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

FORM 10-K

☒ **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: 001-37490

Sierra Oncology, Inc.

(Exact name of registrant as specified in its charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**20-0138994** **(I.R.S. Employer Identification Number)**
1820 Gateway Drive, Suite 110 **San Mateo, California** **(Address of principal executive offices)**	**94404** **(Zip Code)**

(650) 376-8679

(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, $0.001 par value	SRRA	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

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

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

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

Indicate by check mark whether the Registrant has submitted electronically, if any, 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 and post such files). YES ☒ NO ☐

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

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

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

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

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

The aggregate market value of common stock held by non-affiliates of the registrant calculated based on the closing price of $19.47 of the registrant's common stock as reported on The Nasdaq Global Market on June 30, 2021, the last business day of the registrant's most recently completed second quarter, was $128.4 million.

The number of shares of Registrant's Common Stock outstanding as of March 7, 2022 was 23,665,100.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement ("Proxy Statement") relating to the 2022 Annual Meeting of Stockholders will be filed with the Commission within 120 days after the end of the Registrant's 2021 fiscal year and is incorporated by reference into Part III of this Report.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (Annual Report) contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act), and section 27A of the Securities Act of 1933, as amended (Securities Act). All statements contained in this Annual Report other than statements of historical fact are forward-looking statements. The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect," and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements, although not all forward-looking statements contain these words. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements include, but are not limited to:

- our financial condition and performance;
- the sufficiency of our existing cash and cash equivalents to fund our future operating expenses and capital expenditure requirements;
- our ability to obtain funding for our operations, including funding necessary to develop and commercialize our product candidates;
- the ability of our preclinical studies and clinical trials to demonstrate safety and efficacy of our product candidates;
- the success, cost and timing of our development activities, preclinical studies and clinical trials;
- the rate and degree of market acceptance of our product candidates;
- the timing or likelihood of regulatory filings and approvals;
- the timing and focus of our future clinical trials, and the reporting of data from those trials;
- expectations and intentions (including expectations relating to combination studies with momelotinib, SRA515 and SRA737, receipt of regulatory approval for momelotinib and the commercial launch for momelotinib);
- our plans relating to commercializing our product candidates, if approved, including timing relating to a commercial launch;
- our plans and ability to establish and grow our sales, marketing and distribution infrastructure to commercialize any product candidates for which we obtain approval;
- our ability to attract and retain key managerial, scientific and clinical personnel;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the pricing and reimbursement of our product candidates, if approved;
- our reliance on third parties to conduct clinical trials of our product candidates, and for the manufacture of our product candidates for preclinical studies and clinical trials;
- our ability to expand our product candidates into additional indications and patient populations;
- the success of competing therapies that are or may become available;
- the beneficial characteristics, safety and efficacy of our product candidates;
- regulatory developments in the United States and other jurisdictions;
- our ability to obtain and maintain regulatory approval of our product candidates in the United States and other jurisdictions, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;

- future agreements with third parties in connection with the commercialization of our product candidates;
- our plans relating to the further development and manufacturing of our product candidates, including additional indications for which we may pursue regulatory approval;
- our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our expectations regarding the impact of the COVID-19 pandemic on our business;
- the size and growth potential of the markets for our product candidates, if approved for commercial use, and our ability to serve those markets;
- the potential benefits of any strategic collaboration agreements we may enter into;
- the potential future sales under our ATM Program;
- expected timing of the execution of, and expected results from, our exploration of strategic options; and
- our business strategies and objectives for future operations and other statements that are not historical facts.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in Item 1A, "Risk Factors" and elsewhere in this Annual Report. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements to conform these statements to actual results or to changes in our expectations, except as required by law. You should read this Annual Report with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

Unless the context indicates otherwise, as used in this Annual Report, the terms "Sierra Oncology," "the Company," "we," "us" and "our" refer to Sierra Oncology, Inc., a Delaware corporation, and its subsidiaries taken as a whole, unless otherwise noted. Sierra Oncology is our registered trademark. The "Sierra Oncology" logo and all product names are our common law trademarks. This Annual Report contains additional trade names, trademarks and service marks of other companies, which are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

PART I

Item 1. Business.

Overview

We are a late-stage biopharmaceutical company on a mission to deliver targeted therapies that treat rare forms of cancer. Our main focus is the development and potential commercialization of momelotinib, an investigational agent for the treatment of myelofibrosis. In January 2022, we announced positive topline results from our global Phase 3 clinical trial for patients with myelofibrosis called MOMENTUM. Momelotinib achieved a statistically significant benefit on symptoms, anemia and splenic size. MOMENTUM data, combined with data from our earlier clinical trials, will be the basis for a New Drug Application (NDA) we plan to submit to the U.S. Food and Drug Administration (FDA) in the second quarter of 2022. Approximately 1,000 myelofibrosis patients have received momelotinib through clinical trials at different stages of clinical development, and several of our clinical trial patients remain on treatment more than 11 years later.

Momelotinib was acquired from Gilead Sciences, Inc. (Gilead) in the third quarter of 2018. Gilead had already completed several late-stage trials of the drug candidate in patients with myelofibrosis. Myelofibrosis is characterized by progressive anemia and thrombocytopenia and currently approved JAK inhibitor therapies, ruxolitinib and fedratinib, can induce or further exacerbate this myelosuppression, limiting their use in first line treatment and resulting in a population of second line patients who are no longer able to benefit from such therapies. Momelotinib is a novel, orally-bioavailable JAK1 (Janus kinase 1), JAK2 (Janus kinase 2) and ACVR1 (Activin A receptor type 1) inhibitor with a differentiated mechanism of action, enabling it to potentially address all three hallmarks of disease in myelofibrosis: anemia of inflammation, constitutional symptoms and enlarged spleen.

In the second quarter of 2019, we announced that we had obtained regulatory clarity with the FDA concerning the design of a Phase 3 clinical trial intended to support potential registration of momelotinib. We also announced that the FDA had granted Fast Track designation to momelotinib for the treatment of patients with intermediate/high-risk myelofibrosis who have previously received a JAK inhibitor.

Following receipt of this clarity, we announced the design of the MOMENTUM Phase 3 clinical trial in myelofibrosis, which we subsequently launched in the fourth quarter of 2019. MOMENTUM is a randomized double-blind trial that enrolled 195 myelofibrosis patients that were symptomatic and anemic and had been treated previously with a JAK inhibitor. The Primary Endpoint of the trial was the Total Symptom Score (TSS) response rate of momelotinib compared to danazol at Week 24 (99% power; p-value < 0.05). Danazol was selected as an appropriate treatment comparator given its use to ameliorate anemia in myelofibrosis patients, as recommended by National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) guidelines. Patients were randomized 2:1 to receive either momelotinib (n=130) or danazol (n=65). After 24 weeks of treatment, patients on danazol were allowed to crossover to receive momelotinib.

At the 25th European Hematology Association (EHA) Virtual Congress held in the second quarter of 2020, we reported favorable Long-Term Safety and Dose Intensity data for momelotinib from more than 550 patients across the two previously conducted SIMPLIFY Phase 3 studies and their subsequent ongoing extended treatment periods. More than 90 SIMPLIFY-1 and SIMPLIFY-2 patients continued to receive momelotinib for 3.5 years or longer. These data were presented in posters by Professor Claire Harrison, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom, and Dr. Vikas Gupta, Princess Margaret Cancer Centre, Toronto, Canada. The key findings were:

- Consistent with prior data, and reflecting momelotinib's differentiated pharmacological profile, our new long-term safety analyses continue to show a rapid and sustained increase in hemoglobin levels during momelotinib therapy, in contrast to the significant decrease in hemoglobin for patients receiving ruxolitinib. Patients treated with momelotinib also experienced significantly higher mean platelet counts compared to those receiving ruxolitinib. Importantly, patients who switched from ruxolitinib to momelotinib also achieved a sustained improvement in hemoglobin in both studies, and platelets in

SIMPLIFY-1. In addition to an absence of significant rates of high-grade hematological toxicities, long-term tolerability was favorable with no new safety signals or evidence of cumulative toxicity.

- Momelotinib's safety profile and durable benefits facilitated sustained dose intensity across the continuum of JAK inhibitor-naïve and previously JAK inhibitor treated myelofibrosis patients. While the starting doses for ruxolitinib were often attenuated due to low platelets, further reductions in dose intensity were also commonly required for ruxolitinib. In contrast, momelotinib was initiated at full dose for all subjects enrolled to the SIMPLIFY studies and high dose intensity was maintained in the majority over extended durations. Patients who switched from ruxolitinib to momelotinib saw an immediate and sustained improvement in dose intensity.
- The data from the two interrelated presentations suggest that the favorable effect on hemoglobin and platelets allows momelotinib to be initiated at full dose intensity and maintained for the majority of patients at full dose intensity over extended durations while retaining a favorable long-term safety profile. Notably, some patients continued to receive momelotinib 10 years after enrolling in the initial momelotinib Phase 2 trials while 90 Phase 3 SIMPLIFY patients who enrolled into those trials 4 to 6 years ago continued to receive momelotinib. We believe the dosing and safety profile may contribute to momelotinib's potential ability to provide sustained benefits over extended durations.

Later that year at the American Society of Hematology (ASH) Annual Meeting held in December 2020, we released updated analyses from the previously completed Phase 3 SIMPLIFY studies of momelotinib, including overall survival data as well as efficacy data for momelotinib compared to ruxolitinib in patients with low platelet levels. The overall survival data received an oral presentation by Dr. Srdan Verstovsek of the University of Texas MD Anderson Cancer Center in Houston, Texas, USA; efficacy data by platelet strata were presented in a poster by Dr. Jean-Jacques Kiladjian, Saint Louis Hospital, Paris, France. Key findings were:

- Robust overall survival was observed in both JAK inhibitor-naïve and previously ruxolitinib treated patients. Sustained transfusion independence was observed with extended momelotinib treatment, and the median duration of TI in the momelotinib arm has not been reached after more than three years of follow up. We believe these data, in combination with previously reported tolerability data, further highlight where momelotinib may be a viable treatment option for myelofibrosis patients, including those who are not ideal candidates for currently approved therapies.
- The retrospective analysis of the two Phase 3 SIMPLIFY studies demonstrate that the relative benefit-risk profile of momelotinib and ruxolitinib is influenced by baseline platelet count. In SIMPLIFY-1, momelotinib achieved substantially higher Transfusion Independence (TI) and splenic response rates and had a similar symptomatic response relative to ruxolitinib in patients whose platelet count at baseline was <150 x 10^9/L. For patients whose platelet count was 150 – 300 x 10^9/L, momelotinib achieved a higher TI response rate and generally similar splenic and symptom response rates. In patients with platelet counts >300 x 10^9/L, ruxolitinib achieved higher splenic and symptom response rates than momelotinib, and the TI rate remained higher with momelotinib. These updated analyses complement previous findings that demonstrate the ability to initiate and maintain near-maximal momelotinib dose intensity regardless of baseline platelet count, suggesting that this durable dosing contributes to its efficacy profile.

At the EHA Annual Meeting held in June 2021, we announced additional data analyses from the SIMPLIFY studies highlighting transfusion independence with momelotinib is associated with improved overall survival, including in patients with anemia at baseline. In addition, transfusion independence is seen irrespective of baseline degree of anemia, platelet count or transfusion status. Together, these data suggest the goal of achieving transfusion independence should become an important driver of treatment decisions in myelofibrosis.

Also in June 2021, we announced that screening for the MOMENTUM Phase 3 clinical trial had been completed, enrolling 195 patients based on a planned 180 patients. Positive topline data were announced on January 25, 2022. Topline data announced include:

- Primary Endpoint of TSS response rate based on a ≥50% reduction in TSS at Week 24 compared to baseline: 25% in the MMB arm vs. 9% in the control arm (p=0.0095);

- Secondary Endpoint of Transfusion Independence (TI) rate at the end of Week 24: 31% in the MMB arm vs. 20% in the control arm (one-sided p=0.0064; non-inferiority);
- Secondary Endpoint of Splenic Response Rate (SRR) based on a reduction in splenic volume of ≥35% at the end of Week 24 compared to baseline: 23% in the MMB arm vs. 3% in the control arm (p=0.0006);
- The rate of Grade 3 or worse adverse events in the randomized treatment period was 54% in the MMB arm and 65% in the control arm. Serious treatment emergent adverse events were 35% in the MMB arm and 40% in the control arm; and
- Mean baseline characteristics for all patients were TSS of 27, Hemoglobin (Hgb) of 8 g/dL and platelet count of 145 x 10^9/L.

