	$ 36,045,000	$ (3,701,000)

Net cash used in operating activities

Net cash used in operating activities was $19.5 million for the year ended December 31, 2021 and consisted primarily of a net loss of $16.2 million, including a favorable change in fair value of warrant liability of $0.3 million and $0.6 million of noncash stock-based compensation and depreciation expense. Changes in operating assets and liabilities resulted in a net decrease in cash of $3.6 million. Significant changes in operating assets and liabilities included a decrease in accounts payable and accrued liabilities of $3.9 million as a result of the timing of clinical trial and other accruals, and receipt and payment of vendor invoices, and the reduction of prepaid expenses of $0.5 million primarily as a result of recognition of insurance expense. Deferred revenue decreased $0.2 million due to recognition of the unamortized portion of the upfront payment under our collaboration agreement with SymBio.

Net cash used in operating activities was $23.1 million for the year ended December 31, 2020 and consisted primarily of a net loss of $25.2 million, including an unfavorable change in fair value of warrant liability of $0.2 million and $0.4 million of noncash stock-based compensation and depreciation expense. Changes in operating assets and liabilities resulted in a net increase in cash of $1.5 million. Significant changes in operating assets and liabilities included an increase in accounts payable and accrued liabilities of $1.7 million as a result of the timing of clinical trial and other accruals, and receipt and payment of vendor invoices. Deferred revenue decreased $0.2 million due to recognition of the unamortized portion of the upfront payment under our collaboration agreement with SymBio.

Net cash used in investing activities

Net cash used in investing activities was $0 in the 2021 period. Net cash used in investing activities was $15,000 in the 2020 period related to our purchase of information technology assets.

Net cash provided by financing activities

Net cash provided by financing activities for the year ended December 31, 2021 was $55.6 million, which resulted from the proceeds received from the sale of common stock in January, February, and September 2021 and through the at-the-market facility during August and September 2021. An additional $0.5 million was provided by the exercise of common stock warrants. Net cash provided by financing activities for the year ended December 31, 2020 was $19.4 million, which resulted from the proceeds received from the sale of common stock in January 2020 and the exercise of warrants.

Material Cash Requirements

We have not achieved profitability since our inception and we expect to continue to incur net losses for the foreseeable future. We expect net cash expended in 2022 to be slightly higher than 2021. We expect clinical trial costs to increase as we focus on our earlier clinical stage compound, narazaciclib, and increased headcount in our clinical and regulatory groups. We also expect an increase in costs for potential in-licensing, the timing of which will be determined by the timing of any potential in-licensing. We enter into contracts in the normal course of business with third-party contract organizations for clinical trials, preclinical studies, manufacturing and other services and products for operating purposes. These contracts generally provide for termination following a certain period after notice and therefore we believe that, currently, our non-cancelable obligations under these agreements are not material. We believe that our cash and cash equivalents will be sufficient to fund our ongoing trials and operations for at least two years.

We are exploring various sources of funding for continued development of narazaciclib and any potential in-licensed compounds as well as our ongoing operations. We expect to incur significant expenses and operating losses for the foreseeable future as we continue the development and clinical trials of, and seek regulatory approval for, our product candidates, even if milestones under our license and collaboration agreements may be met. If we obtain regulatory approval for any of our product candidates, we expect to incur significant NDA preparation and commercialization expenses. We do not currently have an organization for the sales, marketing and distribution of pharmaceutical products. We may rely on licensing and co-promotion agreements with strategic or collaborative partners for the commercialization of our products in the United States and other territories. If we choose to build a commercial infrastructure to support marketing in the United States for any of our product candidates that achieve regulatory approval, such commercial infrastructure could be expected to include a targeted, oncology sales force supported by sales management, internal sales support, an internal marketing group and distribution support. To develop the appropriate commercial infrastructure internally, we would have to invest financial and management resources, some of which would have to be deployed prior to having any certainty about marketing approval. Furthermore, we have and expect to continue to incur additional costs associated with operating as a public company.

Please see “Risk Factors” for additional risks associated with our substantial capital requirements.

Segment Reporting

We view our operations and manage our business in one segment, which is the identification and development of oncology therapeutics.

Recent Accounting Pronouncements

In June 2016, the FASB issued new guidance on the accounting for credit losses on financial instruments. The guidance was amended in November 2019. The new guidance introduces an expected loss model for estimating credit losses, replacing the incurred loss model. The new guidance also changes the impairment model for available-for-sale debt securities, requiring the use of an allowance to record estimated credit losses (and subsequent recoveries). The

guidance is effective for fiscal years beginning after December 15, 2022, and interim periods within those years, for companies deemed to be smaller reporting companies as of November 15, 2019, with early adoption permitted. We are evaluating the impact of the adoption of the standard on our consolidated financial statements.

ITEM 7A. ***QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK***

As a smaller reporting company, the Company is not required to provide the information otherwise required by this Item.

ITEM 8. ***FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA***

The financial statements and supplementary data required by this item are listed in Item 15 — "Exhibits and Financial Statement Schedules" of this Annual Report.

ITEM 9. ***CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE***

None.

ITEM 9A. ***CONTROLS AND PROCEDURES***

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our President and Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal financial officer), evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2021. Based upon this evaluation, our principal executive officer and principal financial officer concluded that, as of such date, disclosure controls and procedures were effective.

Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control — Integrated Framework issued in 2013. Based upon the assessments, management has concluded that as of December 31, 2021 our internal control over financial reporting was effective to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with GAAP.

This Annual Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to exemptions provided to issuers that are non-accelerated filers or qualify as an "emerging growth company," as defined in Section 2(a) of the Securities Act of 1933, or the Securities Act, as modified by the JOBS Act.

Changes in Internal Control Over Financial Reporting

There has been no change in our internal control over financial reporting during the fiscal quarter ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. ***OTHER INFORMATION***

None.

ITEM 9C. ***DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS***

Not applicable.

PART III

ITEM 10. ***DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE***

Information with respect to this item will be set forth in the Proxy Statement for the 2022 Annual Meeting of Stockholders (the "Proxy Statement") under the headings "Election of Directors," "Executive Officers," "Section 16(a) Beneficial Ownership Reporting Compliance," "Code of Ethics" and "Corporate Governance" and is incorporated herein by reference.

ITEM 11. ***EXECUTIVE COMPENSATION***

Information with respect to this item will be set forth in the Proxy Statement under the headings "Executive Compensation" and "Director Compensation," and is incorporated herein by reference.

ITEM 12. ***SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS***

Information with respect to this item will be set forth in the Proxy Statement under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Executive Compensation," and is incorporated herein by reference.

ITEM 13. ***CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE***

Information with respect to this item will be set forth in the Proxy Statement under the headings "Certain Relationships and Related Party Transactions" and "Corporate Governance" and is incorporated herein by reference.

ITEM 14. ***PRINCIPAL ACCOUNTING FEES AND SERVICES***

Information with respect to this item will be set forth in the Proxy Statement under the heading "Ratification of the Selection of Independent Registered Public Accounting Firm," and is incorporated herein by reference.

PART IV

ITEM 15. ***EXHIBITS AND FINANCIAL STATEMENT SCHEDULES***

(a) (1) Financial Statements: See Index to Consolidated Financial Statements on page F-1.

(3) Exhibits: See Exhibits Index on pages 55 to 59

ITEM 16. ***FORM 10-K SUMMARY***

Information with respect to this item is not required and has been omitted at the Company's option.

EXHIBITS INDEX

Exhibit Number	Exhibit Description
3.1	Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc. *(Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 25, 2013).*
3.2	Certificate of Amendment to Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc. (*Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on May 31, 2016*).
3.3	Certificate of Amendment to Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc., as amended (*Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on March 22, 2018*).
3.4	Certificate of Amendment to Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc., as amended (*Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on June 8, 2018*).
3.5	Certificate of Amendment to Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc., as amended *(Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on September 25, 2018).*
3.6	Certificate of Designation of Series A Convertible Preferred Stock (*Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on February 8, 2018*).
3.7	Certificate of Designation of Series B Convertible Preferred Stock (*Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on April 30, 2018*).
3.8	Certificate of Amendment to the Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc., as amended (*Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on May 20, 2021*).
3.9	Certificate of Amendment to the Tenth Amended and Restated Certificate of Incorporation of Onconova Therapeutics, Inc., as amended (*Incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed on May 20, 2021*).
3.10	Amended and Restated Bylaws of Onconova Therapeutics, Inc. *(Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on July 25, 2013).*
4.1	Form of Certificate of Common Stock *(Incorporated by reference to Exhibit 4.1 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013).*
4.2	Eighth Amended and Restated Stockholders' Agreement, effective as of July 27, 2012, by and among Onconova Therapeutics, Inc. and certain stockholders named therein *(Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on July 11, 2013).*
4.3	Amendment No. 1 to Eighth Amended and Restated Stockholders' Agreement, effective as of July 9, 2013 *(Incorporated by reference to Exhibit 4.2 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013).*
4.4	Form of Warrant Certificate, issued pursuant to Warrant Agreement, dated as of July 27, 2016, by and between Onconova Therapeutics, Inc. and Wells Fargo Bank, N.A., as Warrant Agent (*Incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q filed on August 15, 2016*).