The full data set will be presented at an upcoming medical meeting. Based on these results, we plan to submit an NDA with the FDA in the second quarter of 2022, and if approved, we could anticipate a commercial launch early in the first half of 2023. Additionally, we continue to explore opportunities to expand our pipeline via potential combination studies for momelotinib, including in combination with SRA515.

In August 2021, we entered into an agreement with AstraZeneca AB (AstraZeneca) to acquire an exclusive global license for SRA515 (formerly AZD5153), a potent and selective bromodomain-containing protein 4 (BRD4) bromodomain and extraterminal (BET) inhibitor with a novel bivalent binding mode. We plan to initiate a Phase 2 study examining momelotinib in combination with SRA515 for the treatment of myelofibrosis in the first half of 2022.

Our portfolio also includes SRA737, a selective, orally bioavailable small molecule inhibitor of Checkpoint kinase 1 (Chk1), an emerging target for the treatment of cancer which has a key role in the DNA Damage Response (DDR). In November 2020, we entered into an amendment to the License Agreement with CRT Pioneer Fund (CPF) to allow for the potential future clinical development of SRA737.

We wholly own momelotinib, subject to future milestone payments and royalties, and retain the global commercialization rights to SRA515 and SRA737.

Our Lead Product Candidate – Momelotinib

Myelofibrosis

Myelofibrosis is a disorder involving the stem-cells that give rise to blood cells and is driven by molecular abnormalities that activate the JAK-signal transducers and activators of transcription (JAK-STAT) pathway. The Janus kinases (JAKs) play a central role in the regulation of blood cell production, controlling survival, proliferation, and differentiation of progenitor cells as well as the function of mature cells. Abnormal activation of the JAK-STAT pathway is central to the development of myelofibrosis by driving proliferation, inflammation, fibrosis, and progression of disease.

The three cardinal disease manifestations of myelofibrosis are (1) progressive anemia, often in association with thrombocytopenia (deficiency of platelets in the blood) or other cytopenias (blood cell deficiencies); (2) constitutional symptoms such as fatigue, night sweats, fever, cachexia (wasting), bone pain, pruritus (itching), and weight loss; and (3) organ enlargement, principally of the spleen and less often the liver, due to these organs attempting to produce blood cells, which can cause commonly associated symptoms such as abdominal distension and pain, early satiety, dyspnea (labored breathing), and diarrhea. The median survival for all patients with myelofibrosis is about six years but is considerably worse for intermediate 2- and high-risk patients at 4 years and 2.25 years, respectively. Besides causing disease-related morbidity, myelofibrosis may result in early death from leukemic progression, which can occur in about 20% of patients, and complications arising from progressive bone marrow failure, portal or pulmonary hypertension, infections, clotting, bleeding, and cardiovascular complications.

Myelofibrosis is a relatively rare condition with an incidence of 0.1 to 1 per 100,000 individuals per year, and a prevalence of 6 per 100,000 person-years because of its chronic nature and disabling course. It is estimated that

there are 15,000 symptomatic and anemic myelofibrosis in the United States, representing a potential addressable market of $3.0 billion. Globally there are up to 40,000 myelofibrosis patients. Median age at diagnosis is 67 years. Myelofibrosis may occur de novo as primary myelofibrosis (PMF) or may arise from a preexisting myeloproliferative neoplasm (MPN), including primarily polycythemia vera (PV) or essential thrombocytosis (ET).

Importance of Anemia in Myelofibrosis

Anemia is a cardinal feature of myelofibrosis, and Red Blood Cell (RBC) transfusion dependence is a hallmark of the late-stage disease. Within a year of diagnosis, 45% of patients with myelofibrosis are already RBC transfusion dependent and eventually, nearly all will develop transfusion dependence.

Transfusion dependence is a critical negative prognostic factor for survival for patients with myelofibrosis. Transfusions are associated with both acute and chronic health risks, and they place a significant burden on both the patient and the health care system. Severe anemia and transfusion dependence are independent predictors of poor prognosis and are inversely correlated with quality of life. Conversely, response to anemia-targeted therapies has been associated with improvement in quality of life. The prognostic effect of anemia was recently demonstrated in 1,109 consecutive PMF patients at the Mayo Clinic, 86% of whom presented with some degree of anemia. Even mild anemia impaired survival, while severe anemia (defined as Hgb level of < 8 g/dL or transfusion dependence) was associated with > 1.5-fold increase in risk of death compared with moderate anemia (Hgb level of 8-10 g/dL).

Existing approaches for the management of myelofibrosis associated anemia include transfusion, erythropoiesis-stimulating agents in patients with low erythropoietin levels, corticosteroids, androgens (including danazol), immunomodulators, and splenectomy. Each of these treatments is described by the National Comprehensive Cancer Network (NCCN) as minimally effective.

Momelotinib – A Potent and Selective JAK1, JAK2 and ACVR1 Inhibitor

Momelotinib is a potent, selective, small-molecule inhibitor of JAK1, JAK2 and ACVR1, under development for treatment of patients with myelofibrosis. Momelotinib was discovered by Cytopia Research, which commenced an initial Phase 1/2 clinical trial in the United States in 2009. Cytopia was acquired by YM BioSciences, Inc. in 2010, which continued clinical development of the compound, before its own acquisition by Gilead in 2013. Amongst other clinical studies, Gilead conducted two registration-track Phase 3 trials in subjects with myelofibrosis, GS-US-352-0101 (SIMPLIFY-1) and GS-US-352-1214 (SIMPLIFY-2). In August 2018, we acquired the momelotinib program from Gilead and assumed the role of IND sponsor in September 2018 with the intent to continue development of momelotinib for the treatment of myelofibrosis. Several members of our senior management team were previously executives at Cytopia and/or YM BioSciences and led the early development of momelotinib.

Following our acquisition of the program, we conducted a comprehensive review of data from the two Phase 3 trials of momelotinib, versus ruxolitinib (SIMPLIFY-1) and best available therapy (BAT) (SIMPLIFY-2), as well as GS-US-352-1672, a Phase 2, open-label, translational biology trial of momelotinib in transfusion-dependent subjects with myelofibrosis. In aggregate, our analyses across a variety of datasets show consistent benefit in the three cardinal disease manifestations of myelofibrosis across a spectrum of intermediate-high risk patients with myelofibrosis, both JAK inhibitor-naïve and previously JAK inhibitor-exposed: namely, (1) anemia and transfusion dependency, (2) constitutional symptoms, and (3) enlarged spleen, consistent with the compound's differentiated inhibition of JAK1, JAK2 and ACVR1. Although SIMPLIFY-1 met its primary efficacy endpoint of non-inferior spleen volume reduction, it did not meet its key secondary efficacy endpoint of non-inferior reduction in TSS; and although SIMPLIFY-2 did not meet its primary efficacy endpoint of superior reduction in spleen volume, it did meet its key secondary efficacy endpoint of superior reduction in TSS. In both SIMPLIFY studies, additional secondary endpoints related to transfusion independence rate, transfusion dependence rate, and rate of red blood cell transfusions all favored momelotinib over control and supported the potential for momelotinib to provide meaningful anemia benefits. As such, we have determined that there is substantial clinical justification for further development of momelotinib.

Among the JAK-inhibitor class, momelotinib uniquely inhibits JAK1, JAK2 and ACVR1. All three targets contribute to disease manifestations of myelofibrosis in complex and overlapping ways. The dominant roles for each in driving the various disease manifestations include: JAK1, abnormal cytokine production and immune dysregulation; JAK2, clonal myeloid proliferation; and ACVR1, anemia. Evidence suggests that momelotinib can provide an array of differentiated and compelling anemia-related clinical benefits, while also providing symptomatic and splenic benefits clinically comparable to the approved standard-of-care, ruxolitinib. Specifically, via inhibition of JAK1 and JAK2, momelotinib is uniquely positioned as the only JAK-inhibitor demonstrated to provide

comparable splenic benefit when compared directly to ruxolitinib in the JAK inhibitor treatment-naïve setting, while Phase 3 data strongly suggest the potential for momelotinib to provide substantial symptom benefit for both JAK-inhibitor treatment-naïve and exposed patients with myelofibrosis. In addition, momelotinib induces robust, clinically meaningful and consistent anemia benefits, likely via inhibition of ACVR1 and JAK1, as demonstrated in the two momelotinib Phase 3 trials and in the Phase 2 translational biology trial (GS-US-352-1672) in transfusion-dependent patients.

Myelofibrosis-associated anemia is dependent on a number of factors and involves the hyperactivation of two parallel signal transduction pathways that drive production of the peptide hormone hepcidin. Hepcidin is the master regulator of iron metabolism, and elevated levels in myelofibrosis perturbs iron homeostasis and exacerbates anemia. The principle pathway directing hepcidin expression involves activation of ACVR1, whereas a secondary pathway increases hepcidin in response to inflammation and JAK-STAT signaling. Momelotinib directly inhibits ACVR1, JAK1 and JAK2 to effectively limit hepcidin production. This unique profile induces a dose-dependent decrease in serum hepcidin, restoring iron homeostasis and alleviating anemia.

In a nonclinical anemia model, momelotinib treatment increased circulating plasma iron, RBC production, and Hgb levels consistent with the observed reduction in inflammatory cytokine and hepcidin levels associated with inhibition of JAK1, JAK2 and ACVR1.This effect of momelotinib was further validated by data from trial GS-US-352-1672 in an advanced, transfusion-dependent myelofibrosis population in which 34% and 39% of patients achieved transfusion independence for at least 12 and 8 weeks, respectively. Median plasma hepcidin levels declined acutely after momelotinib dosing and chronically over the entire 24-week dosing period, suggesting momelotinib induced a sustained reduction of both predose (basal) and postdose levels of hepcidin. In an exploratory post-hoc analysis, a substantial reduction in transfusion frequency was also observed in subjects who did not achieve complete transfusion independence.

Similarly, substantially higher rates of transfusion independence and lower rates of transfusion dependency were observed in momelotinib-treated subjects compared with ruxolitinib or BAT-treated subjects in the SIMPLIFY-1 and SIMPLIFY-2 pivotal trials. In an exploratory aggregate analysis including 152 transfusion dependent patients treated with momelotinib across the SIMPLIFY-1, SIMPLIFY-2, and GS-US-352-1672 trials, the combined 8- and 12-week transfusion independence response rates across this continuum of JAK-inhibitor-naïve and exposed, intermediate- and high-risk myelofibrosis patients, were 48.7% and 44.1%, respectively. The rate of transfusion independence in transfusion-dependent subjects, along with other anemia benefits, were broadly consistent across these trials, and are consistent with the empirical findings of a pronounced anemia benefit observed in initial Phase 1/2 momelotinib clinical studies.

In addition, there is extensive evidence of momelotinib's sustained positive effects on hemoglobin (Hgb) and other anemia endpoints. A robust and long-lasting increase in Hgb was observed in the GS-US-352-1672 trial, which enrolled only transfusion-dependent subjects. A similar observation was noted in the JAK inhibitor-naïve SIMPLIFY-1 trial, where a rapid and sustained increase in Hgb was observed in subjects randomized to momelotinib, which contrasted with the acute and profound reduction in Hgb by treatment with the standard-of-care, ruxolitinib. Notably, subjects who crossed over to momelotinib treatment following 24 weeks of ruxolitinib therapy experienced a rapid and substantive increase in Hgb, ultimately achieving sustained Hgb levels that exceeded those observed in the pretreatment baseline period.

In totality, over 1,200 subjects have been treated with momelotinib across more than 20 clinical studies, with approximately 1,000 myelofibrosis patients treated to date. Uniquely among the JAK inhibitor class, this substantive body of clinical data has demonstrated consistent and reproducible therapeutic benefits for momelotinib across all three hallmarks of myelofibrosis, anemia, enlarged spleen and symptoms. In general, momelotinib has proven to be generally well tolerated, with certain patients having received continuous daily dosing of momelotinib for more than 11 years, indicative of momelotinib's potential to provide long-term tolerability and sustained benefit. In the randomized phases of SIMPLIFY-1 and SIMPLIFY-2, the most commonly reported treatment emergent adverse events for subjects treated with momelotinib were thrombocytopenia, diarrhea, headache, asthenia and nausea. The most commonly reported Serious Adverse Events (SAEs) were anemia, atrial fibrillation, diarrhea, pneumonia and cardiac failure. These SAEs include events assessed as both related and unrelated to momelotinib and each occurred in < 4% of subjects.