Exhibit Number	Exhibit Description
4.5	Warrant Agreement, dated as of July 27, 2016, by and between Onconova Therapeutics, Inc. and Wells Fargo Bank, N.A., as Warrant Agent (*Incorporated by reference to Exhibit 4.2 to the Company's Quarterly Report on Form 10-Q filed on August 15, 2016*).
4.6	Form of Pre-Funded Warrants, issued as of July 27, 2016 (*Incorporated by reference to Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q filed on August 15, 2016*).
4.7	Form of Underwriter Warrant, issued as of February 12, 2018 (*Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on February 8, 2018*).
4.8	Form of Preferred Stock Warrant, issued as of February 12, 2018 (*Incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed on February 8, 2018*).
4.9	Form of Pre-Funded Warrant, issued as of February 12, 2018 (*Incorporated by reference to Exhibit 4.3 to the Company's Current Report on Form 8-K filed on February 8, 2018*).
4.10	Form of Preferred Stock Warrant, issued as of May 1, 2018 (*Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on April 30, 2018*).
4.11	Form of Pre-Funded Warrant, issued as of May 1, 2018 (*Incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed on April 30, 2018*).
4.12	First Amendment to Underwriter Series A Convertible Preferred Stock Purchase Warrant, dated as of September 24, 2018 (*Incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q filed on November 14, 2018*).
4.13	Form of Placement Agent Common Stock Purchase Warrant, issued as of September 25, 2019 (*Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on September 25, 2019*).
4.14	Form of Letter Amendment to Warrants, dated as of September 23, 2019 (*Incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q filed on November 12, 2019*).
4.15	Form of Common Stock Purchase Warrant, issued as of November 25, 2019 (*Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on November 26, 2019*).
4.16	Form of Pre-Funded Common Stock Warrant, issued as of November 25, 2019 (*Incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed on November 26, 2019*).
4.17	Form of Placement Agent Common Stock Purchase Warrant, issued as of November 25, 2019 (*Incorporated by reference to Exhibit 4.3 to the Company's Current Report on Form 8-K filed on November 26, 2019*).
4.18	Form of Common Stock Purchase Warrant, issued as of December 10, 2019 (*Incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed on December 10, 2019*).
4.19	Form of Placement Agent Common Stock Purchase Warrant, issued as of December 10, 2019 (*Incorporated by reference to Exhibit 4.2 of the Company's Current Report on Form 8-K filed on December 10, 2019*).
4.20	Form of Common Stock Purchase Warrant, issued as of December 2019 (*Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on December 19, 2019*).
4.21	Form of Placement Agent Common Stock Purchase Warrant, issued as of December 19, 2019 (*Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on December 19, 2019*).
4.21	Form of Placement Agent Common Stock Purchase Warrant, issued as of January 3, 2020 (*Incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed on January 3, 2020).*
4.22	Description of the Company's Securities Registered under Section 12 of the Securities Exchange Act of 1934, as amended (*Incorporated by reference to Exhibit 4.22 to the Company's Annual Report on Form 10-K filed on March 27, 2020).*
10.1*	License Agreement, effective as of July 5, 2011, by and between Onconova Therapeutics, Inc. and SymBio Pharmaceuticals Limited *(Incorporated by reference to Exhibit 10.2 to Pre-Effective Amendment No. 2 the Company's Registration Statement on Form S-1 filed on July 18, 2013).*
10.2*	First Amendment to License Agreement, effective as of September 2, 2011, by and between Onconova Therapeutics, Inc. and SymBio Pharmaceuticals Limited *(Incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).*
10.3*	License Agreement, effective as of January 1, 1999, by and between Onconova Therapeutics, Inc. and Temple University — Of The Commonwealth System of Higher Education *(Incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).*
10.4*	Amendment to License Agreement, effective as of September 1, 2000, by and between Temple University — Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc. *(Incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).*

Exhibit Number	Exhibit Description
10.5*	Amendment #1 to Exclusive License Agreement, effective as of March 21, 2013, by and between Temple University — Of The Commonwealth System of Higher Education and Onconova Therapeutics, Inc. *(Incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).*
10.6+	Onconova Therapeutics, Inc. 2007 Equity Compensation Plan, and forms of agreement thereunder *(Incorporated by reference to Exhibit 10.13 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013).*
10.7+	Consulting Agreement, effective as of January 1, 2012, by and between Onconova Therapeutics, Inc. and E. Premkumar Reddy, Ph.D., including Consultant Agreement Renewal, dated February 27, 2013 *(Incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 filed on June 14, 2013).*
10.8+	Form of Indemnification Agreement entered into by and between Onconova Therapeutics, Inc. and each director and executive officer *(Incorporated by reference to Exhibit 10.24 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013).*
10.9+	Onconova Therapeutics, Inc. 2013 Equity Compensation Plan, and forms of agreement thereunder *(Incorporated by reference to Exhibit 10.25 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013).*
10.10+	Onconova Therapeutics, Inc. 2013 Performance Bonus Plan *(Incorporated by reference to Exhibit 10.26 to Pre-Effective Amendment No. 1 the Company's Registration Statement on Form S-1 filed on July 11, 2013).*
10.11+	Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Mark Guerin *(Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on February 17, 2016).*
10.12+	Amended and Restated Employment Agreement, effective as of July 1, 2015, by and between Onconova Therapeutics, Inc. and Steven M. Fruchtman, M.D. *(Incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed on August 13, 2015).*
10.13*	License, Development and Commercialization Agreement, dated as of March 2, 2018, by and between Onconova Therapeutics, Inc. and Pint International SA (*Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on May 15, 2018*).
10.14	Securities Purchase Agreement, dated as of March 2, 2018, by and between Onconova Therapeutics, Inc. and Pint Pharma GmbH (*Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on May 15, 2018*).
10.15.1+	Amended and Restated Employment Agreement, effective as of June 19, 2018, by and between Onconova Therapeutics, Inc. and Steven M. Fruchtman, M.D. (*Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 14, 2018*).
10.15.2+	Amendment to Employment Agreement, dated as of March 18, 2021, by and between Onconova Therapeutics, Inc. and Steven M. Fruchtman, M.D.
10.16+	Onconova Therapeutics, Inc. 2018 Omnibus Incentive Compensation Plan, as approved by the stockholders (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on June 29, 2018*).
10.17+	Form of Nonqualified Stock Option Award Agreement under the Onconova Therapeutics, Inc. 2018 Omnibus Incentive Compensation Plan (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 30, 2018*).
10.18+	Employment Agreement, effective as of November 5, 2018, by and between Onconova Therapeutics, Inc. and Richard C. Woodman, M.D. (*Incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q filed on November 14, 2018*).
10.19	License and Collaboration Agreement, effective as of May 10, 2019, by and between Onconova Therapeutics, Inc. and HanX Biopharmaceuticals, Inc. (*Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 14, 2019*).
10.20	Securities Purchase Agreement, effective as of May 10, 2019, by and between Onconova Therapeutics, Inc. and HanX Biopharmaceuticals, Inc. (*Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 14, 2019*).
10.21	Securities Purchase Agreement, effective as of May 10, 2019, by and between Onconova Therapeutics, Inc. and Abundant New Investments Ltd. (*Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed on August 14, 2019*).

Exhibit Number	Exhibit Description
10.22	Form of Securities Purchase Agreement, effective as of September 23, 2019, by and between Onconova Therapeutics, Inc. and each purchase identified on the signature pages thereto (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on September 25, 2019*).
10.23**	Distribution, License and Supply Agreement, effective as of November 20, 2019, by and between Onconova Therapeutics, Inc. and Knight Therapeutics, Inc. (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 21, 2019*).
10.24	Form of Securities Purchase Agreement, effective as of November 21, 2019, by and between Onconova Therapeutics, Inc. and each purchaser identified on the signature pages thereto (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 26, 2019*).
10.25	Form of Securities Purchase Agreement, effective as of December 6, 2019, by and between Onconova Therapeutics, Inc. and each purchaser identified on the signature pages thereto (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 10, 2019*).
10.26**	Distribution, License and Supply Agreement, by and between Onconova Therapeutics, Inc. and Specialised Therapeutics Asia Pte. Ltd., effective as of December 18, 2019 (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 19, 2019*).
10.27	Form of Securities Purchase Agreement, by and between Onconova Therapeutics, Inc. and each purchaser identified on the signature pages thereto, effective as of December 17, 2019 (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on December 19, 2019*).
10.28	Form of Securities Purchase Agreement, by and between Onconova Therapeutics, Inc. and each purchaser identified on the signature pages thereto, effective as of December 31, 2019 (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 3, 2020).*
10.29+	Form of Stock Appreciation Right Award Agreement (for Employees) (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on July 10, 2020).*
10.30	Form of Purchase Agreement, dated as of January 7, 2021, by and among Onconova Therapeutics, Inc. and the investors party thereto (*Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on January 8, 2021).*
10.31	Underwriting Agreement, dated February 10, 2021, by and between Onconova Therapeutics, Inc. and Guggenheim Securities, LLC (*Incorporated by reference as Exhibit 1.1 to the Company's Current Report of Form 8-K filed on February 12, 2021*).
10.32+	Form of Stock Appreciation Right Award Agreement (for Non-Employee Directors) (*Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on November 16, 2020).*
10.33+	Form of Performance Stock Unit Award Agreement (*Incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed on July 10, 2020).*
10.34+	Employment Agreement, dated June 14, 2021, by and between Onconova Therapeutics, Inc. and Mark Stephen Gelder, M.D. *(Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on August 16, 2021*).
10.35+	Employment Agreement, dated March 9, 2021, by and between Onconova Therapeutics, Inc. and Abraham N. Oler *(Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on August 16, 2021*).
10.36	Equity Distribution Agreement, dated as of August 20, 2021, by and between Onconova Therapeutics, Inc. and Piper Sandler & Co. (*Incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed on August 20, 2021*).
10.37	Underwriting Agreement, dated September 23, 2021, by and between Onconova Therapeutics, Inc. and Guggenheim Securities, LLC (*Incorporated by reference as Exhibit 1.1 to the Company's Current Report of Form 8-K filed on September 24, 2021*).
10.38+	Form of Restricted Stock Unit Agreement *(Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 15, 2021*).
10.39+	Form of Non-Qualified Stock Option Agreement *(Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed on November 15, 2021*).
21.1	Subsidiaries of Onconova Therapeutics, Inc.
23.1	Consent of Ernst & Young, LLP.
31.1	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

Exhibit Number	Exhibit Description
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File – The cover page interactive data file does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document

+ Indicates management contract or compensatory plan.

* Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

** Portions of the exhibit have been omitted.

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.

Date: March 21, 2022

Onconova Therapeutics, Inc.

By: /s/ Steven M. Fruchtman, M.D.
Steven M. Fruchtman
Chief Executive Officer

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

Signature	Title	Date
/s/ Steven M. Fruchtman, M.D. Steven M. Fruchtman, M.D.	Director, President and Chief Executive Officer (Principal Executive Officer)	March 21, 2022
/s/ Mark Guerin Mark Guerin	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 21, 2022
/s/ James J. Marino James J. Marino	Chairman, Board of Directors	March 21, 2022
/s/ Jerome E. Groopman, M.D. Jerome E. Groopman, M.D.	Director	March 21, 2022
/s/ Viren Mehta, Ph.D. J Viren Mehta, Ph.D.	Director	March 21, 2022
/s/ Mary Teresa Shoemaker Mary Teresa Shoemaker	Director	March 21, 2022
/s/ Jack E. Stover Jack E. Stover	Director	March 21, 2022

ONCONOVA THERAPEUTICS, INC. AND SUBSIDIARIES

Index to Consolidated Financial Statements

All common stock, equity, share and per share amounts have been retroactively adjusted to reflect a one-for-fifteen reverse stock split which was effective May 20, 2021.

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Onconova Therapeutics, Inc.

Opinion on the Financial Statements

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

Basis for Opinion

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

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

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

Critical Audit Matter

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

Clinical Trial Expense Accruals

Description of the Matter	As described in Note 2 to the consolidated financial statements, the Company records accruals for estimated costs of research and development activities that include contract services for clinical trials. At December 31, 2021, the Company recorded accrued expenses for clinical trial accruals, which are included in accrued expenses and other current liabilities on the consolidated balance sheet. Clinical trial activities performed by third parties are accrued based upon estimates of the proportion of work completed over the life of the individual clinical trial in accordance with agreements established with contract research organizations, clinical trial sites and other third parties.