Momelotinib – Next Steps

During the first quarter of 2022, we announced positive topline results from the MOMENTUM clinical trial for patients with myelofibrosis. The randomized double-blind global Phase 3 trial demonstrated a statistically significant improvement in symptoms, anemia and splenic response, as compared to danazol. The trial enrolled 195 myelofibrosis patients who were symptomatic, anemic and had been treated previously with a JAK inhibitor. Based on the positive results, we plan to submit an NDA with the FDA in the second quarter of 2022. Data from MOMENTUM, along with data from more than 820 myelofibrosis patients previously treated with momelotinib, will form the basis of the global registration strategy for momelotinib. Additionally, the initiation of a Phase 2 study examining momelotinib in combination with SRA515—our novel BRD 4 BET inhibitor—for the treatment of myelofibrosis is planned for the first half of 2022.

Our BET Inhibitor – SRA515

SRA515 (formerly AZD5153), a selective BRD4 BET inhibitor with a unique bivalent binding mode

Inhibitors of the Bromodomain and Extra-terminal Domain (BET protein family consisting of BRD2, BRD3, BRD4 and BRDT) can modify a range of pathological cellular processes, including the initiation and continuation of transcription and cell cycle control. BET inhibition can lead to decreased inflammatory cytokine release, anti-fibrotic activity and reduced mutant cell proliferation, all of which are indicative of disease-modifying effects. Several BET inhibitors are under clinical investigation in multiple solid tumor and hematologic indications, including myelofibrosis.

SRA515 is a selective BRD4 inhibitor with a novel bivalent binding mode that inhibits both protein bromodomains, resulting in improved potency. Unlike currently available JAK inhibitors, momelotinib is not overtly myelosuppressive in contrast to the approved JAK inhibitors, therefore the combination of momelotinib and SRA515 may provide an efficacy and safety advantage over other JAK inhibitor plus BET inhibitor combinations and allow for prolonged dose intensity and treatment duration. This trial will be designed to provide preliminary proof of concept for a future confirmatory study and support potential additional studies of momelotinib with other novel agents in development for myelofibrosis. Trial initiation is anticipated to begin in the first half of 2022.

Clinical overview of SRA515

Clinical experience includes dosing of a total of 61 patients thus far:

- 34 patients with monotherapy; variety of solid tumors;
- 15 patients in combination with olapraib; ovarian and pancreatic tumors;
- 4 patients in combination with acalabrutinib; relapsed/refractory lymphoma;
- 8 patients in combination with venetoclax; AML; and
- Duration treatment range (<1 - ~19 months); last reported median duration of 1.3 months.

Our DDR Candidate – SRA737

SRA737, a Potent, Highly Selective, Orally Bioavailable Chk1 Inhibitor

SRA737 is a potent, highly selective, orally bioavailable small molecule inhibitor of Checkpoint kinase 1, an emerging target for the treatment of cancer which has a key role in the DNA Damage Response. SRA737 was investigated in two Phase 1/2 clinical trials that were initiated in the third quarter of 2016 in the United Kingdom under a Clinical Trial Authorization (CTA). SRA737 was licensed to us in September 2016 and in January 2017, we successfully transferred sponsorship of the trials to Sierra.

Checkpoint kinase 1 (Chk1) is a serine-threonine kinase and master regulator of cell cycle progression and the DNA Damage Response (DDR) replication stress response. One of the hallmarks of cancer is genomic instability. A major source of genomic instability in certain tumors arises as a consequence of dysregulated cell cycle checkpoints and aberrant DNA replication, resulting in high replication stress (RS), which is manifested by stalled replication forks and associated DNA damage. Chk1 regulates multiple cell-cycle phases, temporarily inhibiting the progression

of cell replication and division in order to ensure proper replication of the genome and repair of collapsed or damaged replication forks. Chk1 stabilizes stalled replication forks, manages origin firing to avoid further replication stress, and mediates DNA repair via homologous recombination in the event of fork collapse. Tumors with high RS become reliant on Chk1 to mitigate the potentially catastrophic consequences of excess genomic instability. As such, Chk1 represents a promising therapeutic target in cancers with high RS, as inhibiting Chk1 drives excessive genomic instability which can result in replication catastrophe and tumor cell death.

During the second quarter of 2019, we reported preliminary efficacy and tolerability data from these two trials at the 2019 ASCO Annual meeting. In the fourth quarter of 2020, we announced an amendment to the license agreement with CPF to allow for the potential future clinical development of SRA737.

SRA737-01 Phase 1/2 Monotherapy Trial

This signal-seeking Phase 1/2 study (NCT02797964) was designed to investigate the safety and tolerability of continuous, oral daily dosing of SRA737, as well as to survey a broad range of cancer indications and genetic contexts in the expansion phase, in order to evaluate preliminary anti-tumor activity and delineate potential genetic signatures and/or tumor indications that might warrant additional therapeutic investigation.

At the 2019 ASCO Annual meeting, we reported preliminary efficacy and tolerability data from this trial. Evidence of anti-tumor activity was observed in subjects with high grade serous ovarian carcinomas, colorectal, prostate and non-small cell lung cancers; no RECIST partial responses or complete responses were confirmed, but several noteworthy tumor reductions were recorded.

SRA737-02 Phase 1/2 Low-Dose Gemcitabine Combination Trial

Extensive preclinical data, as well as emerging clinical data, support the synergistic interaction between Chk1 inhibition and gemcitabine. Gemcitabine profoundly depletes DNA replication building blocks, and targets proliferating cells by inducing replication stress through induction of stalled replication forks and double-strand breaks. Low concentrations of gemcitabine cause a prolonged cell cycle S-phase and induce hallmarks of replication stress without inducing overt cytotoxicity. The critical role of Chk1 in mediating cellular responses to replication stress affords the opportunity to combine SRA737 with sub-therapeutic concentrations of the replication stress-inducing agent gemcitabine.

This signal-seeking Phase 1/2 study (NCT02797977) was designed to investigate the safety and tolerability of SRA737 in combination with sub-therapeutic, low dose gemcitabine (LDG), as well as to evaluate preliminary anti-tumor activity of SRA737 potentiated by LDG in tumors with genetic alterations predicted to confer increased intrinsic RS and Chk1i sensitivity. Relative to standard-of-care, gemcitabine doses tested were approximately 10-25% of a standard chemotherapeutic dose.

At the 2019 ASCO Annual meeting, we reported preliminary efficacy and tolerability data from this trial. Overall, Partial Responses were observed in six subjects and 41 subjects had a best response of Stable Disease (SD); durable SD lasting ≥ 4 months was recorded in 32 subjects and was observed in all expansion cohorts. The combination of SRA737+LDG was generally well tolerated.

Asset Purchase Agreement

In August 2018, we entered into an Asset Purchase Agreement with Gilead whereby we acquired worldwide rights to the pharmaceutical product momelotinib, an investigational orally-bioavailable JAK1, JAK2 and ACVR1 inhibitor together with all related intellectual property rights and certain other related assets. Pursuant to the agreement, we made a one-time upfront payment of $3.0 million in August 2018. In October 2019, we entered into an amendment to the Asset Purchase Agreement in which we agreed to issue, subject to certain conditions, shares of common stock and a warrant to purchase common stock to Gilead in consideration for meaningfully reduced royalty rates and elimination of a near term milestone payment in the Asset Purchase Agreement. In January 2020, we entered into a securities purchase agreement with Gilead, pursuant to which we issued to Gilead 725,283 shares of our common stock and a warrant to purchase 725,283 shares of common stock at a price per share of $13.20 (see Note 11 to our Consolidated Financial Statements under Item 8 of this Form 10-K for information pertaining to exercise of the warrant subsequent to December 31, 2021). Pursuant to the amended agreement, milestone payments

of up to an aggregate of $190.0 million may become payable to Gilead upon the achievement of certain regulatory and commercial milestone events, including a milestone payment of $25.0 million due upon the approval of momelotinib from the U.S. FDA. In addition, we are required to pay Gilead low double-digit to high-teens percent tiered combined royalties based upon net sales.

License Agreements

AstraZeneca License Agreement

In August 2021, we entered into a license agreement with AstraZeneca for an exclusive global license for SRA515 and related compounds, which selectively inhibit BRD4. Under the agreement, we have an exclusive license to develop, manufacture and commercialize SRA515 for all therapeutic, prophylactic, palliative and diagnostic uses in humans and animals. We made a one-time upfront cash payment of $8.0 million to AstraZeneca. Pursuant to the license agreement, future aggregate milestone payments of up to $208.0 million may become payable to AstraZeneca upon the achievement of certain development, regulatory and commercial milestones. In addition, we are required to pay AstraZeneca a tiered royalty on worldwide net sales ranging from high single-digits to low double-digits.

The license agreement will expire on the date of expiration of our obligation to pay royalties to AstraZeneca and in any event no later than the 10th anniversary of the expiration of the last valid claim of an AstraZeneca patent. Either party may terminate the license agreement if the other party materially breaches the license agreement, subject to certain cure provisions, and AstraZeneca may terminate the license agreement in certain limited circumstances as described in the license agreement. The license agreement may also be terminated at any time by us upon 60 days' prior written notice to AstraZeneca.

CRT Pioneer Fund LP License Agreement

In September 2016, we entered into an exclusive license agreement with CRT Pioneer Fund LP (CPF) for worldwide rights, know-how and materials to develop SRA737, a small molecule inhibitor targeting Checkpoint kinase 1, an emerging target to treat cancer which has a key role in the DNA Damage Response. Pursuant to the agreement, we made a one-time upfront payment of $7.0 million to CPF in October 2016 and paid $2.0 million to CPF in January 2017 for the successful transfer of two ongoing Phase I clinical trials. Pursuant to the original license agreement, additional milestone payments of up to an aggregate of $319.5 million may have become payable to CPF upon the achievement of certain milestones. In November 2020, we entered into an amendment to the license agreement with CPF, which amended the terms and reduced the amounts of certain future milestones. Pursuant to the amended agreement, future milestone payments of up to an aggregate of $290.0 million may become payable to CPF upon the achievement of certain developmental, regulatory and commercial milestones, including a milestone payment of $2.0 million upon the dosing of the first patient of the first trial of SRA737 following the effective date of the amendment. In addition, we are required to pay CPF, on a product-by-product and country-by-country basis, tiered high single-digit to low double-digit royalties on the net sales of any product successfully developed until the later of (i) the date when such licensed product is no longer covered by a valid patent claim within the licensed intellectual property, (ii) the expiration of any data, marketing or other statutory exclusivity rights covering the licensed product, or (iii) a specified period after the first commercial sale of the licensed product. Such royalties will be reduced on a product-by-product and country-by-country basis under certain conditions, including if certain generic competition exists in such country, or if we are required to pay royalties to third parties in order to develop or commercialize the licensed product.

The license agreement will expire on the date of expiration of our obligation to pay royalties to CPF. Either party may terminate the license agreement if the other party materially breaches the license agreement, subject to certain cure provisions, and CPF may terminate the license agreement in certain limited circumstances as described in the license agreement. The license agreement may also be terminated at any time by us upon 90 days' prior written notice to CPF.

Carna Biosciences, Inc. Collaboration Agreement

In May 2016, we entered into an exclusive license agreement with Carna Biosciences, Inc. (Carna) for worldwide rights to develop and commercialize SRA141, a small molecule kinase inhibitor targeting Cdc7. In exchange for this exclusive right, we paid Carna an upfront payment of $0.9 million in June 2016. In June 2020, we entered into a collaboration agreement with Carna effectively terminating the license agreement. Pursuant to the collaboration agreement, Carna paid an upfront fee of $0.3 million for the exclusive worldwide rights for SRA141 and other transition services. In addition, we may be entitled to single-digit royalties on product sales, on a product-by-product basis, and low to mid-teen profit share on royalty and non-royalty income.