	Auditing management's clinical trial expense accruals is especially challenging because of the judgment applied by management to determine the progress or stage of completion of the activities under the Company's research and development agreements and the cost and extent of work performed during the reporting period for services not yet billed by contracted third-party vendors. The testing of the Company's accrued clinical trial expense models also involves a significant level of effort to test the high volume of data from third parties.
How We Addressed the Matter in Our Audit	To test the clinical trial expense accruals, our audit procedures included, among others, testing the completeness and accuracy of the underlying data used in the estimates and evaluating the significant assumptions including, but not limited to, expected patient enrollment, costs per patient/visit, and site activation, that are used by management to estimate the recorded accruals. To assess the reasonableness of the significant assumptions, we corroborated the progress of clinical trials with the Company’s clinical personnel. We also tested subsequent invoicing received from such third parties and inspected the Company’s contracts with third parties to assess the impact to the accrual through the balance sheet date and compared that to the Company’s estimates.

/s/ Ernst & Young LLP

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

Philadelphia, Pennsylvania

March 21, 2022

ONCONOVA THERAPEUTICS, INC.

Consolidated Balance Sheets

	December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 55,070,000	$ 19,025,000
Receivables	28,000	37,000
Prepaid expenses and other current assets	332,000	722,000
Total current assets	55,430,000	19,784,000
Property and equipment, net	38,000	52,000
Other non-current assets	10,000	150,000
Total assets	$ 55,478,000	$ 19,986,000
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,757,000	$ 4,833,000
Accrued expenses and other current liabilities	3,132,000	4,962,000
Deferred revenue	226,000	226,000
Total current liabilities	6,115,000	10,021,000
Warrant liability	—	321,000
Deferred revenue, non-current	3,243,000	3,469,000
Total liabilities	9,358,000	13,811,000
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.01 par value, 5,000,000 authorized at December 31, 2021 and December 31, 2020, none issued and outstanding at December 31, 2021 and December 31, 2020	—	—
Common stock, $0.01 par value, 125,000,000 and 250,000,000 authorized at December 31, 2021 and December 31, 2020, 20,895,563 and 12,396,219 shares issued and outstanding at December 31, 2021 and December 31, 2020	209,000	124,000
Additional paid in capital	490,644,000	434,593,000
Accumulated deficit	(444,719,000)	(428,556,000)
Accumulated other comprehensive (loss) income	(14,000)	14,000
Total stockholders' equity	46,120,000	6,175,000
Total liabilities and stockholders' equity	$ 55,478,000	$ 19,986,000

See accompanying notes to consolidated financial statements.

ONCONOVA THERAPEUTICS, INC.

Consolidated Statements of Operations

	Years ended December 31,	
	2021	2020
Revenue	$ 226,000	$ 231,000
Operating expenses:		
General and administrative	9,425,000	8,326,000
Research and development	7,297,000	16,898,000
Total operating expenses	16,722,000	25,224,000
Loss from operations	(16,496,000)	(24,993,000)
Change in fair value of warrant liability	321,000	(208,000)
Other income, net	12,000	48,000
Net loss before income taxes	(16,163,000)	(25,153,000)
Income tax expense	—	4,000
Net loss	(16,163,000)	(25,157,000)
Net loss per share, basic and diluted	$ (0.96)	$ (2.17)
Basic and diluted weighted average shares outstanding	16,832,198	11,602,391

See accompanying notes to consolidated financial statements.

ONCONOVA THERAPEUTICS, INC.

Consolidated Statements of Comprehensive Loss

	Years ended December 31,	
	2021	2020
Net loss	$ (16,163,000)	$ (25,157,000)
Other comprehensive (loss) income, net of tax:		
Foreign currency translation adjustments, net	(28,000)	32,000
Other comprehensive (loss) income, net of tax	(28,000)	32,000
Comprehensive loss	$ (16,191,000)	$ (25,125,000)

See accompanying notes to consolidated financial statements.

ONCONOVA THERAPEUTICS, INC.

Consolidated Statements of Stockholders' Equity

	Stockholders' Equity					
	Common Stock		Additional Paid in Capital	Accumulated deficit	Accumulated other comprehensive income (loss)	Total
	Shares	Amount				
Balance at December 31, 2019	7,411,157	$ 74,000	$ 414,917,000	$ (403,399,000)	$ (18,000)	$ 11,574,000
Net loss	—	—	—	(25,157,000)	—	(25,157,000)
Other comprehensive income	—	—	—	—	32,000	32,000
Stock-based compensation	—	—	369,000	—	—	369,000
Issuance of common stock, net	1,844,168	18,000	9,044,000	—	—	9,062,000
Issuance of common stock upon exercise of common warrants	3,057,560	31,000	10,263,000	—	—	10,294,000
Issuance of common stock upon exercise of pre-funded warrants	83,334	1,000	—	—	—	1,000
Balance at December 31, 2020	12,396,219	$ 124,000	$ 434,593,000	$ (428,556,000)	$ 14,000	$ 6,175,000
Net loss	—	—	—	(16,163,000)	—	(16,163,000)
Other comprehensive loss	—	—	—	—	(28,000)	(28,000)
Stock-based compensation	—	—	576,000	—	—	576,000
Exercise of stock options	4,642	—	24,000	—	—	24,000
Shares issued in connection with reverse stock split	104	—	—	—	—	—
Issuance of common stock, net	8,329,598	83,000	54,958,000	—	—	55,041,000
Issuance of common stock upon exercise of warrants	165,000	2,000	493,000	—	—	495,000
Balance at December 31, 2021	20,895,563	$ 209,000	$ 490,644,000	$ (444,719,000)	$ (14,000)	$ 46,120,000

See accompanying notes to consolidated financial statements.

ONCONOVA THERAPEUTICS, INC.

Consolidated Statements of Cash Flows

	Year Ended December 31,	
	2021	2020
Operating activities:		
Net loss	$ (16,163,000)	$ (25,157,000)
Adjustment to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	14,000	13,000
Change in fair value of warrant liabilities	(321,000)	208,000
Stock compensation expense	576,000	369,000
Changes in assets and liabilities:		
Receivables	9,000	61,000
Prepaid expenses and other current assets	530,000	(72,000)
Accounts payable	(2,076,000)	562,000
Accrued expenses and other current liabilities	(1,830,000)	1,167,000
Deferred revenue	(226,000)	(226,000)
Net cash used in operating activities	(19,487,000)	(23,075,000)
Investing activities:		
Payments for purchase of property and equipment	—	(15,000)
Net cash used in investing activities	—	(15,000)
Financing activities:		
Proceeds from the sale of common stock and warrants, net of costs	55,041,000	9,062,000
Proceeds from the exercise of common warrants	495,000	10,294,000
Proceeds from the exercise of pre-funded warrants	—	1,000
Proceeds from the exercise of stock options	24,000	—
Net cash provided by financing activities	55,560,000	19,357,000
Effect of foreign currency translation on cash	(28,000)	32,000
Net increase (decrease) in cash and cash equivalents	36,045,000	(3,701,000)
Cash and cash equivalents at beginning of period	19,025,000	22,726,000
Cash and cash equivalents at end of period	$ 55,070,000	$ 19,025,000

See accompanying notes to consolidated financial statements.

ONCONOVA THERAPEUTICS, INC.

Notes to Consolidated Financial Statements

1. Nature of Business

The Company

Onconova Therapeutics, Inc. (the "Company") was incorporated in the State of Delaware on December 22, 1998 and commenced operations on January 1, 1999. The Company's headquarters are located in Newtown, Pennsylvania. The Company is a clinical-stage biopharmaceutical company focused on discovering and developing novel products for patients with cancer. The Company has proprietary targeted anti-cancer agents designed to disrupt specific cellular pathways that are important for cancer cell proliferation. The Company believes that the product candidates in its pipeline have the potential to be efficacious in a variety of cancers with unmet medical need. The Company has the following two clinical-stage programs: 1. narazaciclib (ON 123300), a multi-kinase inhibitor in solid tumors; and 2. oral rigosertib alone or in combination with PD-1 inhibitors for treatment of KRAS-mutated solid tumors. During 2012, Onconova Europe GmbH was established as a wholly owned subsidiary of the Company for the purpose of further developing business in Europe.

On May 20, 2021, the Company amended its certificate of incorporation to effect a one-for-fifteen reverse stock split of its common stock. All common stock, equity, share and per share amounts in the financial statements and notes have been retroactively adjusted to reflect this one-for-fifteen reverse stock split.

On May 20, 2021, the Company amended its certificate of incorporation to decrease the number of authorized shares of common stock par value $0.01 per share from 250,000,000 to 125,000,000.

Liquidity

The Company has incurred recurring operating losses since inception. For the year ended December 31, 2021, the Company incurred a net loss of $16,163,000 and as of December 31, 2021 the Company had generated an accumulated deficit of $444,719,000. The Company anticipates operating losses to continue for the foreseeable future due to, among other things, costs related to research, development of its product candidates and its preclinical programs, strategic alliances and its administrative organization. At December 31, 2021, the Company had cash and cash equivalents of $55,070,000. The Company will require substantial additional financing to fund its ongoing clinical trials and operations, and to continue to execute its strategy.

On January 3, 2020, the Company closed on an offering of common stock. The Company issued 1,844,168 shares of common stock and net proceeds were approximately $9.0 million. In addition, during the year ended December 31, 2020 3,057,560 warrants were exercised, resulting in proceeds of $10.3 million.

On January 11, 2021, the Company closed on an offering of common stock. The Company issued 1,303,408 shares of common stock and net proceeds were approximately $8.5 million. On February 16, 2021, the Company closed on an offering of common stock. The Company issued 1,916,667 shares of common stock and net proceeds were approximately $26.7 million. On September 28, 2021, the Company closed on an offering of common stock. The Company issued 5,000,000 shares of common stock and net proceeds were approximately $19.5 million.

On August 20, 2021, the Company entered into an at-the-market equity distribution agreement for the sale of up to $25.0 million of common stock. Through September 30, 2021, the Company sold 109,523 shares under the agreement at a weighted average price of $5.32 per share. Net proceeds after commissions and offering expenses were approximately $0.5 million.

Following the unsuccessful conclusion of the INSPIRE trial, the Company took steps to reduce its cash expenditures. From September 2020 to December 2020, the Company implemented a workforce reduction of employees in research and development who were primarily focused on preparing the NDA for the use of rigosertib in higher risk

MDS. In total, 10 employees were terminated, representing approximately 43% of the Company's workforce at that time. A severance related charge of approximately $1,207,000, which includes a non-cash charge of approximately $29,000 related to the accelerated vesting of outstanding stock options, was recorded in the year ended December 31, 2020. The accrued severance balance was included in accrued expenses and other liabilities on the balance sheet. The accrued severance balance remaining at December 31, 2020 was $1,045,000 and was paid in periodic amounts through September 2021. On October 30, 2020, the Company notified its landlord of its intention to not renew its office space lease. The lease expired in February 2021 and was modified to a month-to-month lease for a portion of the space. The lease terminated in June 2021 and the Company has relocated to temporary office space with all employees working remotely.

The Company has and may continue to delay, scale-back, or eliminate certain of its research and development activities and other aspects of its operations until such time as the Company is successful in securing additional funding. The Company is exploring various dilutive and non-dilutive sources of funding, including equity financings, strategic alliances, business development and other sources. The future success of the Company is dependent upon its ability to obtain additional funding. There can be no assurance, however, that the Company will be successful in obtaining such funding in sufficient amounts, on terms acceptable to the Company, or at all. The Company believes that its cash and cash equivalents will be sufficient to fund its ongoing trials and business operations for more than twelve months from the date of this filing.