The collaboration agreement will expire on the date of expiration of Carna's obligation to pay royalties to us. We may terminate the collaboration agreement if Carna materially breaches the agreement, subject to certain cure provisions. The collaboration agreement may also be terminated at any time by Carna upon 30 days' prior written notice to us.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for momelotinib, SRA515 and SRA737 and future product candidates, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary or intellectual property rights. Our strategy is to seek to protect our proprietary position and intellectual property position by, among other methods, filing patent applications related to our proprietary technology and product candidates in the United States and in foreign jurisdictions. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We have acquired all rights to patent portfolios directed to compositions of matter and methods of use related to momelotinib and other JAK 1/2 and ACVR1 inhibitors. As of December 31, 2021, these rights included three issued U.S. patents and one pending U.S. divisional application comprising claims directed to compositions and analogs of momelotinib and methods of using momelotinib for the treatment of myelofibrotic indications as a single agent. Two of these patents will expire in 2028 while the third patent will expire in 2030, absent any extensions. Any patent issuing from the pending U.S. application is expected to expire in 2028. It should be noted that for issued U.S. patents, up to five years of patent term extension is available for a single patent directed to the composition of momelotinib, bringing the possible patent exclusivity in the U.S. out to 2035. As of December 31, 2021, these rights also include 54 issued foreign patents in 48 jurisdictions, including Australia, Canada, China, several countries in Europe, Japan, Korea, Mexico, Russia and others comprising claims directed to compositions of momelotinib for the treatment of myelofibrotic indications as a single agent. These foreign patents, and any patent issuing from the pending foreign patent application, are expected to expire in 2028, absent any extension. It should be noted that for issued European patents, up to five years of term extension is available via a Supplementary Protection Certificate (SPC) for a single patent directed to the composition of momelotinib, bringing the possible patent exclusivity in Europe out to 2033. As of December 31, 2021, these rights also included one issued U.S. utility patent and one reissued U.S. utility patent, and one pending reissue application comprising claims directed to different polymorph and salt forms of momelotinib, and methods of their use for the treatment of myelofibrotic indications. These patents will expire in 2035, absent any extension. As of December 31, 2021, these rights also included 51 issued foreign patents, and 13 pending foreign patent applications in 52 jurisdictions and one regional office, including Australia, Brazil, Canada, China, several countries in Europe, EPO, Hong-Kong, India, Israel, New Zealand, Mexico, Japan, Korea, Singapore and Taiwan comprising claims directed to different polymorph and salt forms of momelotinib. These foreign patents, and any patent issuing from these pending foreign patent applications, are expected to expire in 2035, absent any extension. As of December 31, 2021, these rights also included four issued foreign patents in four jurisdictions, including Australia, New Zealand, Singapore and South Africa comprising claims directed to methods of using momelotinib for the treatment of anemia. As of December 31, 2021, these rights also included one issued U.S. patent comprising claims directed to methods of using momelotinib for the treatment of ACVR1-mediated diseases. This U.S. patent will expire in 2037, absent any extensions. Additionally, as of December 31, 2021, these rights also included one pending U.S. patent application and 16 foreign pending applications in 14 jurisdictions and two regional patent offices including Argentina, Australia, Brazil, Canada, China, Eurasian Patent Office, European Patent Office, Japan, Korea and others comprising claims directed to platelet count-agnostic

methods of using momelotinib for the treatment of myelofibrosis. Additionally, as of December 31, 2021, these rights also included one pending Patent Cooperation Treaty application comprising claims directed to methods of using momelotinib for the treatment of joint inflammation. We have filed and will continue to file patent applications directed to the composition of matter and methods of use related to various aspects of momelotinib as they develop.

We have exclusively licensed rights to SRA515 (AZD5153) patents owned by AstraZeneca AB directed to compositions of matter and methods of use related to SRA515, a selective BRD4 BET inhibitor, and its analogs. As of December 31, 2021, these rights included three issued U.S. patents and one pending U.S. continuation application comprising claims directed to compositions and analogs of SRA515 and methods of using SRA515 for the treatment of cancer. The three issued patents will expire in 2035, absent any extensions. Any patent issuing from the pending U.S. application is expected to expire in 2035. As of December 31, 2021, these rights also included 71 issued foreign patents, and 19 pending foreign patent applications in 88 jurisdictions, including Australia, Brazil, Canada, China, several countries in Europe, Japan, Korea, Mexico, Russia and others comprising claims directed to claims directed to composition, and its analogs of SRA515 and methods of using SRA515 for the treatment of cancer. These foreign patents, and any patent issuing from these pending foreign patent applications, are expected to expire in 2035, absent any extension. Additionally, as of December 31, 2021, these rights also included one pending Patent Cooperation Treaty application comprising claims directed to the methods of using SRA515 and venetoclax as a combination therapy for the treatment of a hematological malignancy. We will continue to file patent applications directed to the composition of matter and methods of use related to various aspects of SRA515 as they develop.

We have exclusively licensed CPF's rights to patents owned by Cancer Research Technology (CPF), a subsidiary of Cancer Research UK (CRUK), directed to compositions of matter and methods of use related to SRA737 and other Chk1 inhibitors. As of December 31, 2021, these rights included two issued U.S. patents and two pending U.S. patent application comprising claims directed to compositions of SRA737 and methods of using SRA737 for the treatment of cancer indications as a single agent, or in combination with a DNA damaging agent. The two issued U.S. patents and any patents issuing from the pending U.S. utility application are expected to expire in 2033, absent any adjustments or extensions. As of December 31, 2021, these rights also included 28 issued foreign patents and 7 pending foreign patent applications in 28 foreign jurisdictions, including Australia, Canada, China, Europe and Japan comprising claims directed to compositions of SRA737 and methods of using SRA737 for the treatment of cancer indications as a single agent, or in combination with a DNA damaging agent. These foreign patents, and any patents issuing from these pending foreign patent applications, are expected to expire in 2033, absent any extensions. As of December 31, 2021, these rights also included, one pending U.S. application and 4 pending foreign applications comprising claims directed to biomarkers and patient selection when using SRA737 to treat cancer indications. Any patents issuing from these pending patent applications are expected to expire in 2038, absent any adjustments or extensions. As of December 31, 2021, these rights also included one pending U.S. application and 8 pending foreign applications comprising claims directed to methods of using SRA737 in combination with PARP inhibitors for inhibiting tumor reduction. Any patents issuing from these pending patent applications are expected to expire in 2038, absent any adjustments or extensions. As of December 31, 2021, these rights also included one pending U.S. application and 8 pending foreign applications comprising claims directed to methods of using SRA737 as a monotherapy or in combination therapy to treat cancer indications. Any patents issuing from these pending patent applications are expected to expire in 2039, absent any adjustments or extensions. As of December 31, 2021, these rights also included one pending U.S. patent application and 2 pending foreign patent applications filed by the Company and The University of Texas M.D. Anderson Cancer Center comprising claims directed to methods of using SRA737 to treat cancer indications. Any patents issuing from these pending patent applications are expected to expire in 2040, absent any adjustments or extensions. Additionally, as of December 31, 2021, these rights also included one pending U.S. patent application and 9 pending foreign patent applications comprising claims directed to methods of using SRA737 in the treatment of cancer associated with an intermediate mutational burden (TMB), or genetic abnormality in one or more particular genes associated with replicative stress. Any patents issuing from these pending patent applications are expected to expire in 2040, absent any adjustments or extensions. Additionally, as of December 31, 2021, these rights included one pending Patent Cooperation Treaty application comprising claims directed to methods for the synthesis of CHK1 inhibitors. We have filed and will continue to file patent applications directed to the composition of matter and methods of use related to various aspects of SRA737 as they develop.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. In the future, if and when our product candidates receive approval by the FDA, the European Medicines Agency (EMA) or other foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each product candidate and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

As with other oncology companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, patent applications that we may file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Our issued patents and any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before momelotinib, SRA515, or SRA737 can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our scientific advisors and consultants, and invention assignment agreements with our employees. 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 our relationship with a third party.

Competition

The hematology and oncology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We may face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies that are available for the indication or indications for which they are approved and new therapies that may become available in the future.

To our knowledge, there are currently three approved myelofibrosis drugs that specifically rely on JAK inhibition, ruxolitinib, marketed by Incyte Corporation as Jakafi® in the United States and by Novartis as Jakavi in the rest of the world and fedratinib, marketed by Celgene Corporation (now part of Bristol Meyers Squibb (BMS)) as Inrebic® in the United States and Europe. Both of these are approved for intermediate and high-risk myelofibrosis. Recently, pacritinib, marketed by CTI Biopharma Corp as Vonjo® was approved for a subset of myelofibrosis patients with platelet counts less than 50,000/uL. However, to our knowledge, there are no drugs that target JAK1, JAK2 and ACVR1/ALK2 on the market, nor in development. Other competitors developing myelofibrosis therapeutics include BMS, Morphosys (formerly Constellation Pharma), AbbVie, Kartos, Incyte and Geron. BMS is developing luspatercept in a Phase 3 clinical trial for myelofibrosis. Morphosys is developing pelabresib (CPI-0610), a BET inhibitor in Phase 3 clinical trial in combination with ruxolitinib. AbbVie is currently conducting two Phase 3 clinical trials in combination with ruxolitinib for JAKi naïve and previously JAKi treated patients. Kartos announced clinical trial plans for KRT-232, a MDM2 inhibitor for JAKi relapsed or refractory myelofibrosis patients. Incyte is conducting Phase 3 clinical trials to evaluate parsaclisib, in combination with ruxolitinib. Geron is conducting a Phase 3 trial for imetelstat for relapsed and refractory myelofibrosis. In addition, there are several Phase 1 and Phase 2 clinical trials being conducted in myelofibrosis by various companies, including a Phase 2 study of a deuterated

form of momelotinib being run by Zelgen Biopharmaceuticals in China. Several additional companies are advancing assets in the early stages of development potentially for the myelofibrosis market. If momelotinib is approved, it will compete with existing therapies for the indication or indications for which it is approved. While we believe that momelotinib may have the ability to provide an anemia benefit in addition to treating the other manifestations of myelofibrosis, which we believe is unique within the JAK inhibitor class of agents, the market for momelotinib is competitive, and physicians and other prescribers may not recommend or prescribe momelotinib over competing products.

To our knowledge, there are no approved drugs that specifically target BET inhibitors. BMS, Incyte, Morphosys and AbbVie are all developing BET inhibitors as monotherapy or in combination with approved JAK inhibitors, across various stages of clinical development. Plexxicon and Zenith Epigenetics are also developing BET inhibitors in combination for solid and hematological malignancies. To our knowledge, SRA515 is the only bivalent, BRD4 specific inhibitor in clinical development. If SRA515 is approved, it will compete with existing therapies and currently marketed drugs for the indication or indications for which it is approved.

To our knowledge, there are no approved drugs that specifically target Chk1 on the market, but there are a number of competitors in clinical development, at a similar stage of development or more advanced than us. To our knowledge, Esperas Pharma is conducting a Phase 1/2 clinical trial of an oral Chk1 inhibitor as monotherapy and in combination with gemcitabine in patients with advanced or metastatic cancer. Acrivon Therapeutics recently in-licensed the Chk1/Chk2 inhibitor ACR-368 (formally prexasertib) from Eli Lilly and intends to develop in various solid tumors. There are also preclinical programs focused on developing Chk1 inhibitors. If SRA737 is approved, it will compete with existing therapies and currently marketed drugs for the indication or indications for which it is approved.

Many of the companies against which we may compete have significantly greater financial and other resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the hematology and oncology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our momelotinib program. Development efforts and clinical results of other companies may be unsuccessful or terminated, which could result in a negative perception of momelotinib, decreases in our stock price and adverse regulatory impacts, which could have a material and adverse effect on our ongoing development programs and our business.

Our commercial opportunity could be reduced or eliminated if any competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain FDA or foreign regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors who may place restrictions on patient access to our drugs in seeking to encourage the use of generic or cheaper drugs. If we fail to compete effectively, our business and operating results would be harmed.

Sales and Marketing

We are currently establishing our commercialization and distribution capabilities. We intend to grow our commercial operations functions substantially in preparation for the potential FDA approval of momelotinib. We plan to invest resources to develop the appropriate commercial infrastructure to launch momelotinib in the United States, if approved. We are also exploring options for potential strategic partnerships, collaborations and alliances or licensing arrangement with third parties for the commercialization of momelotinib in certain global regions.

Manufacturing

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third parties for the manufacture and supply of preclinical study and clinical trial materials in relation to our lead product

candidate, momelotinib, including materials for any combination trials that we may undertake, and any future potential product candidates that we may develop for preclinical and clinical testing, as well as for commercial manufacture if momelotinib receives marketing approval.

We do not currently have arrangements in place for redundant supply. We believe that our manufacturers have sufficient capacity to meet our current demand and, in the event that they fail to meet our demand, adequate alternative sources for such materials exist. However, there is a risk that if supplies are interrupted or result in poor yield or quality, it would materially harm our business. We will continue to evaluate product demand requirements and qualify alternate sources for momelotinib, and our other product candidates on an as-needed basis.