COVID-19

While the Company is not aware of a material impact from the novel coronavirus disease ("COVID-19") pandemic through December 31, 2021, the full extent to which COVID-19 will directly or indirectly impact the Company's business, results of operations and financial condition, including manufacturing, clinical trials and research and development costs, depends on future developments that are uncertain at this time.

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements are prepared in conformity with accounting principles generally accepted in the United States ("GAAP"). The financial statements include the consolidated accounts of the Company and its wholly-owned subsidiary, Onconova Europe GmbH. All significant intercompany transactions have been eliminated.

All common stock, equity, share and per share amounts have been retroactively adjusted to reflect a one-for-fifteen reverse stock split which was effective May 20, 2021.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one segment, which is the identification and development of oncology therapeutics.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses, other comprehensive income and related disclosures. On an ongoing basis, management evaluates its estimates, including estimates related to clinical trial accruals, warrant liability, and allocation of consideration for revenue recognition. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash and cash equivalents. The Company maintains a portion of its cash and cash equivalent balances in the form of money market accounts with financial institutions that management believes are creditworthy. The Company has no financial instruments with off-balance sheet risk of loss.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original or remaining maturity from the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents include bank demand deposits, marketable securities with maturities of three months or less at purchase, and money market funds that invest primarily in certificates of deposit, commercial paper and U.S. government and U.S. government agency obligations. Cash equivalents are reported at fair value.

Fair Value of Financial Instruments

The carrying amounts reported in the accompanying consolidated financial statements for cash and cash equivalents, accounts payable, and accrued liabilities approximate their respective fair values because of the short-term nature of these accounts. The fair value of the warrant liability is discussed in Note 8, “Fair Value Measurements.”

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets. Leasehold improvements are amortized over the useful life of the asset or the lease term, whichever is shorter. Maintenance and repairs are expensed as incurred. The following estimated useful lives were used to depreciate the Company’s assets:

	Estimated Useful Life
Lab equipment	5-6 years
Software	3 years
Computer and office equipment	5-6 years
Leasehold improvements	Shorter of the lease term or estimated useful life

Upon retirement or sale, the cost of the disposed asset and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is recognized.

The Company reviews long-lived assets for impairment when events or changes in circumstances indicate that the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the assets’ book value to future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceeds their fair value, which is measured based on the projected discounted future net cash flows generated from the assets. No impairment losses have been recorded through December 31, 2021.

Warrant Accounting

Common stock warrants are accounted for in accordance with applicable accounting guidance provided in ASC Topic 815, *Derivatives and Hedging—Contracts in Entity’s Own Equity* (ASC Topic 815), as either derivative liabilities or as equity instruments depending on the specific terms of the warrant agreement. (See Note 4).

The Company’s warrants that are classified as liabilities are recorded at fair value. The warrants are subject to remeasurement at each balance sheet date and any change in fair value is recognized as a component of change in fair value of warrant liability in the consolidated statements of operations. The Company has had both tradable and non-

tradable warrants. At December 31, 2020, the tradable warrants were classified as level 1 liabilities and the Company used the Nasdaq quoted market price to estimate the fair value of the related derivative warrant liability. The non-tradable warrants are classified as level 3 liabilities and the Company uses the Black-Scholes pricing model to estimate the fair value of the related derivative warrant liability. All of the tradable and non-tradable warrants that were classified as liabilities at December 31, 2020 expired in July 2021. (See Note 8 for a discussion of the fair value hierarchy).

Foreign Currency Translation

The reporting currency of the Company and its U.S. subsidiaries is the U.S. dollar. The functional currency of the Company's non-U.S. subsidiary is the local currency. Assets and liabilities of the foreign subsidiary are translated into U.S. dollars based on exchange rates at the end of the period. Revenues and expenses are translated at average exchange rates during the reporting period. Gains and losses arising from the translation of assets and liabilities are included as a component of accumulated other comprehensive income. Gains and losses resulting from foreign currency transactions are reflected within the Company's results of operations. The Company has not utilized any foreign currency hedging strategies to mitigate the effect of its foreign currency exposure.

Revenue Recognition

The Company recognizes revenue in accordance with Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* (ASC 606). The Company applies ASC 606 to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. In accordance with ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that it will collect the consideration it is entitled to in exchange for the goods and services it transfers to the customer. At contract inception, the Company assesses the goods or services promised within each contract that falls under the scope of ASC 606, determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company derives revenue from collaboration and licensing agreements and from the sale of products associated with material transfer, collaboration and supply agreements.

License, Collaboration and Other Revenues

The Company enters into licensing and collaboration agreements, under which it licenses certain of its product candidates' rights to third parties. The Company recognizes revenue related to these agreements in accordance with ASC 606. The terms of these arrangements typically include payment from third parties of one or more of the following: non-refundable, up-front license fees; development, regulatory and commercial milestone payments; and royalties on net sales of the licensed product.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligation under each of its agreements, the Company performs the five steps described above. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement of personnel costs, discount rates and probabilities of technical and regulatory success.

Licensing of Intellectual Property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is

able to use and benefit from the license. For licenses that are bundled with other performance obligations, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front-fees. The Company evaluates the measure of progress each reporting period, and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone Payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal will not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensees, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in their period of adjustment.

Manufacturing supply services. Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer's discretion are generally considered as options. The Company assesses if these options provide material rights to the licensee and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the customer exercises these options, any additional payments are recorded when the customer obtains control of the goods, which is upon shipment.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and for which the license is deemed to be the predominant item to which royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some of all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue from its license agreements.

Research and Development Expenses

Research and development costs are charged to expense as incurred. These costs include, but are not limited to, license fees related to the acquisition of in-licensed products; employee-related expenses, including salaries, benefits and travel; expenses incurred under agreements with contract research organizations and investigative sites that conduct clinical trials and preclinical studies; the cost of acquiring, developing and manufacturing clinical trial materials; facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies; and costs associated with preclinical activities and regulatory operations.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued research and development expense, as the case may be.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources.

Leases

The Company accounts for leases in accordance with Accounting Standards Codification Topic 842, *Leases* (ASC 842). The Company determines whether an arrangement is a lease at contract inception by establishing if the contract conveys the right to control the use of identified property, plant, or equipment for a period of time in exchange for consideration.

Right of Use (ROU) Assets and Lease Liabilities are recognized at the lease commencement date based on the present value of all minimum lease payments over the lease term. The Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of lease payments, when the implicit rate is not readily determinable. Lease terms may include options to extend or terminate the lease. These options are included in the lease term when it is reasonably certain that the Company will exercise that option. Operating lease expense is recognized on a straight-line basis over the lease term.

The Company has elected the following policy elections on adoption: use of portfolio approach on leases of assets under master service agreements, exclusion of short-term leases (term of 12 months or less) on the balance sheet, and not separating lease and non-lease components.

The Company does not have any material lease agreements.

Income Taxes

The Company accounts for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. The deferred tax asset primarily includes net operating loss and tax credit carry forwards, accrued expenses not currently deductible and the cumulative temporary differences related to certain research and patent costs, which have been charged to expense in the accompanying statements of operations but have been recorded as assets for income tax purposes. The portion of any deferred tax asset for which it is more likely than not that a tax benefit will not be realized must then be offset by recording a valuation allowance. A full valuation allowance has been established against all of the deferred tax assets (see Note 9, “Income Taxes”), as it is more likely than not that these assets will not be realized given the Company’s history of operating losses. The Company recognizes the tax benefit from an uncertain tax position only if it is more likely than not to be sustained upon examination based on the technical merits of the position. The amount for which an exposure exists is measured as the largest amount of benefit determined on a cumulative probability basis that the Company believes is more likely than not to be realized upon ultimate settlement of the position.

Stock-Based Compensation Expense

The Company applies the provisions of FASB Accounting Standards Codification (“ASC”) Topic 718, *Compensation—Stock Compensation* (“ASC 718”), which requires the measurement and recognition of compensation expense for all stock-based awards made to employees and non-employees, including employee stock options, stock appreciation rights performance stock units and restricted stock units.

Share-based payment transactions with employees are recognized as compensation expense over the requisite service period based on their estimated fair values. ASC 718 also requires significant judgment and the use of estimates, particularly surrounding Black-Scholes assumptions such as stock price volatility over the term and expected lives, to estimate the grant date fair value of equity-based compensation and requires the recognition of the fair value of stock compensation in the statement of operations.

Clinical Trial Expense Accruals

As part of the process of preparing its financial statements, the Company is required to estimate its expenses resulting from its obligations under contracts with vendors, clinical research organizations and consultants and under

clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company's objective is to reflect the appropriate trial expenses in its financial statements by matching those expenses with the period in which services are performed and efforts are expended. The Company accounts for these expenses according to the progress of the trial as measured by patient progression and the timing of various aspects of the trial. The Company determines accrual estimates through financial models taking into account discussion with applicable personnel and outside service providers as to the progress or state of consummation of trials, or the services completed. During the course of a clinical trial, the Company adjusts its clinical expense recognition if actual results differ from its estimates. The Company makes estimates of its accrued expenses as of each balance sheet date based on the facts and circumstances known to it at that time. The Company's clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in it reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2021 and 2020, there were no material adjustments to the Company's prior period estimates of accrued expenses for clinical trials.

Basic and Diluted Net Loss Per Share of Common Stock

Basic net loss per share of common stock is computed by dividing net loss applicable to common stockholders by the weighted-average number of shares of Common Stock outstanding during the period, excluding the dilutive effects of stock options and warrants. Diluted net loss per share of common stock is computed by dividing the net loss applicable to common stockholders by the sum of the weighted-average number of shares of Common Stock outstanding during the period plus the potential dilutive effects of stock options and warrants outstanding during the period calculated in accordance with the treasury stock method but are excluded if their effect is anti-dilutive. Because the impact of these items is anti-dilutive during periods of net loss, there was no difference between basic and diluted net loss per share of Common Stock for the years ended December 31, 2021 and 2020.

Recent Accounting Pronouncements

In June 2016, the FASB issued new guidance on the accounting for credit losses on financial instruments. The guidance was amended in November 2019. The new guidance introduces an expected loss model for estimating credit losses, replacing the incurred loss model. The new guidance also changes the impairment model for available-for-sale debt securities, requiring the use of an allowance to record estimated credit losses (and subsequent recoveries). The guidance is effective for fiscal years beginning after December 15, 2022, and interim periods within those years, for companies deemed to be smaller reporting companies as of November 15, 2019, with early adoption permitted. The guidance is not expected to have a material effect on the Company.

3. Property and Equipment

Property and equipment and related accumulated depreciation are as follows:

	December 31,	
	2021	2020
Computer and office equipment	$ 70,000	$ 70,000
Less accumulated depreciation	(32,000)	(18,000)
	$ 38,000	$ 52,000

Depreciation and amortization expense was $14,000 and $13,000 for the years ended December 31, 2021 and 2020, respectively. On October 30, 2020, the Company notified its landlord of its intention to not renew its office space lease which expired in February 2021. Most of the property and equipment was disposed of. This property and equipment was fully depreciated and there was no gain or loss on disposal.

4. Warrants

Common stock warrants are accounted for in accordance with applicable accounting guidance provided in ASC Topic 815, *Derivatives and Hedging-Contracts in Entity's Own Equity* (ASC Topic 815), as either derivative liabilities or as equity instruments depending on the specific terms of the warrant agreement. Some of the Company's warrants were classified as liabilities because in certain circumstances they could have required cash settlement.

Warrants outstanding at December 31, 2020 and 2021, and warrant activity for the year ended December 31, 2021 is as follows (reflects the number of common shares as if the warrants were converted to common stock):

Description	Classification	Exercise Price	Expiration Date	Balance December 31, 2020	Warrants Issued	Warrants Exercised	Warrants Expired	Balance December 31, 2021
Non-tradable warrants	Liability	$ 2,587.50	July 2021	430	—	—	(430)	—
Tradable warrants	Liability	$ 1,107.00	July 2021	14,187	—	—	(14,187)	—
Non-tradable pre-funded warrants	Equity	$ 2.25	July 2023	26	—	—	—	26
Non-tradable warrants	Equity	$ 24.00	December 2022	26,189	—	—	—	26,189
Non-tradable warrants	Equity	$ 211.50	March 2021	333	—	—	(333)	—
Non-tradable warrants	Equity	$ 317.25	March 2021	556	—	—	(556)	—
Non-tradable warrants	Equity	$ 116.8425	June 2021	1,000	—	—	(1,000)	—
Non-tradable pre-funded warrants	Equity	$ 2.25	none	3,522	—	—	—	3,522
Non-tradable warrants	Equity	$ 24.00	December 2022	120,407	—	—	—	120,407
Non-tradable pre-funded warrants	Equity	$ 2.25	none	4,974	—	—	—	4,974
Non-tradable warrants	Equity	$ 30.00	September 2023	7,306	—	—	—	7,306
Non-tradable warrants	Equity	$ 3.00	November 2024	409,500	—	(165,000)	—	244,500
Non-tradable warrants	Equity	$ 6.54375	December 2024	16,953	—	—	—	16,953
Non-tradable warrants	Equity	$ 6.75450	December 2024	46,263	—	—	—	46,263
Non-tradable warrants	Equity	$ 6.77850	December 2023	29,968	—	—	—	29,968
				681,614	—	(165,000)	(16,506)	500,108

5. Net Loss Per Share of Common Stock

The following table sets forth the computation of basic and diluted earnings per share for the years ended December 31, 2021 and 2020:

	Year ended December 31, 2021	2020
Basic and diluted net loss per share of common stock:		
Net loss attributable to Onconova Therapeutics, Inc.	$(16,163,000)	$(25,157,000)
Weighted average shares of common stock outstanding	16,832,198	11,602,391
Net loss per share of common stock—basic and diluted	$ (0.96)	$ (2.17)

The following potentially dilutive securities outstanding at December 31, 2021 and 2020 have been excluded from the computation of diluted weighted average shares outstanding, as they would be antidilutive (reflects the number of common shares as if the dilutive securities had been converted to common stock):

	December 31, 2021	2020
Warrants	491,586	673,092
Stock options	452,999	57,939
	944,585	731,031

6. Revenue

The Company recognized revenue under its license and collaboration agreement with SymBio as follows (See Note 14):

	Year ended December 31,	
	2021	2020
Symbio		
Upfront license fee recognition over time	$ 226,000	$ 226,000
Supplies	—	5,000
	$ 226,000	$ 231,000

Deferred revenue is as follows:

	Symbio Upfront Payment
Deferred balance at December 31, 2020	$ 3,695,000
Recognition to revenue	226,000
Deferred balance at December 31, 2021	$ 3,469,000

7. Balance Sheet Detail

Prepaid expenses and other current assets are as follows:

	December 31,	
	2021	2020
Research and development	$ 15,000	$ 189,000
Manufacturing	29,000	90,000
Insurance	253,000	263,000
Other	35,000	180,000
	$ 332,000	$ 722,000

Accrued expenses and other current liabilities are as follows:

	December 31,	
	2021	2020
Research and development	$ 1,759,000	$ 2,541,000
Employee compensation	1,217,000	2,239,000
Professional fees	156,000	182,000
	$ 3,132,000	$ 4,962,000

8. Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

The Company utilizes a valuation hierarchy for disclosure of the inputs to the valuations used to measure fair value. This hierarchy prioritizes the inputs into three broad levels as follows. Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities. Level 2 inputs are quoted prices for similar assets and liabilities in active markets or inputs that are observable for the asset or liability, either directly or indirectly through market corroboration, for substantially the full term of the financial instrument. Level 3 inputs are unobservable inputs based on the

Company's own assumptions used to measure assets and liabilities at fair value. A financial asset or liability's classification within the hierarchy is determined based on the lowest level input that is significant to the fair value measurement.

The following fair value hierarchy table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis as of December 31, 2021 and 2020:

	Fair Value Measurement as of:							
	December 31, 2021				December 31, 2020			
	Level 1	Level 2	Level 3	Balance	Level 1	Level 2	Level 3	Balance
Tradable warrants liability	$ —	$ —	$ —	$ —	$ 321,000	$ —	$ —	$ 321,000
Non-tradable warrants liability	—	—	—	—	—	—	—	—
Total	$ —	$ —	$ —	$ —	$ 321,000	$ —	$ —	$ 321,000

The tradable warrants were listed on the Nasdaq Capital Market. The Company determined that an active and orderly market for the tradable warrants developed and that the Nasdaq Capital Market price was the best indicator of fair value of the warrant liability. The quoted market price was used to determine the fair value at December 31, 2020. The fair value of the non-tradable warrants was estimated using the Black-Scholes pricing model at December 31, 2020. All of the tradable and non-tradable warrants that were classified as liabilities expired in July 2021. There were no transfers between Levels in any of the periods reported.

9. Income Taxes

The Company accounts for income taxes under FASB ASC 740 ("ASC 740"). Deferred income tax assets and liabilities are determined based upon differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

Income taxes have been based on the following income (loss) before income tax expense:

	December 31,	
	2021	2020
Domestic	$(16,153,000)	$(25,167,000)
Foreign	(10,000)	14,000
	$(16,163,000)	$(25,153,000)

The provision for income taxes consists of the following:

	December 31,	
	2021	2020
Current		
US Federal	$ —	$ —
State and Local	—	—
Foreign	—	4,000
Total Current	$ —	$ 4,000
Deferred		
US Federal	$ —	$ —
State and Local	—	—
Foreign	—	—
Total Deferred	$ —	$ —
Total (Benefit) Expense	$ —	$ 4,000

As of December 31, 2021, the Company had federal net operating loss ("NOL") carry forwards of $293,691,000, state NOL carry forwards of $251,285,000, federal research and development tax credit carry forwards of $87,870,000,

and state research and development tax credit carry forwards of $1,077,000, which may be available to reduce future taxable income. There are $210,499,000 of federal NOLs that were generated in tax periods prior to 2018 that will begin to expire at various dates starting in 2022 and ending in 2037. The NOLs that were generated in 2018 through 2021 of $83,192,000 will carry forward indefinitely and not expire pursuant to changes in tax laws but will be limited in a single tax year to 80 percent of federal taxable income. The state NOL carry forwards will begin to expire at various dates starting in 2025. The NOL carry forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carry forwards may become subject to an 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 of 1986, as amended, as well as similar state tax provisions. The Company believes such a change occurred and may impact available net operating losses and carry over research credits generated. The Company has not performed any detailed analysis as it expects these to expire before utilization and has provided for a full valuation allowance. The Company will complete a full Section 382 and 383 analysis prior to any utilization of any NOL and tax credit carry forwards. The amount of the annual limitation, if any, will be determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

The Company's reserves related to taxes are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized. The Company recognized no material adjustment for unrecognized income tax benefits. Through December 31, 2021, the Company had no unrecognized tax benefits or related interest and penalties accrued.

The principal components of the Company's deferred tax assets are as follows:

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryovers	$ 81,468,000	$ 76,631,000
R&D tax credits	88,721,000	87,529,000
Non-qualified stock options	2,194,000	2,448,000
Deferred revenue	1,002,000	1,068,000
Charitable contributions	4,000	4,000
Accrued expenses	447,000	647,000
Stock Appreciation Rights	19,000	19,000
Deferred tax assets	173,855,000	168,346,000
Deferred tax liabilities:		
Fixed Assets	(1,000)	(2,000)
Deferred tax liabilities	(1,000)	(2,000)
Less valuation allowance	(173,854,000)	(168,344,000)
Net deferred tax assets	$ —	$ —

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a full valuation allowance against its deferred tax assets at December 31, 2021. The Company experienced a net change in valuation allowance of $5,510,000 and $7,319,000 for the years ended December 31, 2021 and 2020, respectively.

A reconciliation of income tax (expense) benefit at the statutory federal income tax rate and income taxes as reflected in the financial statements is as follows:

	December 31,	
	2021	2020
Federal income tax expense at statutory rate	21.0 %	21.0 %
Permanent items	0.4	(0.2)
State income tax, net of federal benefit	8.0	7.8
Tax credits	7.4	11.0
Change in valuation allowance	(34.1)	(29.1)
Deferred tax adjustment	(2.6)	(10.5)
Other	(0.1)	(0.1)
Effective income tax rate	(0.0)%	(0.1)%

10. Stock-Based Compensation

The 2018 Omnibus Incentive Compensation Plan (the "2018 Plan") was unanimously approved by the Company's Board of Directors on May 24, 2018 and was approved by the Company's stockholders on June 27, 2018.

Under the 2018 Plan, the Company may grant incentive stock options, non-qualified stock options, stock awards, stock units, stock appreciation rights and other stock-based awards to employees, non-employee directors and consultants, and advisors. The maximum aggregate number of shares of the Company's common stock that may be issued under the 2018 Plan is 26,823.

The 2018 Plan was amended and restated following unanimous approval of the Company's Board of Directors on April 24, 2019 and was approved by the Company's shareholders on June 17, 2019. The amended 2018 Plan (the "Amended 2018 Plan") allowed for an additional 39,300 shares of the Company's common stock that may be issued under the Amended 2018 Plan with respect to awards made on and after June 17, 2019.

The 2021 Incentive Compensation Plan (the "2021 Plan") was unanimously approved by the Company's shareholders on July 30, 2021. Upon stockholders' approval of the 2021 Plan, no further awards will be made under the Amended 2018 Plan. Under the 2021 Plan, the Company may grant incentive stock options, non-qualified stock options, stock awards, stock units, stock appreciation rights and other stock-based awards to employees, non-employee directors and consultants, and advisors. The maximum aggregate number of shares of the Company's common stock that may be issued under the 2021 Plan is 1,300,000. At December 31, 2021, there were 902,101 shares available for future issuance.