Due to the COVID-19 pandemic, we have recently begun to experience some supply chain delays including resourcing constraints by some of our manufacturing partners. There is a risk that if our supply chain is further interrupted, it would limit our ability to source drug substance and drug product for our clinical trials and may result in delays to the timing of our commercialization plans and could potentially increase our costs which would materially harm our business.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our contract manufacturing organizations are required to comply with current good manufacturing practice (cGMP) regulations, which are regulatory requirements for the production of pharmaceuticals that will be used in humans.

Government Regulation

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or FDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, consent decrees, fines, refusal of government contracts, restitution, disgorgement, civil or criminal penalties, and criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

Pharmaceutical product development for a new product or certain changes to an approved product in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the product candidate for each indication for which FDA approval is sought. 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.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies, and formulation studies in accordance with FDA's good laboratory practice requirements and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent IRB ethics committee, either centralized or with respect to each clinical site, before each clinical trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA after completion of all pivotal trials;
- determination by the FDA within 60 days of its receipt of an NDA to accept the filing for substantive review;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP requirements to ensure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality, and purity, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Prior to beginning the first clinical trial with a product candidate in the United States, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices (GLPs). The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational new drug to eligible human subjects under the supervision of a qualified investigator. Clinical trials must be conducted (i) in compliance with federal regulations; (ii) in compliance with good clinical practice (GCP), an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors, and which includes the requirement that all research subjects provide their informed consent for their participation in any clinical study; and (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness 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 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. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board (IRB) for approval. An IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects and has the authority to approve, require modifications in (to secure approval), or disapprove research. IRB review serves an important role in the protection of the rights and welfare of human research subjects. Regulatory authorities, the IRB, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the clinical trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of

qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which may review data and endpoints at designated check points, make recommendations and/or halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

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

- Phase 1: The product candidate is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism, and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- Phase 2: The product candidate is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages, and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3: The product candidate is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

Post-approval clinical trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality, and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

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

Further, as a result of the COVID-19 pandemic, we may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus. For example, the FDA has issued guidance on conducting clinical trials during the pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including certain reporting requirements, and additional guidance on the good manufacturing practice considerations for responding to COVID-19 infection and other topics. We may be required to make further adjustments to our clinical trials or business operations based on current or future guidance and regulatory requirements as a result of the COVID-19 pandemic.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development nonclinical and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information

are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA 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. Once the submission is accepted for filing, the FDA begins a substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing.

The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review drug products are reviewed within ten to twelve months; most applications for priority review drugs are reviewed in six to eight months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment or provide a treatment where no adequate therapy exists. For biologics, priority review is further limited only for drugs intended to treat a serious or life-threatening disease relative to the currently approved products. The review process for both standard and priority review may be extended by FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that 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. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with current good manufacturing practices (cGMPs) is satisfactory and the NDA contains data that provide evidence that the drug is safe and effective in the indication studied. If the FDA determines that the application, manufacturing process, or manufacturing facilities are not acceptable, it will outline the deficiencies in a Complete Response Letter and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After 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 will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase 3 clinical trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies, or manufacturing. If a Complete Response Letter is issued, the sponsor must resubmit the NDA, addressing all of the deficiencies identified in the letter to the FDA satisfaction, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. If, 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. FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. As a condition of NDA approval, the FDA may require Risk Evaluation and Mitigation Strategies (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 (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 REMS can materially affect the potential market and profitability of the drug, and typically require substantial documentation and communication with the FDA.

Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may also require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could impact the timeline for regulatory approval or otherwise impact ongoing development programs.

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.

Pediatric Information

Under the Pediatric Research Equity Act (PREA), NDAs or 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. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA generally does not apply to a drug for an indication for which orphan designation has been granted; however, beginning in 2020, PREA will apply to NDAs for orphan-designated drugs if the drug is molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that FDA has determined is substantially relevant to the growth or progression of a pediatric cancer. The Best Pharmaceuticals for Children Act (BPCA) provides NDA holders a six-month extension of any exclusivity—patent or non-patent—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, FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Expedited Development and Review Programs

The FDA has a Fast Track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. With regard to a Fast Track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

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

In addition, a product may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. In addition, the FDA currently requires pre-approval of promotional materials as a condition for accelerated approval, which could adversely impact the timing of the commercial launch of the product. Accelerated approval

or Fast Track programs do not reduce the amount of clinical data necessary to establish the drug is both safe and effective or the standards for approval.

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

Fast Track designation, priority review, accelerated approval, and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process. We previously announced that the FDA has granted Fast Track designation to momelotinib for the treatment of patients with intermediate/high-risk myelofibrosis who have previously received a JAK inhibitor. Even if a product qualifies for Fast Track designation or any of these other programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may continue to explore some of these opportunities for our product candidates as appropriate.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly-available information to gain knowledge regarding the progress of development programs.

Post-Approval Requirements

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

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on post-approval or Phase IV clinical studies, if applicable;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases, and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising, and promotion of drug products. A company can only promote the indications that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. In many cases, physicians view such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory agencies have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA-approved labelling.

The Hatch-Waxman 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. 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 generic competitors in support of approval of an abbreviated new drug application (ANDA). An ANDA provides for marketing of a 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.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product 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 applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carve 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 the listed patents, the ANDA application will not be approved 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 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 once the ANDA has been accepted for filing by the FDA. 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 approving the ANDA 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 applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Marketing Exclusivity and Patent Term Extension

Market exclusivity provisions authorized under the FDCA can delay the submission and approval of certain marketing applications for products containing the same active ingredient. Upon NDA approval of a new chemical entity (NCE), which is a drug that contains no active moiety that has been approved by FDA in any other NDA, that drug receives five years of marketing exclusivity during which FDA cannot receive any ANDA seeking approval of a generic version of that drug. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which FDA cannot approval an ANDA for a generic drug that includes the change. An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent term extension. 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). The time can be shortened if FDA determines that the applicant did not pursue testing and review with due diligence. The total patent term after the extension may not exceed 14 years from NDA approval. For patents that might expire during the review phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The Director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted. Up to five years of patent term extension is potentially available for a single US issued patent directed to the momelotinib composition of matter upon NDA approval. We have acquired patent rights including two issued U.S. utility patents and one pending reissue application comprising claims directed to a polymorph and salt form of momelotinib. These patents will expire in 2035, absent any extension. If five years of patent term extension is applied to one of these patents, the patent exclusivity for momelotinib in the U.S. would extend to either 2040 or the maximum allowable 14-year limit from NDA approval, whichever is sooner.

During the exclusivity period, the FDA may not approve or even accept for review an abbreviated new drug application (ANDA) or an NDA submitted under Section 505(b)(2) (505(b)(2) NDA), submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal

right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

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

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

Other Healthcare Laws

In the U.S., the research, manufacturing, distribution, sale and promotion of drug products that we are developing are subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, state Attorneys General, and other state and local government agencies. For example, sales, marketing and scientific/educational grant programs must comply with applicable health care fraud and abuse laws, such as the federal Anti-Kickback Statute, the federal False Claims Act, Stark law, and implementing regulations, and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Other laws and regulations that may apply to prescription drug manufacturers include the Sunshine Act, prescription drug price reporting requirements, and various state transparency and reporting laws. All business activities of prescription drug manufacturers are also potentially subject to federal and state consumer protection and unfair competition laws.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act (PPACA) amended the intent element of the federal statute so that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to commit a violation. This statute has been interpreted broadly to apply to arrangements between pharmaceutical manufacturers on the one hand and any referral source on the other, including prescribers, purchasers and formulary managers. The term “remuneration” has been broadly interpreted to include anything of value, including, for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests, and service fees, unless expressly exempted or protected by a safe harbor. Further, the statute has been interpreted to cover any arrangement where one purpose of the remuneration was to obtain remuneration in exchange for referral or to induce further referrals for an item or service. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria of an applicable safe harbor for protection from liability under the federal Anti-Kickback

Statute. The reach of the Anti-Kickback Statute was broadened by PPACA, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute such that the government does not need to prove that a person had the intent to specifically violate the statute in order to find a violation. In addition, the PPACA 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 false or fraudulent claim for purposes of the federal False Claims Act (discussed below) or the civil monetary penalties statute, which imposes fines against any person who is determined to have presented or caused to be presented claims 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. Additionally, many states have adopted laws similar to the federal Anti-Kickback Statute, and some of these state prohibitions apply to referral of patients for healthcare items or services reimbursed by any third-party payer, not only the Medicare and Medicaid programs in at least some cases, and do not expressly provide for certain safe harbors or impose different requirements for safe harbor protection under applicable state laws.

The federal False Claims Act imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false or fraudulent claim for payment by a federal healthcare program. The qui tam provisions of the False Claims Act allow a private individual to bring civil actions on behalf of the federal government alleging that the defendant has submitted or cause to be submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically. In addition, various states have enacted false claims laws analogous to the False Claims Act. Many of these state laws apply where a claim is submitted to any third-party payer and not merely a federal healthcare program. There are many potential bases for liability under the False Claims Act. Liability arises, primarily, when an entity knowingly submits, or causes another to submit, a false claim for reimbursement to the federal government. The False Claims Act has been used to assert liability on the basis of inadequate care, kickbacks and other improper referrals, improperly reported government pricing metrics such as Best Price or Average Manufacturer Price, improper use of Medicare billing numbers when detailing the provider of services, improper promotion of off-label uses (i.e., uses not expressly approved by FDA in a drug's label), and allegations as to misrepresentations with respect to the services rendered. Our future activities relating to the reporting of discount and rebate information and other information affecting federal, provincial, state and third party reimbursement of our products, and the sale and marketing of our products and our service arrangements or data purchases, among other activities, may be subject to scrutiny under these laws. We are unable to predict whether we would be subject to actions under the False Claims Act or a similar state law, or the impact of such actions. However, the cost of defending such claims, as well as any sanctions imposed, could adversely affect our financial performance. Also, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including healthcare fraud, and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers. The false statements statute prohibits 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.

In addition, we may be subject to, or our marketing activities may be limited by, data privacy and security regulation in the U.S. and foreign jurisdictions in which we conduct our business, including jurisdictions in which we conduct our clinical trials. For example, HIPAA and its implementing regulations established uniform federal standards for certain "covered entities" (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information. The American Recovery and Reinvestment Act of 2009 included expansion of HIPAA's privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates"—independent contractors, service providers or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, 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.

The Physician Payment Sunshine Act, or the Sunshine Act, requires applicable manufacturers and certain distributors of prescription drugs, among other products, that are available for coverage by Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Secretary of HHS: (i) payments and or other transfers of value made by that entity, or by a third-party as directed by that entity, to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician healthcare professionals (such as physician assistants and nurse practitioners, among others) and teaching hospitals,

or to third parties on behalf of physicians or teaching hospitals; and (ii) physician ownership (including immediate family ownership) and investment interests in the entity. There are also an increasing number of state and local "sunshine" or transparency and reporting laws that require applicable manufacturers to make reports to states on pricing and marketing information. The U.S. federal government discloses the reported information on a publicly available website. 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 certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. These federal, state, and local laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. If we fail to track and report as required by these laws or otherwise comply with these laws, we could be subject to the penalty provisions of the pertinent state and federal authorities.

Because of the breadth of these health care 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 or refusal to allow us to enter into supply contracts, including government contracts, the curtailment or restructuring of our operations, and corporate integrity agreement, which impose certain compliance, certification and reporting obligations, 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 or if we contract with vendors or independent contractors outside of the U.S., we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-approval requirements, including safety surveillance, anti-corruption/anti-bribery laws, anti-kickback laws, healthcare fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals. While we are not aware of any current issues, we are unable to predict whether we will be subject to actions under applicable healthcare laws, or the impact of such actions on our business. However, the costs of defending such actions or claims, as well as any sanctions imposed, could result in a material adverse effect on our business or financial condition.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. Sales of pharmaceutical products for which we receive regulatory approval for commercial sale will depend, in part, on the availability of third-party coverage and adequate reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. These third-party payers may deny coverage or reimbursement for a product or therapy in whole or in part if they determine that the product or therapy was not medically appropriate or necessary. Third-party payers may attempt to control costs by limiting coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication, and by limiting the amount of reimbursement for particular procedures or drug treatments.