Stock-based compensation expense includes stock options granted to employees and non-employees and has been reported in the Company's statements of operations and comprehensive loss in either research and development expenses or general and administrative expenses depending on the function performed by the optionee. No net tax benefits related to the stock-based compensation costs have been recognized since the Company's inception. The Company recognized stock-based compensation expense related to stock options and restricted stock units as follows for the years ended December 31, 2021 and 2020:

	Year ended December 31,	
	2021	2020
General and administrative	$ 490,000	$ 160,000
Research and development	86,000	209,000
	$ 576,000	$ 369,000

A summary of stock option activity for the twelve months ended December 31, 2021 is as follows:

		Options Outstanding			
	Shares Available for Grant	Number of Shares	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Balance, December 31, 2020	12,339	57,939	$ 368.10	8.38	$ —
Authorized	1,300,000	—			
Granted	(413,575)	413,575	$ 5.19	9.59	—
Exercised	—	(4,642)	$ 4.65	8.86	$ 21,636
Forfeitures	3,337	(13,873)	$ 949.54	6.60	
Balance, December 31, 2021	902,101	452,999	$ 20.71	9.42	$ —
Exercisable at December 31, 2021		24,261	$ 293.44	7.37	$ —

The Company accounts for all stock-based payments made to employees, non-employees and directors using an option pricing model for estimating fair value. Accordingly, stock-based compensation expense is measured based on the estimated fair value of the awards on the date of grant. Compensation expense is recognized for the portion that is ultimately expected to vest over the period during which the recipient renders the required services to the Company using the straight-line single option method.

The Company uses the Black-Scholes option-pricing model to estimate the fair value of stock options at the grant date. The Black-Scholes model requires the Company to make certain estimates and assumptions, including assumptions related to the expected price volatility of the Common Stock, the period during which the options will be outstanding, the rate of return on risk-free investments and the expected dividend yield for the Company's stock.

As of December 31, 2021, there was $1,597,000 of unrecognized compensation expense related to the unvested stock options which is expected to be recognized over a weighted-average period of approximately 2.22 years.

The weighted-average assumptions underlying the Black-Scholes calculation of grant date fair value include the following:

	Year ended December 31,	
	2021	2020
Risk-free interest rate	0.89 %	0.45 %
Expected volatility	133.77 %	105.14 %
Expected term	5.93 years	6.00 years
Expected dividend yield	0 %	0 %
Weighted average grant date fair value	$ 4.60	$ 0.25

The weighted-average valuation assumptions were determined as follows:

- Risk-free interest rate: The Company based the risk-free interest rate on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected option term.

- Expected term of options: Due to its lack of sufficient historical data, the Company estimates the expected life of its employee stock options using the "simplified" method, as prescribed in Staff Accounting Bulletin (SAB) No. 107, whereby the expected life equals the arithmetic average of the vesting term and the original contractual term of the option.

- Expected stock price volatility: Expected volatility is based on the historical volatility of the Company's Common Stock.

- Expected annual dividend yield: The Company has never paid, and does not expect to pay, dividends in the foreseeable future. Accordingly, the Company assumed an expected dividend yield of 0.0%.

On August 2, 2021, the compensation committee of the board of directors approved restricted stock unit grants to the Company's employees ("2021 RSU"). An aggregate of 104,700 service-based RSUs were issued at a grant date fair value of $5.19. The 2021 RSU awards will be settled in stock, vest 33% on each of the first and second anniversary of the date of grant, and vest 34% on the third anniversary of the date of grant. The 2021 RSU awards were granted under the 2021 Plan. There were no vesting events, expirations, forfeitures, or cancelations of the 2021 RSUs during the period. At December 31, 2021, the unrecognized compensation cost related to unvested service-based RSUs was $468,000, which will be recognized over the remaining service period. During the twelve months ended December 31, 2021, the Company recognized $75,000 of stock-based compensation expense related to the 2021 RSUs, which is included in additional paid-in capital.

Grants of PSUs and SARs

On July 9, 2020, the compensation committee of the board of directors and the board approved a cash bonus program of cash-settled stock appreciation right ("2020 SAR") awards and cash-settled performance stock unit ("2020 PSU") awards to the Company's employees. An aggregate of 2020 SAR awards with respect to 256,713 shares of common stock and 2020 PSU awards with respect to 124,220 shares of common stock were granted to the Company's employees. The 2020 SAR awards will be settled in cash, vest 33% on the first anniversary of the date of grant, and the remaining 67% monthly over the next 24 months, have a per-share base amount of $8.40, which was the closing sales price of a share of the Company's common stock on the grant date, and are in all cases subject to the terms and conditions of the Company's form of SAR award agreement. The 2020 SAR awards are cash-settled and were granted outside of the 2018 Plan and the 2021 Plan.

The 2020 PSU awards vest 50% upon the submission of a new drug application ("NDA") to the U.S. FDA for rigosertib in higher-risk myelodysplastic syndromes ("HR-MDS") and 50% upon U.S. FDA approval of rigosertib for HR-MDS. The 2020 PSU awards have a maximum value of $21.60 per share. The maximum price per share is the per-share value based on the Company's market capitalization at $250 million and the Company's outstanding shares of common stock, which was 11,611,829 shares on July 9, 2020. In all cases, the 2020 PSU awards are subject to the terms and conditions of the Company's form of PSU award agreement. The 2020 PSU awards are cash-settled and were granted outside of the 2018 Plan and the 2021 Plan.

In addition, on July 9, 2020, based on the recommendation of the compensation committee, the board approved a change in the non-employee director compensation policy that would provide for an annual SAR award ("2020 Director SAR") with respect to 8,333 shares of common stock for each of the Company's non-employee directors. No other changes to the non-employee director compensation policy were approved and, on July 9, 2020, the Board approved the initial 8,333 2020 Director SAR award to each of the non-employee directors for an aggregate total of 58,333 2020 Directors SAR awards granted. The 2020 Director SAR awards vest on the first anniversary of grant subject to the director's continued service and will be settled in cash, have a per-share base amount of $8.40, and are in all cases subject to the terms and conditions of the Company's form of 2020 Director SAR award agreement.

Each SAR subject to a 2020 SAR award represents the right to a cash payment equal to the excess, if any, of (i) the fair market value of each underlying share of the Company's common stock, determined on the date of exercise of the SAR minus (ii) the base amount. Pursuant to the terms of the SAR awards, in no event may the cash payment for each SAR exceed $13.20, which is the maximum price per share of $21.60, minus the base amount of $8.40, subject to adjustment in accordance with the terms of the Stock Appreciation Right Award Agreement. The maximum price per share is the per-share value based on the Company's market capitalization at $250 million and the Company's outstanding shares of common stock, which was 11,611,829 shares on July 9, 2020.

On February 17, 2021, the compensation committee of the board of directors and the board approved a cash bonus program of cash-settled stock appreciation right ("2021 SAR") awards and cash-settled performance stock unit ("2021 PSU") awards to the Company's employees. An aggregate of 2021 SAR awards with respect to 100,000 shares of common stock and 2021 PSU awards with respect to 100,000 shares of common stock were granted to the Company's

employees. The 2021 SAR awards will be settled in cash, vest 33% on the first anniversary of the date of grant, and the remaining 67% monthly over the next 24 months, have a per-share base amount of $22.65, which was the closing sales price of a share of the Company's common stock on the grant date, and are in all cases subject to the terms and conditions of the Company's form of SAR award agreement. Each SAR subject to a 2021 SAR award represents the right to a cash payment equal to the excess, if any, of (i) the fair market value of each underlying share of the Company's common stock, determined on the date of exercise of the 2021 SAR minus (ii) the base amount. Pursuant to the terms of the 2021 SAR awards, in no event may the cash payment for each SAR exceed $15.45, which is the maximum price per share of $38.10, minus the base amount of $22.65, subject to adjustment in accordance with the terms of the Stock Appreciation Right Award Agreement. The maximum price per share is the per-share value based on the Company's market capitalization at $600 million and the Company's outstanding shares of common stock, which was 15,767,492 shares on February 17, 2021. The 2021 SAR awards are cash-settled and were granted outside of the 2018 Plan and the 2021 Plan.

The 2021 PSU awards vest 20% upon the initiation of a new clinical program with an in-licensed compound, 20% for reaching the recommended Phase 2 dose for any compound, 20% for the first patient enrolled in the expansion cohort of the Phase 1 ON123300 clinical trial, 20% for the first patient enrolled in a registrational study for any compound, and 20% for the topline data of a registrational study for any compound. The 2021 PSU awards have a maximum value of $38.10 per share. The maximum price per share is the per-share value based on the Company's approximate market capitalization at $600 million and the Company's outstanding shares of common stock, which was 15,767,492 shares on February 17, 2021. In all cases, the 2021 PSU awards are subject to the terms and conditions of the Company's form of PSU award agreement. The 2021 PSU awards are cash-settled and were granted outside of the 2018 Plan and the 2021 Plan.

The fair value of the 2021 and 2020 SARs granted has been estimated using the Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year ended December 31,	
	2021	2020
Risk-free interest rate	0.95 %	0.30 %
Expected volatility	129.79 %	111.57 %
Expected term	6.50 years	6.35 years
Expected dividend yield	0 %	0 %
Weighted average grant date fair value	$ 0.62	$ 0.47

During the years ended December 31, 2021 and 2020, the Company recognized $519,000 and $67,000, respectively, of compensation expense related to the SARs and PSUs. Included in compensation expense related to SARs in 2021 is $442,000 of expense resulting from the exercise of 2020 SARs during February 2021. As of December 31, 2021, the SARs and PSUs liability was $66,000 and is included in accrued expenses. As of December 31, 2021, there was $19,000 of unrecognized compensation cost related to the 2020 SARs and PSUs and $233,000 of unrecognized compensation cost related to the 2021 SARs and PSUs.

11. Employee Benefit Plan

The Company has a 401(k) Retirement Savings Plan. Employees are eligible to participate in the plan as soon as they join the Company if they are at least 21 years of age and work a minimum of 1,000 hours per year. The Company matches $0.75 for every dollar of the first 6% of payroll that employees invest, up to the legal limit. Employer contributions vest immediately. For the years ended December 31, 2021 and 2020, the Company contributed $114,000 and $146,000, respectively.

12. Commitments and Contingencies

Employment agreements

The Company has entered into employment agreements with certain of its executives. The agreements provide for, among other things, salary, bonus and severance payments.

13. Research Agreements

The Company has entered into various licensing and right-to-sublicense agreements with educational institutions for the exclusive use of patents and patent applications, as well as any patents that may develop from research being conducted by such educational institutions in the field of anticancer therapy, genes and proteins. Results from this research have been licensed to the Company pursuant to these agreements. Under one of these agreements with Temple University ("Temple"), the Company is required to make annual maintenance payments to Temple and royalty payments based upon a percentage of sales generated from any products covered by the licensed patents, with minimum specified royalty payments. As no sales had been generated through December 31, 2021 under the licensed patents, the Company has not incurred any royalty expenses related to this agreement. In addition, the Company is required to pay Temple a percentage of any sublicensing fees received by the Company. No sublicense fees were incurred during 2021 or 2020.