The cost of pharmaceuticals continues to generate substantial governmental and third-party payer interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. The product candidates that we develop may not be considered medically necessary or cost-effective. A payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Some third-party payers also require pre-approval or prior authorization of coverage for new or innovative drug therapies before they will reimburse healthcare providers who prescribe such therapies or patients

who use such prescription drugs. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, these requirements or any announcement or adoption of such proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and to operate profitably.

The marketability of any product candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. There can be no assurance that our products will be considered medically reasonable and necessary for a specific indication, that our products will be considered cost-effective by third-party payers, that coverage or an adequate level of reimbursement will be available or that the third-party payers' reimbursement policies will not adversely affect our ability to sell our products profitably.

In addition, in many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the United States and generally prices tend to be significantly lower.

Healthcare Reform

In the U.S. and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs.

Enacted in March 2010, the Patient Protection and Affordable Care Act, as amended, or PPACA, is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. Among other things, PPACA revises the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with healthcare practitioners and a significant number of provisions are not yet, or have only recently become, effective. For example, in 2020, HHS and CMS issued various rules that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of these rules implemented during the Trump administration. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies. The impact of these lawsuits as well as legislative, executive, and administrative actions of the Biden administration on us and the pharmaceutical industry as a whole is unclear.

There have been judicial and Congressional challenges and amendments to certain aspects of the PPACA. In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013, which will remain in effect through 2031, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. In January 2013, the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations.

There have been legislative and judicial efforts to repeal, replace, or change some or all of the PPACA, including measures taken during the Trump administration. For example, in June 2021 the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the PPACA, dismissing the case on procedural grounds without specifically ruling on the constitutionality of the PPACA. Thus, the PPACA will remain in effect in its current form. It is possible that the PPACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and healthcare measures promulgated by the Biden administration will impact the PPACA, our business, financial condition and results of operations. The Bipartisan Budget Act of 2018, or the BBA, among other things, also amended the PPACA, effective January 1, 2019, by increasing from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In addition, CMS published a final rule that would give states greater flexibility, effective January 1, 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the PPACA for plans sold through such marketplaces.

Further, there have been several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. In addition, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases and allowing Medicare to negotiate pricing for certain covered drug products. The impact of these regulations and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is currently unknown. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, a number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. We expect additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

Other Governmental Regulation

Our business activities may be subject to the Foreign Corrupt Practices Act of 1977, as amended, or FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything

of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the SEC and the Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing, among other things, research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drugs, and reimbursement requirements. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority. 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 studies or marketing of the product in those countries. Certain countries outside of the U.S. have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies. The approval process varies from country to country and the time may be longer or shorter than that required to obtain FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country and may require us to perform additional pre-clinical or clinical testing.

In the European Union, Member States require both regulatory clearances by the national competent authority and a favorable ethics committee opinion prior to the commencement of a clinical trial. Under the European Union regulatory systems, marketing authorization applications may be submitted under either a centralized or decentralized procedure or national procedure. An additional route (mutual recognition procedure) is based on the recognition of granted marketing authorizations by one or more EU countries. The centralized procedure is compulsory for certain types of medicines, including human medicines containing new active substances to treat cancer.

We would be subject to the centralized authorization procedure, which provides for the grant of a single marketing authorization by the European Commission that is valid for all 27 European Union Member States, as well as Iceland, Liechtenstein and Norway (who, together with the European Union Member States) are members of the European Economic Area (EEA). Under the centralized procedure, pharmaceutical companies submit a single marketing authorization application to the EMA. By law, a company can only start to market a medicine once it has received a marketing authorization.

The UK is no longer a member of the EU, but EU law remains applicable in Northern Ireland. There are a number of new marketing authorization routes available in the UK, Great Britain (England, Scotland and Wales) or Northern Ireland, in addition to the national procedure. As with the EU position, a company can only start to market a medicine in the UK once it has received a marketing authorization.

European Regulation of Clinical Trials and Grant of Marketing Authorization

Pharmaceutical products in the European Union are subject to regulation under comprehensive legislation enacted by the European Commission in the European Medicinal Products Directive (Directive 2001/83/EC), as amended. Centrally authorized products are also regulated by Regulation (EC) No. 726/2004. This legislation is binding on all Member States together with ancillary legislation governing research. In the UK, the main legislative texts relating to human medicines is the Medicines Act 1968 and the Human Medicines Regulation 2012.

Clinical Trial Authorization

Clinical trials in the European Union are regulated under European Council Directive 2001/20/EC (Clinical Trials Directive) on the implementation of GCP in the conduct of clinical trials of medicinal products for human use. The Clinical Trials Directive requires the sponsor of an investigational medicinal product to obtain a CTA, much like an IND in the United States, from the national competent authority of a European Union Member State in which the clinical trial is to be conducted. The application for CTA must satisfy detailed requirements for the protection of trial subjects including requirements relating to consent and specific rules for minors and adults unable to consent by reason of incapacity. The CTA application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the Council Directive and corresponding national laws of the Member States and further detailed in applicable guidance, including the European Commission Communication 2010/C 82/01. A clinical trial may only be commenced after an Ethics Committee has given its approval.

A sponsor of a clinical trial must also follow certain procedures, including obtaining a unique EudraCT number by entering specified relevant information in the EudraCT Community Clinical Trial System. In addition, Member States require that the manufacture and/or importation of investigational medicinal products be authorized. Sponsors of investigational medicinal products must ensure compliance with, among other things, GCP and good manufacturing practice (GMP) as well as requirements pertaining to safety reporting.

In April 2014, Regulation EU No 536/2014 (Clinical Trials Regulation) was adopted to replace the Clinical Trials Directive. The Clinical Trials Regulation entered into application on January 31, 2022 and is intended to simplify the current rules for clinical trial authorization and standards of performance. For instance, there will be a streamlined application procedure via a single-entry point, a European Union portal and database. The new clinical trial portal and database will be maintained by the EMA in collaboration with the European Commission and the European Union Member States. The objectives of the new Regulation include consistent rules for conducting trials throughout the European Union, consistent data standards and adverse events listing, and consistent information on the authorization status. Additionally, information on the conduct and results of each clinical trial carried out in the European Union will be made publicly available.

The main legislation that applies to clinical trials in the UK is the UK Medicines for Human Use (Clinical Trials) Regulations 2004, which transposes the Clinical Trials Directive into domestic law. Consequently, the requirements and obligations that relate to the conduct of clinical trials in the UK currently remain largely aligned with the EU position. A CTA will be required to conduct a clinical trial in the UK, together with Ethics Committee approval. However, the sponsor of a clinical trial in the UK must be established in the UK or a country on an approved list (currently limited to the EU Member States plus Iceland, Liechtenstein and Norway) or appoint a legal representative who is established on one of the aforementioned countries. Clinical trials should also be registered on an established international register such as ISRCTN registry or ClinicalTrials.gov. The UK also requires the manufacture and/or importation of investigational medicinal products to be authorised. There is no mutual recognition agreement between the UK and EU on GMP, so medicines manufactured in the UK would be subject to GMP release in the EU.

Procedural Routes for Marketing Authorization in the European Union and UK

The European Union system for authorization of medicinal products for human use offers several routes: the centralized procedure, the decentralized procedure, and the mutual recognition procedure, as well as domestic national routes. The centralized procedure provides for the grant of a single marketing authorization that is valid for

all European Union Member States as well as the EEA countries of Iceland, Liechtenstein and Norway. The centralized procedure is mandatory for certain categories of investigational products, including human products containing a new active substance indicated for the treatment of certain diseases, including cancer, AIDS, diabetes and neurodegenerative illness; orphan medicinal products; and medicinal products manufactured using biotechnological processes. Applications for marketing authorization for such medicines must be submitted to the EMA, in which the Committee for Medicinal Products for Human Use (CHMP) is generally responsible for conducting the initial assessment of a product.

The decentralized and mutual recognition procedures are applicable to the majority of conventional medicinal products and are both based on the principle of recognition of a marketing authorization by one or more Member States. The decentralized procedure is available for applicants who wish to market a product in various European Union Member States where such product has not received marketing approval in any European Union Member State before. In this procedure, an application for marketing authorization is submitted simultaneously in several Member States, one of them being chosen as the "Reference Member State." At the end of the procedure, national marketing authorizations are granted in the Reference and in the concerned Member States. The mutual recognition procedure is compulsory when a medicinal product has already received a marketing authorization in one Member State and is to be marketed in a Member State other than that in which it was first authorized. Any national marketing authorization granted by a European Union Member State's national authority can be used to support an application for its mutual recognition by other Member States. Marketing authorization applications can also be submitted directly to the Member State's national competent authority under the national route (if the centralized route is not compulsory). There are now multiple routes to obtain a marketing authorization in the UK, Great Britain or Northern Ireland, which are broadly categorized as either (1) national routes (i.e. the innovative licensing and access procedure (ILAP), the national procedure, rolling review, EC Decision Procedure (ECDP), the MR/DC reliance procedure and unfettered access from Northern Ireland); or (2) international routes (i.e. Access Consortium to market a medicine in the UK, Australia, Canada, Singapore and/or Switzerland; or the Project Orbis program for cancer treatments). The application procedure will depend on the relevant procedure chosen.

All granted centrally authorized marketing authorizations automatically became Great Britain (GB) marketing authorizations on 1 January 2021. Though there are several ways to obtain a marketing authorization for GB (and Northern Ireland) discussed above, the EDRCP is available for marketing authorizations approved under the centralized procedure. Under this procedure the UK's regulator, the MHRA, can rely on the decision of the European Commission on the approval of a new marketing authorization under centralized procedure for a period of two years from 1 January 2021 when determining an application for a GB marketing authorization. Applicants submit a letter of intent to submit an EDRCP to the MHRA at least 4 weeks before the submission of the application for the EDRCP marketing authorization application. The marketing authorization application is submitted after receipt of the positive opinion from the CHMP.

Standard for Approval of a Marketing Authorization in the European Union and UK

The objective of the EMA is the comprehensive evaluation of benefit/risk profile of a new medicinal product going through the centralized procedure. This evaluation involves showing that the product has significant efficacy and safety, together with a satisfactory plan for risk management post-marketing. The CHMP is the EMA's expert committee responsible for human medicinal products. The CHMP is responsible for conducting the initial review of centrally authorized marketing authorization applications and for assessing modifications or extensions (variations) to an existing marketing authorization. It also considers the recommendations of the Pharmacovigilance Risk Assessment Committee on the safety of medicines on the market and when necessary, recommends to the European Commission changes to a medicine's marketing authorization, or its suspension or withdrawal from the market. The marketing authorization application is similar to the NDA in the United States. All application procedures require an application in the common technical document (CTD), which includes the submission of detailed information about the manufacturing and quality of the product, and non-clinical and clinical trial information. The main scientific principle used by the CHMP in the evaluation of medicinal products is the benefit/risk ratio based on quality, efficacy, safety, and risk management considerations. The CHMP assesses whether the data it reviews comply with the ICH-harmonized Good Practices published for GCP, GMP and good laboratory practice (GLP). The CHMP also considers whether studies concluding efficacy and safety of products have sufficient statistical power.

Marketing authorizations for the UK are submitted to the MHRA. As the Medicinal Products Directive is transposed into domestic law, the standards of clinical efficacy, safety, chemical control and manufacture as at 31 December 2020 (the end of the transition period for the UK's exit from the EU) are retained. As Northern Ireland continues to apply EU law, medicines regulation for Great Britain is likely to be closely aligned with the EU for some time.

Other Regulatory Issues

An exemption to the rule requiring marketing authorization permits Member States of the European Union (and the UK) to make a product available for compassionate use to patients with a chronically or seriously debilitating disease or whose disease is considered life threatening, and who cannot be treated satisfactorily by an authorized medicinal product. The medicinal product concerned must be undergoing clinical trials or the subject of application for marketing authorization.

Quality of the medicinal products in question is governed by the GMP Directives. These lay down the legal framework for GMP for both marketed medicinal products and investigational products in clinical trials. The Directive obliges manufacturers to comply with GMP for an effective pharmaceutical quality assurance, quality control, systems for recording and reviewing complaints and a system for prompt recall of products in the distribution network. With regards to post–marketing safety of newly authorized products, the EMA monitors and supervises the safety of medicines that have been authorized in the EU to ensure their benefits outweigh their risks. Volume 4 of EudraLex published by the European Commission provides GMP guidelines used to interpret the principles of GMP laid down in the GMP Directives.