14. License and Collaboration Agreements

SymBio Agreement

In July 2011, the Company entered into a license agreement with SymBio Pharmaceuticals Limited ("SymBio"), which has been subsequently amended, granting SymBio an exclusive, royalty-bearing license for the development and commercialization of rigosertib in Japan and Korea. Under the SymBio license agreement, SymBio is obligated to use commercially reasonable efforts to develop and obtain market approval for rigosertib inside the licensed territory and the Company has similar obligations outside of the licensed territory. The Company has also entered into an agreement with SymBio providing for it to supply SymBio with development-stage product. Under the SymBio license agreement, the Company also agreed to supply commercial product to SymBio under specified terms that will be included in a commercial supply agreement to be negotiated prior to the first commercial sale of rigosertib. The supply of development-stage product and the supply of commercial product will be at the Company's cost plus a defined profit margin. Sales of development-stage product have been de minimis. The Company has additionally granted SymBio a right of first negotiation to license or obtain the rights to develop and commercialize compounds having a chemical structure similar to rigosertib in the licensed territory.

Under the terms of the SymBio license agreement, the Company received an upfront payment of $7,500,000 in 2011. In addition, the Company could receive regulatory, development and sales-based milestone payments as well as royalty payments at percentage rates ranging from the mid-teens to 20% based on net sales of rigosertib by SymBio.

Royalties will be payable under the SymBio agreement on a country-by-country basis in the licensed territory, until the later of the expiration of marketing exclusivity in those countries, a specified period of time after first commercial sale of rigosertib in such country, or the expiration of all valid claims of the licensed patents covering rigosertib or the manufacture or use of rigosertib in such country. If no valid claim exists covering the composition of matter of rigosertib or the use of or treatment with rigosertib in a particular country before the expiration of the royalty term, and specified competing products achieve a specified market share percentage in such country, SymBio's obligation to pay the Company royalties will continue at a reduced royalty rate until the end of the royalty term. In addition, the applicable royalties payable to the Company may be reduced if SymBio is required to pay royalties to third-parties for licenses to intellectual property rights necessary to develop, use, manufacture or commercialize rigosertib in the licensed territory. The license agreement with SymBio will remain in effect until the expiration of the royalty term. However, the SymBio license agreement may be terminated earlier due to the uncured material breach or bankruptcy of a party, or force majeure. If SymBio terminates the license agreement in these circumstances, its licenses to rigosertib will survive, subject to SymBio's milestone and royalty obligations, which SymBio may elect to defer and offset against any damages that may be determined to be due from the Company. In addition, the Company may terminate the license agreement in

the event that SymBio brings a challenge against it in relation to the licensed patents, and SymBio may terminate the license agreement without cause by providing the Company with written notice within a specified period of time in advance of termination.

The Company assessed the SymBio arrangement in accordance with ASC 606 and determined that its performance obligations under the SymBio agreement include the exclusive, royalty-bearing, sublicensable license to rigosertib, the research and development services to be provided by the Company and its obligation to serve on a joint committee. The Company concluded that the license was not distinct since it was of no benefit to SymBio without the ongoing research and development services and that, as such, the license and the research and development services should be bundled as a single performance obligation. Since the provision of the license and research and development services are considered a single performance obligation, the $7,500,000 upfront payment is being recognized as revenue ratably through December 2037, the expected period over which the Company expects the research and development services to be performed.

SymBio's purchases of rigosertib as development-stage product or for commercial requirements represent options under the agreement and revenues are therefore recognized when control of the product is transferred, which is typically when shipped. If SymBio orders the supplies from the Company, the Company expects the pricing for this supply to equal its third-party manufacturing cost plus a pre-negotiated percentage, which will not result in a significant incremental discount to market rates. In January 2018, the agreement was amended to provide SymBio a discount of 35% on future purchases, limited to a cumulative total amount of $300,000.

HanX Narazaciclib (ON 123300) Agreement

In December 2017, the Company entered into a license and collaboration agreement with HanX Biopharmaceuticals, Inc. ("HanX"), a company focused on development of novel oncology products, for the further development, registration and commercialization of narazaciclib in Greater China. Narazaciclib is a preclinical compound which the Company believes has the potential to overcome the limitations of current generation CDK 4/6 inhibitors. The key feature of the collaboration was that HanX provided all funding required for the Chinese IND enabling studies necessary in order to seek IND approval by the National Medical Products Administration (Chinese FDA). The Chinese IND was approved in January 2020. The Company and HanX also intended for these studies underlying the Chinese IND approval, to meet the US FDA standards for IND approval. Accordingly, such studies were used by the Company for an IND filing with the US FDA in November 2020. In September 2020, a Phase 1 Study with narazaciclib in cancer patients was initiated in China. The Company maintains global rights to the study and study data outside of China. The US FDA Study May Proceed letter was issued in December 2020. Enrollment into the US phase 1 study (Study 19-01) commenced in May 2021.

Pursuant to the agreement, the Company received a $450,000 upfront payment on April 11, 2018. If the compound receives regulatory approval and is commercialized, the Company would receive regulatory and commercial milestone payments, as well as royalties on sales in the Greater China territory.

The Company assessed the HanX arrangement for revenue recognition in accordance with ASC 606 and determined that the license was distinct and that control of the license had been transferred during the first quarter of 2018. As such, the Company recognized the $450,000 allocated to the license at that time.

Pint Agreement

On March 2, 2018, the Company entered into a License, Development and Commercialization Agreement (the "Pint License Agreement") and a Securities Purchase Agreement (the "Pint Securities Purchase Agreement") with Pint International SA (which, together with its affiliate Pint Pharma GmbH, are collectively referred to as "Pint").

Under the terms of the Pint License Agreement, the Company granted Pint an exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to develop and commercialize any pharmaceutical product (the "Pint Licensed Product") containing rigosertib in all uses of rigosertib in humans in Latin American countries (the "Pint Territory," including Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica,

Cuba, Dominican Republic, Ecuador, El Salvador, French Guiana, British Guiana, Suriname, Guatemala, Haiti, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Uruguay and Venezuela).

Pint agreed to make an upfront equity investment in the Company's common stock. In addition, the Company could receive additional regulatory, development and sales-based milestone payments, an additional equity investment, as well as tiered, double digit royalties based on net aggregate net sales in the Pint Territory. Pint and the Company have also agreed to enter into a supply agreement providing for Pint purchasing rigosertib and the Pint Licensed Product from the Company within 90 days of the FDA approval of an a NDA for the Pint Licensed Product.

Pint may terminate the Pint License Agreement in whole (but not in part) at any time upon 45 days' prior written notice. The Pint License Agreement also contains certain provisions for termination by either party in the event of breach of the Pint License Agreement by the other party, subject to a cure period, or bankruptcy of the other party.

Under the terms of the Pint Securities Purchase Agreement, Pint agreed to make an upfront equity investment in the Company at a specified premium to the Company's share price. Pursuant to the Pint Securities Purchase Agreement, closing of the upfront equity investment occurred on April 4, 2018 and Pint purchased 3,631 shares of common stock for $1,250,000. The total amount of the premium was $319,000 and this amount was allocated to the license.

In addition, under the Pint Securities Purchase Agreement, if the FDA approves the NDA for the Pint Licensed Product, Pint will reimburse the Company for certain research and development expenses. Half of the reimbursement amount will be paid in cash, the other half of the amount will be by an equity investment at a premium to the average of the volume weighted average price of common stock for the ten consecutive trading days ended on the day the FDA approves the NDA.

Pursuant to the Pint Securities Purchase Agreement, the common stock purchased by Pint is subject to certain lock-up restrictions and Pint is entitled to certain registration and participation rights.

The Company assessed the Pint arrangement for revenue recognition in accordance with ASC 606 and determined that the license was distinct and that control of the license had been transferred during the second quarter of 2018. As such, the Company recognized the $319,000 allocated to the license at that time.

Knight Agreement

In November 2019, the Company entered into a Distribution, License and Supply Agreement (the "Knight License Agreement") with Knight Therapeutics Inc. ("Knight"). Under the terms of the Knight License Agreement, the Company granted Knight (i) a non-exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to develop and manufacture any product (the "Knight Licensed Product") containing rigosertib for Canada (and Israel should Knight exercise its option) (the "Knight Territory") and in human uses (the "Knight Licensed Field"), and (ii) an exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to commercialize the Knight Licensed Product in the Knight Territory and in the Knight Licensed Field.

Knight has also agreed to obtain from the Company all of Knight's requirements of the Knight Licensed Products for the Knight Territory, and the Company has agreed to supply Knight with all of its requirements of the Knight Licensed Products. The Company may, at its discretion, use the services of a contract manufacturer to manufacture and package the Knight Licensed Products.

In addition, the Company has granted Knight an exclusive right of first refusal with respect to all or any part of the Knight Territory, to store, market, promote, sell, offer for sale and/or distribute any ROFR Products. As used in the Knight License Agreement, "ROFR Products" means all products other than the Knight Licensed Product that are owned, licensed, or controlled by the Company as of the effective date and all improvements thereto.

The Company received an upfront payment of $100,000 and is eligible to receive clinical, regulatory and sales-based milestone payments. The Company is also eligible to receive tiered double-digit royalties based on net sales in the Knight Territory.

The Knight License Agreement is for a term of 15 years from the launch on a country by country basis in the Knight Territory and contains customary provisions for termination by either party in the event of breach of the Knight License Agreement by the other party (subject to a cure period), bankruptcy of the other party, or challenges to the patents by any sublicensee or assignee.

The Company assessed the Knight License Agreement for revenue recognition in accordance with ASC 606 and determined that the license was distinct and that control of the license had been transferred during the fourth quarter of 2019. As such, the Company recognized the $100,000 allocated to the license at that time.

Specialised Therapeutics Asia Pte. Ltd. Agreement

On December 18, 2019, the Company entered into a Distribution, License and Supply Agreement (the "STA License Agreement") with Specialised Therapeutics Asia Pte. Ltd. ("STA"). Under the terms of the STA License Agreement, the Company granted STA (i) a non-exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to develop and manufacture any product (the "STA Licensed Product") containing rigosertib for Australia and New Zealand (the "STA Territory") and in human uses (the "Field"), and (ii) an exclusive, royalty-bearing license, with the right to sublicense, under certain Company patent rights and know-how to commercialize the STA Licensed Product in the STA Territory and in the Field.

STA has also agreed to obtain from the Company all of STA's requirements of the STA Licensed Products for the STA Territory, and the Company has agreed to supply STA with all of its requirements of the STA Licensed Products. The Company may, at its discretion, use the services of a contract manufacturer to manufacture and package the STA Licensed Products.

There was an upfront fee of $50,000 and the Company may be entitled to receive clinical, regulatory and sale-based milestone payments. The Company may also be entitled to receive tiered double-digit royalties based on net sales in the Territory.