The pharmacovigilance legislation imposes a duty on Member States to collect information on the risks of products with regards to patients' or public health. That information must refer to adverse events arising from the use of the medicinal product within the terms of the marketing authorization as well as use outside the authorized indication and use associated with occupational exposure.

There is a similar obligation on the marketing authorization holder (MAH) to operate a robust pharmacovigilance system equivalent to that of the relevant Member State. The MAH must evaluate all safety and effectiveness information scientifically, consider the options for risk minimization and take appropriate measures as necessary. As part of the pharmacovigilance system, the MAH must have permanently and continuously an appropriately qualified person responsible for pharmacovigilance, maintain a pharmacovigilance master file, operate a risk management system for each medicinal product, monitor the outcome of risk minimization measures contained in the risk management program and continually update the risk management system and monitor the pharmacovigilance system to determine whether there are new risks or changes to the risk-benefit profile of the product(s).

Two recent developments have been introduced which further expand the European regulatory framework: the Falsified Medicines Directive and the Pharmacovigilance Directive. The Falsified Medicines Directive obliges manufacturers of medicinal products to audit their suppliers of active substances to ensure compliance with GMP. It also introduces a new obligation on product manufacturers to inform the competent authority (e.g., ANSM) and the marketing authorization holder if they become aware that these products may be falsified, whether they are being distributed through the legitimate supply chain or by illegal means. The Pharmacovigilance Directive obliges marketing authorization holders to monitor the safety of authorized products and detect any change in their risk-benefit profile. A new pan-European clinical trial data information database has been created that will be complementary to the database established for pharmacovigilance (Regulation (EC) No 726/2004 with respect to centrally authorized medicinal products). In addition, Commission Implementing Regulation (EU) No 520/2012 outlines the practical implications for marketing authorization holders, national competent authorities, and the EMA. Also, Commission Delegated Regulation (EU) No 357/2014 on post-authorization efficacy studies specifies the situations in which such studies may be required. Post-authorization efficacy studies may be required where concerns relating to some aspects of efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed, or where the understanding of the disease, the clinical methodology or the use of the medicinal product under real-life conditions indicate that previous efficacy evaluations might have to be revised significantly. Brexit will disrupt the operation of pre- and post-authorization clinical trial infrastructure. The rules around GMP and pharmacovigilance in the UK currently remain similar to the EU requirements. However, the

Falsified Medicines Directive will not apply in Great Britain though it is likely that the UK will implement a procedure to minimise the risk of falsified medicines.

In addition, in May 2016, the EU formally adopted the General Data Protection Regulation, or GDPR, which applies to all EU member states from May 25, 2018 and replaced the European Union Data Protection Directive. The GDPR has imposed many new or additional requirements including, but not limited to, obtaining consent of the individuals to whom the personal data relates, the nature and scope of notifications provided to the individuals, the security and confidentiality of the personal data, data breach notification and using third party processors in connection with the processing of the personal data. Failure to comply with the GDPR could subject us to regulatory sanctions, delays in clinical trials, criminal prosecution and/or civil fines or penalties. Additionally, GDPR creates a direct cause of action by individual data subjects. The GDPR is a complex law and the regulatory guidance is still evolving, including with respect to how the GDPR should be applied in the context of clinical trials or other transactions from that we may gain access to personal data. Beginning in 2021, the UK will be a "third country" under the GDPR. These changes in the law will increase our costs of compliance and result in greater legal risks. Other countries maintain different privacy laws that we are subject to.

Approval Outside the United States/European Union

For marketing outside the United States and the European Union, we are subject to foreign regulatory requirements governing human clinical testing and marketing approval for our products. Whether or not FDA or European Commission approval has been obtained for a product, approval of the product by comparable regulatory authorities of countries outside of the United States or the European Union, as the case may be, must be obtained prior to marketing the product in those countries. Approval in one country does not assure that a product will be approved in another country. In certain countries, regulatory requirements and approval processes are similar to those in the United States and the European Union, where approval decisions by regulators are based on the regulators' review of the results of clinical trials performed for specific indications. Other countries may have a less comprehensive review process in terms of data requirements and may rely on prior marketing approval from a foreign regulatory authority in other countries such as the United States or the European Union. In many countries outside of the United States, approvals for pricing, coverage and reimbursement offered by third-party payers, including government payers and private insurance plans, are also required.

Human Capital

As of December 31, 2021, we had 109 active employees, of which 23 had M.D. or doctorate degrees and 70 were engaged in research and development activities. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good. Developing a diverse, equitable and inclusive culture is critical to our success in attracting and retaining the top talent necessary to deliver on our growth strategy. We continue to invest in the creation of a work environment where our employees can feel inspired to deliver their best at the workplace.

Diversity, Equity and Inclusion

We are committed to intentionally cultivating a culture of inclusion where all feel welcomed and valued for their backgrounds, perspectives and experiences. We believe our company is stronger because of the diversity in experiences and backgrounds our employees bring to work. Our commitment to diversity extends through our recruitment, retention, learning and engagement. Our objective is to appreciate each other as individuals with unique experiences rather than define one another by traits such as race, sexual orientation or geographic location. We also mandated training for all managers to prevent workplace harassment.

Compensation and Benefits, Professional Development and Performance Management

We strive to provide compensation and benefits that are competitive to market and equitable within the organization. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success

of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives. In addition, we offer comprehensive benefits and services that help meet the varying needs of our employees.

We invest in the professional development of our team members through regular informal feedback and guidance, as well as formal performance reviews to evaluate performance against pre-established objectives. In addition, we support targeted learning and development opportunities, such as conference attendance, to meet demonstrated needs.

Employee Safety

A safe, healthy and secure work environment is our top priority for all employees. In response to the COVID-19 pandemic, we have continued to prioritize employee safety and follow local, state, federal and Centers for Disease Control and Preventions (CDC) guidelines. Clear COVID-19 policies and safety protocols have been established and updates are provided to all employees.

Corporate Information

We were incorporated in Delaware in May 2003 as Phenome Systems, Inc. and changed our name to ProNAi Therapeutics, Inc. in April 2004. Shortly thereafter, we merged with SenseGene Therapeutics Inc., a Michigan corporation, with ProNAi Therapeutics, Inc. being the surviving corporation. We changed our name to Sierra Oncology, Inc. in January 2017. Our principal executive offices are located at 1820 Gateway Drive, Suite 110, San Mateo, California 94404, and our telephone number is (650) 376-8679. Our website address is www.sierraoncology.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report, and you should not consider information on our website to be part of this Annual Report.

Available Information

We file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other information with the Securities and Exchange Commission (SEC). Our filings with the SEC are available free of charge on the SEC's website at *www.sec.gov* and on our website under the "Investors" tab as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this report, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment.

Summary Risk Factors

The below summary of risk factors provides an overview of many of the risks we are exposed to in the normal course of our business activities. As a result, the below summary risks do not contain all of the information that may be important to you, and you should read the summary risks together with the more detailed discussion of risks set forth following this section under the heading "Risk Factors," as well as elsewhere in this Annual Report on Form 10-K. Additional risks, beyond those summarized below or discussed elsewhere in this Annual Report on Form 10-K, may apply to our activities or operations as currently conducted or as we may conduct them in the future or in the markets in which we operate or may in the future operate. Consistent with the foregoing, we are exposed to a variety of risks, including risks associated with the following:

- We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- Our business is highly dependent on the success of momelotinib. If we are unable to successfully develop, obtain regulatory approval for and commercialize momelotinib, or experience significant delays in doing so, our business will be materially harmed.
- If further preclinical development or clinical trials of momelotinib, or any other future product candidates that we may develop or acquire fail to demonstrate acceptable safety and efficacy or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of current or future product candidates.
- Our business, results of operations and financial condition have been adversely affected and may be materially adversely affected by the COVID-19 pandemic.
- We may form or seek strategic alliances, licensing arrangements or other collaborations in the future or enter into a strategic transaction. We may be unable to form or enter into such alliances or arrangements, and we may not realize the expected benefits of any such transaction.
- Past and future acquisitions could disrupt our business and harm our financial condition and operating results.
- The manufacture of momelotinib and SRA515 requires outsourced, custom manufacturing and we may encounter difficulties in production, particularly with respect to formulation, process development or scaling up of our manufacturing capabilities. If our third-party manufacturers or suppliers encounter such difficulties, our ability to provide supply of momelotinib for preclinical studies, clinical trials or our products for patients, if approved, or danazol for the MOMENTUM trial could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.
- Our reliance on third-party manufacturing partners or suppliers may cause our supply of research and development, preclinical and clinical development materials to become limited or interrupted or fail to be of satisfactory quantity or quality.
- We face significant competition from other hematology and oncology companies, and our operating results will suffer if we fail to compete effectively.
- If we are unable to adequately prepare the market for the potential future commercialization of a product, we may not be able to generate product revenue once marketing authorization is obtained. We currently are establishing our marketing and sales organization and have limited experience in

marketing products. If we are unable to successfully establish marketing and sales capabilities or enter into agreements with third parties to market and sell momelotinib or any future product candidates, we may not be able to generate product revenue.

- We may be unable to obtain U.S. or foreign regulatory approval of momelotinib, and, as a result, we may be unable to commercialize momelotinib.
- Our internal information technology systems, or those used by our CROs or other contractors or consultants, may fail or suffer security breaches.
- If we or any of our independent contractors, consultants, collaborators, manufacturers, vendors or service providers fail to comply with healthcare and data privacy laws and regulations, we or they could be subject to enforcement actions, which could result in penalties and affect our ability to develop, market and sell momelotinib or any future product candidates and may harm our reputation.
- If we are not able to obtain and enforce patent protection for our technologies or momelotinib, development and commercialization of our product candidates may be adversely affected.
- We have a significant number of outstanding warrants which may cause significant dilution to our stockholders, have a material adverse impact on the market price of our common stock, make it more difficult for us to raise funds through future equity offerings and discourage an acquisition of us by a third party.

Risks Related to Our Business and Industry

We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses for the foreseeable future.

We are a clinical stage hematology and oncology company with a limited operating history. Since inception, we have incurred significant operating losses. Our net losses were $94.7 million, $80.9 million and $88.3 million for the years ended December 31, 2021, 2020 and 2019 respectively. As of December 31, 2021, we had an accumulated deficit of $941.2 million. Investment in hematology and oncology product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval and become commercially viable. For example, in June 2016, we decided to suspend the development of our former lead product candidate PNT2258 after an interim analysis of data from a Phase 2 clinical trial of PNT2258 indicated only modest efficacy. We have also decided to suspend the continued development of SRA141, which was licensed to Carna Biosciences in June 2020, to focus our resources on the clinical development of momelotinib, SRA515 and potentially SRA737. We have no products approved for commercial sale and have not generated any revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue the development of product candidates, fund research and preclinical studies and clinical trials, seek to identify additional product candidates, in-license additional products or technologies, seek regulatory approval, prepare for potential commercialization which will require a significant investment in areas related to contract manufacturing and inventory buildup and continue to operate as a public company.

Even if we succeed in commercializing momelotinib, if approved, or any future product candidates we may acquire or develop, we will continue to incur substantial research and development and other expenditures to develop and market these and other product candidates for which we obtain marketing authorization. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our business is highly dependent on the success of momelotinib. If we are unable to successfully obtain regulatory approval for and commercialize momelotinib, or experience significant delays in doing so, our business will be materially harmed.

Our business and future success depend on our ability to successfully obtain regulatory approval for and commercialize momelotinib, a potent, selective and orally bioavailable JAK1, JAK2 and ACVR1 / activin receptor-like kinase-2 (ALK2) inhibitor. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis, and we launched our MOMENTUM Phase 3 clinical trial for momelotinib in the fourth quarter of 2019 after receiving regulatory feedback concerning the design of the trial.

While momelotinib is a late-stage product candidate for which our Phase 3 clinical trial data suggest the potential to provide promising safety and efficacy in patients who are JAK inhibitor-naïve and in patients who have previously received a JAK inhibitor such as ruxolitinib, FDA may disagree with our interpretation of the data and may require additional clinical testing before we can seek regulatory approval and begin commercialization, if at all. While the FDA has provided regulatory clarity concerning the design of MOMENTUM, our Phase 3 clinical trial for momelotinib, there is no guarantee that we will obtain regulatory approval and be able to begin commercialization on the timeline as we anticipate. Before we can generate any revenue from sales of momelotinib, we must complete additional development activities, including the submission of a marketing application such as a NDA or foreign equivalent, for regulatory review and approval in at least one jurisdiction, make substantial investments, obtain access to sufficient commercial manufacturing capacity and engage in significant marketing and commercial access efforts.