The License Agreement is for a term of 15 years from the launch on a country by country basis in the Territory and contains customary provisions for termination by either party in the event of breach of the License Agreement by the other party (subject to a cure period), bankruptcy of the other party, or challenges to the patents by any sublicensee or assignee.

The Company assessed the License Agreement for revenue recognition in accordance with ASC 606 and determined that the license was distinct and that control of the license had been transferred during the fourth quarter of 2019. As such, the Company recognized the $50,000 allocated to the license at that time.

15. Related-Party Transactions

The Company entered into a research agreement, as subsequently amended, with the Mount Sinai School of Medicine ("Mount Sinai"), with which a former member of its board of directors and a stockholder is affiliated. The agreement expired in June 2020 and was not renewed. The board member left the Company's board in August 2020. Mount Sinai undertook research on behalf of the Company on the terms set forth in the agreements. Payments to Mount Sinai under this research agreement for the years ended December 31, 2021 and 2020 were $0 and $201,000, respectively. At both December 31, 2021 and 2020, the Company had $77,000 payable to Mount Sinai under this agreement.

The Company entered into a consulting agreement with a member of its board of directors, which was cancelled in June 2020. The board member left the Company's board in August 2020. The former board member provided consulting services to the Company on the terms set forth in the agreement. Payments to this board member under this agreement for the years ended December 31, 2021 and 2020 were $0 and $66,000, respectively. At both December 31, 2021 and 2020, the Company had $0 payable under this agreement.

16. Securities Registrations and Sales Agreements

January 2020 Offering

On December 31, 2019, the Company entered into definitive securities purchase agreements with institutional investors for the issuance and sale in a registered direct offering of 1,844,168 shares of the Company's common stock at an offering price of $5.4225 per share.

Pursuant to the December 2019 HCW Engagement Letter, HCW agreed to serve as exclusive placement agent for the offering. In connection with the offering, the Company paid HCW an aggregate cash fee equal to 7.0% of the gross proceeds in the offering, management fee equal to 1.0% of the gross proceeds raised in the offering, $85,000 for non-accountable expenses; and $10,000 for clearing fees. The Company also issued to HCW or its designees placement agent warrant to purchase up to 92,208 shares of common stock at an exercise price of $6.7785 per share. The placement agent warrants are immediately exercisable and will expire on December 31, 2023.

The net proceeds to the Company from the offering, after deducting HCW's placement agent fees and expenses and other estimated offering expenses payable by the Company were approximately $9.0 million and were received in January 2020.

The offering was pursuant to a prospectus dated December 28, 2017, and a prospectus supplement dated as of December 31, 2019 filed in connection with a takedown from the Company's shelf registration statement on Form S-3 (File No. 333-221684). The offering closed on January 3, 2020.

January 2021 Offering

On January 7, 2021, the Company entered into a purchase agreement with certain institutional and accredited investors for the sale of an aggregate of 1,303,408 shares of the Company's common stock, at a purchase price of $6.675 per share.

Under the purchase agreement, subject to certain exceptions, the Company is prohibited from effecting or entering into an agreement to effect any "variable rate transactions" as defined in the purchase agreement for a period of five years following the closing of the offering.

In connection with the offering, pursuant to the purchase agreement the Company reimbursed Lincoln Park Capital Fund, LLC, as the lead investor ("Lincoln Park"), an aggregate of $100,000 for expenses incurred in connection with the offering, including any due diligence expenses and legal fees. Furthermore, pursuant to the purchase agreement, the Company granted Lincoln Park certain rights to participate at fair value with other investors in up to 50% of the amount of any future offerings of common stock or securities exercisable for or convertible into common stock that the Company seeks to complete within one year after the closing of the offering, other than a firm commitment public offering.

The net proceeds to the Company from the offering, after deducting Lincoln Park's expenses and other estimated offering expenses payable by the Company were approximately $8.5 million.

The shares sold in the offering were offered and sold by the Company directly to the investors, without a placement agent, underwriter, broker or dealer, pursuant to an effective shelf registration statement on Form S-3 (File No. 333-237844) declared effective by the SEC on May 18, 2020, and the base prospectus contained therein. The offering closed on January 11, 2021.

February 2021 Offering

On February 10, 2021, the Company entered into an underwriting agreement with Guggenheim Securities, LLC, as representative of several underwriters, for the public offering of 1,666,667 shares of the Company's common stock, at a public offering price of $15.00 per share. Under the terms of the underwriting agreement, the Company granted the

underwriters an option, exercisable for 30 days, to purchase up to an additional 250,000 shares of common stock at the same price. The option was exercised prior to closing.

In connection with the offering, the Company paid the underwriters a cash fee equal to 6% of the gross proceeds in the offering and $100,000 in legal fees and expenses.

The net proceeds to the Company from the offering, including exercise of the underwriters' option, were approximately $26.7 million, after deducting fees and estimated offering expenses payable by the Company.

The offering was made pursuant to a registration statement (No. 333-237844) on Form S-3, which was initially filed by the Company with the SEC on April 24, 2020, amended on Form S-3/A that was filed with the SEC on May 15, 2020, and was declared effective by the SEC on May 18, 2020. The offering closed on February 16, 2021.

August 2021 Equity Distribution Agreement

On August 20, 2021, the Company entered into an Equity Distribution Agreement (the "Equity Distribution Agreement") with Piper Sandler & Co. ("Piper Sandler") under which the Company may offer and sell, from time to time at its sole discretion, shares of the Company's common stock, with aggregate gross sales proceeds of up to $25.0 million through an "at the market" equity offering program under which Piper Sandler is the sales agent.

Under the Equity Distribution Agreement, the Company has the right to 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, limitations 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 Equity Distribution Agreement, Piper Sandler may sell the shares by methods deemed to be an "at the market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made through The Nasdaq Capital Market or any other trading market for the Company's common stock. The Equity Distribution Agreement provides that Piper Sandler is entitled to compensation for its services equal to 3.0% of the gross proceeds of any shares of common stock sold through Piper Sandler under the Equity Distribution Agreement. The Company has no obligation to sell any shares under the Equity Distribution Agreement, and may at any time suspend solicitation and offers under the Equity Distribution Agreement. Through September 30, 2021, the Company sold 109,523 shares under the agreement at a weighted average price of $5.32 per share. Net proceeds after commissions and offering expenses were approximately $0.5 million.

The shares are issued pursuant to the Company's shelf registration statement on Form S-3 (File No. 333-237844). The Company filed a prospectus supplement, dated August 20, 2021 with the Securities and Exchange Commission in connection with the offer and sale of the shares pursuant to the Equity Distribution Agreement.

September 2021 Offering

On September 23, 2021, the Company entered into an underwriting agreement with Guggenheim Securities, LLC, as representative of several underwriters, for the public offering of 5,000,000 shares of the Company's common stock, at a public offering price of $4.20 per share. Under the terms of the underwriting agreement, the Company granted the underwriters an option, exercisable for 30 days, to purchase up to an additional 750,000 shares of common stock at the same price. The option was not exercised.

In connection with the offering, the Company paid the underwriters a cash fee equal to 6% of the gross proceeds in the offering and $100,000 in legal fees and expenses.

The net proceeds to the Company from the offering, including exercise of the underwriters' option, were approximately $19.5 million, after deducting fees and estimated offering expenses payable by the Company.

The offering was made pursuant to a registration statement (No. 333-237844) on Form S-3, which was initially filed by the Company with the SEC on April 24, 2020, amended on Form S-3/A that was filed with the SEC on May 15, 2020, and was declared effective by the SEC on May 18, 2020. The offering closed on September 28, 2021.

Exhibit 21.1

Subsidiary	Jurisdiction of Incorporation
Onconova Europe GmbH	Germany

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

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

(1) Registration Statement (Form S-8 No. 333-191161) pertaining to the Onconova Therapeutics, Inc. 2013 Equity Compensation Plan

(2) Registration Statement (Form S-8 No. 333-194228) pertaining to the Onconova Therapeutics, Inc. 2013 Equity Compensation Plan

(3) Registration Statement (Form S-8 No. 333-204210) pertaining to the Onconova Therapeutics, Inc. 2013 Equity Compensation Plan

(4) Registration Statement (Form S-8 No. 333-210694) pertaining to the Onconova Therapeutics, Inc. 2013 Equity Compensation Plan

(5) Registration Statement (Form S-8 No. 333-215575) pertaining to the Onconova Therapeutics, Inc. 2013 Equity Compensation Plan

(6) Registration Statement (Form S-8 No. 333-222400) pertaining to the Onconova Therapeutics, Inc. 2013 Equity Compensation Plan

(7) Registration Statement (Form S-8 No. 333-226199) pertaining to the Onconova Therapeutics, Inc. 2018 Omnibus Incentive Compensation Plan

(8) Registration Statement (Form S-8 No. 333-233410) pertaining to the Onconova Therapeutics, Inc. 2018 Omnibus Incentive Compensation Plan

(9) Registration Statement (Form S-8 No. 333-258336) pertaining to the Onconova Therapeutics, Inc. 2021 Omnibus Incentive Compensation Plan

(10) Registration Statement (Form S-3 No. 333-237844) of Onconova Therapeutics, Inc.

(11) Registration Statement (Form S-3 No. 333-230744) of Onconova Therapeutics, Inc.

(12) Registration Statement (Form S-1 No. 333-211769) of Onconova Therapeutics, Inc.

(13) Registration Statement (Form S-1 No. 333-222374) of Onconova Therapeutics, Inc.

(14) Registration Statement (Form S-1 No. 333-224315) of Onconova Therapeutics, Inc.

(15) Registration Statement (Form S-1 No. 333-234360) of Onconova Therapeutics, Inc.

of our report dated March 21, 2022, with respect to the consolidated financial statements of Onconova Therapeutics, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
March 21, 2022

Exhibit 31.1

CERTIFICATIONS

I, Steven Fruchtman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Onconova Therapeutics, Inc.;

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 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 the registrant's board of directors (or other 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.

/S/ STEVEN FRUCHTMAN, M.D.
Steven Fruchtman, M.D.
President and Chief Executive Officer
(Principal Executive Officer and Principal Operating Officer)

Dated: March 21, 2022

Exhibit 31.2

CERTIFICATIONS

I, Mark Guerin, certify that:

1. I have reviewed this Annual Report on Form 10-K of Onconova Therapeutics, Inc.;

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 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 the registrant's board of directors (or other 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.

/s/ MARK GUERIN
Mark Guerin
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Dated: March 21, 2022

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Onconova Therapeutics, Inc. (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Steven Fruchtman, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, based on my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ STEVEN FRUCHTMAN, M.D.
Steven Fruchtman, M.D.
President and Chief Executive Officer
(Principal Executive Officer and Principal Operating Officer)

Dated: March 21, 2022

Exhibit 32.2

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

In connection with the Annual Report on Form 10-K of Onconova Therapeutics, Inc. (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Mark Guerin, Chief Financial Officer, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, based on my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ MARK GUERIN
Mark Guerin
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Dated: March 21, 2022