We cannot commercialize momelotinib in the United States without first obtaining regulatory approval from the FDA. Similarly, we cannot commercialize momelotinib outside of the United States without obtaining regulatory approval from similar regulatory authorities outside of the United States, such as the EMA in Europe and the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom. Applications for regulatory approval and regulatory approval of momelotinib in any jurisdiction could be delayed or be denied for many reasons, including but not limited to the following:

- the FDA or foreign regulatory authorities may disagree with the number, design or implementation of our clinical trials;
- the population studied in the clinical trial may not be considered sufficiently broad or representative to assure safety in the full population for which we seek approval;
- the FDA or foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of momelotinib may not meet the level of statistical or clinical significance required by the FDA or foreign regulatory authorities or may otherwise not be sufficient to support the submission of an NDA, marketing authorization application or other submission or to obtain regulatory approval in the United States, the European Union or elsewhere;
- the FDA or foreign regulatory authorities may require us to conduct additional preclinical studies and clinical trials;
- we may be unable to demonstrate to the FDA or foreign regulatory authorities that our product candidate’s response rate, duration of response or risk-benefit ratio for its proposed indication is acceptable;
- the FDA or foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications applicable to the manufacture of momelotinib, the facilities of third-party manufacturers with which we contract for clinical and commercial supplies may fail to maintain a compliance status acceptable to the FDA or foreign regulatory authorities or foreign regulatory authorities may fail to approve facilities of third-party manufacturers with which we contract for clinical and commercial supplies;

- we or any third-party service providers may be unable to demonstrate compliance with current good manufacturing practices (cGMPs) and/or good clinical practices (GCPs) to the satisfaction of the FDA or foreign regulatory authorities, which could result in delays in regulatory approval;
- the regulations or policies of the FDA or foreign regulatory authorities may change in a manner rendering our clinical data insufficient for approval; or
- political factors surrounding the approval process, such as government shutdowns, political instability or global pandemics such as the outbreak of the novel strain of coronavirus, COVID-19.

Even if momelotinib were to be approved by the FDA or foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified patient populations, age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for momelotinib or any future product candidate in one or more jurisdictions, or if any approval contains significant limitations, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the marketing or commercialization of momelotinib or any future product candidate. If competitive products developed by third parties show significant benefit in the indications in which we are developing momelotinib, any planned supportive or primary registration trials may be delayed, altered, terminated or not initiated and any future product candidates may never receive regulatory approval. Our clinical development programs for momelotinib or any future product candidates may also not receive regulatory approval if we have inadequate financial or other resources to advance these product candidates through the clinical trial process. Furthermore, even if we obtain regulatory approval for momelotinib or any future product candidates, we will still need to develop sales, marketing and commercialization infrastructure, or collaborate with a third party for the commercialization of such product candidates, establish commercially viable pricing and obtain approval for coverage and adequate reimbursement from third parties, including government payors. If we are unable to successfully commercialize momelotinib or any future product candidate, we may not be able to generate sufficient revenues to continue our business.

If further preclinical development or clinical trials of momelotinib, or any other future product candidates that we may develop or acquire fail to demonstrate acceptable safety and efficacy or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of current or future product candidates.

Before obtaining marketing approval from regulatory authorities, including the FDA, for the sale of momelotinib or any future product candidates, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of such product candidates in humans.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later preclinical testing and clinical trials, and interim results of a clinical trial do not necessarily predict final results. Many companies in the biotechnology industry have suffered significant setbacks in later-stage clinical trials after achieving positive results in early-stage development, and there is a high failure rate for product candidates proceeding through clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. For example, in June 2016, we announced that we decided to suspend the development of our former lead product candidate PNT2258 after an interim analysis of data from a Phase 2 clinical trial of PNT2258 indicated only modest efficacy. We cannot guarantee that we will be successful in obtaining the required efficacy and safety profile for momelotinib, or any future product candidate. A failure of one or more preclinical studies or clinical trials can occur at any stage of testing.

We previously acquired from Gilead momelotinib, a potent, selective and orally bioavailable JAK1, JAK2 and ACVR1/ALK2 inhibitor. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis, SIMPLIFY-1 and SIMPLIFY-2. Based on the results of the prespecified analyses, neither trial was considered sufficiently compelling to justify the submission of an application for regulatory approval. Although SIMPLIFY-1 met its primary efficacy endpoint of non-inferior spleen volume reduction, it did not meet its key secondary efficacy endpoint of non-inferior reduction in Total Symptom Score (TSS); and although SIMPLIFY-2 did not meet its primary efficacy endpoint of superior reduction in spleen volume, it did meet its key secondary

efficacy endpoint of superior reduction in TSS. In both SIMPLIFY studies, additional secondary endpoints related to transfusion independence rate, transfusion dependence rate, and rate of red blood cell transfusions all favored momelotinib over control and supported the potential for momelotinib to provide meaningful anemia benefits. Based on post hoc analyses of the data for these trials that we subsequently conducted, we believe the trials showed promising substantive spleen and constitutional symptom control. In addition, we believe momelotinib has the potential to provide a differentiated therapeutic profile encompassing anemia-related benefits. As such, we have determined that there is substantial clinical justification for further development of momelotinib.

While we believe the safety and efficacy profile of momelotinib in patients with myelofibrosis appears promising based on the Phase 3 trial results including the MOMENTUM Phase 3 trial, preclinical and clinical data are often susceptible to varying interpretations and analyses, and even if the trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit momelotinib for approval. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. To the extent that the results of our studies and trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, approval of momelotinib may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of momelotinib.

We may experience numerous unforeseen events during, or as a result of, preclinical studies and clinical trials, including the completion of our MOMENTUM clinical trial, that could delay or prevent our ability to receive marketing approval or commercialize momelotinib or other product candidates, including, but not limited to:

- undesirable side effects or other unexpected characteristics of momelotinib or other product candidates, causing us or our investigators, regulators or IRBs to suspend or terminate the trials;
- regulators or IRBs may not authorize us or our investigators to initiate a clinical trial, conduct a clinical trial at a prospective trial site, or amend a clinical trial;
- government or regulatory delays and changes in regulatory requirements, policy and guidelines, including as a result of the COVID-19 pandemic;
- delays in reaching or failure to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites and contract research organizations (CROs), or failure by such CROs or trials sites to carry out the clinical trial in accordance with the terms of our agreements with them;
- negative or inconclusive results of preclinical studies or clinical trials;
- issues with data retention due to lack of adherence to privacy and data protection legislation;decision by us to conduct additional preclinical studies or clinical trials or abandon product development programs;
- a higher number of patients being required for clinical trials or higher than expected drop out rates;
- clinical sites electing to terminate their participation in one of our clinical trials, which would likely have a detrimental effect on subject enrollment;
- delays or difficulties with respect to our clinical trials as a result of the COVID-19 pandemic, such as delays or difficulties in the distribution of clinical trial materials, study monitoring and data analysis;
- failure of third-party contractors to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- inability or unwillingness of patients or medical investigators to follow our clinical trial protocols;
- suspension or termination of clinical trials for various reasons, including unacceptable health risks;
- imposition of a clinical hold for safety reasons or following an inspection of our clinical trial operations or site by the FDA or foreign regulatory authorities;
- greater than expected cost of clinical trials;

- insufficient supply or quality of product candidates or other materials, necessary to conduct clinical trials;
- FDA rejecting or disagreeing with our statistical plan;
- FDA disagreeing with the interpretation of our clinical data;
- delays or additional costs as a result of the United Kingdom's decision to leave the European Union and resulting need to decouple the United Kingdom's regulatory system from that of the European Union; and
- revision of legal or regulatory requirements for approving product candidates.

If we are required to conduct additional preclinical studies or clinical trials or other testing of momelotinib or other product candidates beyond those that we currently contemplate, if we are unable to successfully complete preclinical studies and clinical trials of momelotinib or other product candidates or other testing, or if the results of these studies, trials or tests do not reflect an acceptable safety or efficacy profile, we may:

- be delayed or unable to submit additional CTAs or equivalents in one or more countries;
- not have the permission of the FDA or other health authorities to commence clinical trials, or may have a clinical hold placed on one or more of our clinical trials;
- be delayed in obtaining marketing approval;
- not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any preclinical studies or clinical trials will continue as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical studies and clinical trial delays also could allow our competitors to bring products to market before we do and could impair our ability to successfully commercialize momelotinib or other product candidates, any of which may harm our business and results of operations.

Our business, results of operations and financial condition have been adversely affected and may be materially adversely affected by the COVID-19 pandemic, and a similar public health crises could have a material adverse impact on our business, financial condition and results of operations, including the execution of our clinical trials and the use and sufficiency of our existing cash.

The extent to which the COVID-19 pandemic impacts our business, financial condition and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning the COVID-19 pandemic, the emergence of new variants and increased cases which have led to the reimplementation of restrictions in many areas and the actions to contain the virus or treat its impact.

For instance, our MOMENTUM Phase 3 clinical trial for momelotinib was and other trials may be affected by the COVID-19 pandemic. We launched MOMENTUM in the fourth quarter of 2019 and participant dosing, distribution of clinical trial materials, study monitoring and data analysis were and other trials may be delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward COVID-19 pandemic efforts, or other reasons related to the COVID-19 pandemic. Additionally, some participants and clinical investigators may not be able to comply with clinical trial protocols. For example, quarantines or other travel

limitations (whether voluntary or required) may impede participant movement, affect sponsor access to study sites, or interrupt healthcare services, and we may be unable to conduct our clinical trial. Any such delays to our planned clinical timelines could also impact the use and sufficiency of our existing cash reserves, and we may be required to raise additional capital.

We currently utilize third parties to, among other things, manufacture raw materials, drug product, components, parts, and consumables, perform quality testing and distribute drug product. The COVID-19 pandemic and its adverse effects have become more prevalent in the locations where our third-party manufacturing partners and suppliers conduct business and as a result, we have recently begun to experience some supply chain delays including resourcing constraints by some of our manufacturing partners. There is a risk that if our supply chain is further interrupted, it may limit our ability to source drug substance and drug product for our clinical trials and may result in delays to the timing of our commercialization and potentially increase our costs which could materially harm our business. We may experience constrained supply of momelotinib, SRA515 or, with respect to our planned clinical trials, we could again experience delays in planned site initiations and activations, or experience delays in enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis that could materially adversely impact our business, results of operations and overall financial performance in future periods. Specifically, we may experience impact from changes in how we and companies worldwide conduct business due to the COVID-19 pandemic, including but not limited to restrictions on travel and in-person meetings, prioritization of hospital resources toward pandemic effort, delays in review by the FDA and comparable foreign regulatory agencies, and further disruptions in our supply chain for momelotinib or SRA515. Any such delays to our planned development timelines and pre-commercialization efforts could also impact the use and sufficiency of our existing cash reserves, and we may be required to raise additional capital. Challenging and uncertain economic conditions can make capital raising costly and dilutive. We may be unable to raise additional capital if and when needed, which may result in delays or suspension of our development and potential commercial launch plans.

Further, infections and deaths related to the COVID-19 pandemic are disrupting certain healthcare and healthcare regulatory systems globally. Such disruptions could divert healthcare resources away from, or materially delay review by, the FDA and comparable foreign regulatory agencies. As a result of the FDA's updated industry guidance for conducting clinical trials issued on March 18, 2020, as subsequently updated by the FDA, we may be required to make certain adjustments to our clinical trials, which could delay the submission of our NDA and regulatory approval and increase our costs. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trial or delay in regulatory review resulting from such disruptions could materially adversely affect the development and study of our product candidates. The COVID-19 pandemic may also impact the resources and the availability of FDA to provide feedback and regulatory review or to conduct pre-approval inspections on a timely basis, which will delay our regulatory approval and increase our costs.

In response to the COVID-19 pandemic, many of our employees continue their work outside of our office. In the event of a shelter-in-place order or other mandated local travel restrictions, third parties conducting clinical or manufacturing activities may not be able to access laboratory or manufacturing space, and our core activities may be significantly limited or curtailed, possibly for an extended period of time.

The spread of COVID-19, which has caused a broad impact globally, including restrictions on travel and quarantine policies put into place by businesses and governments, may have a material adverse effect on our business. While the potential economic impact brought by and the duration of the COVID-19 pandemic may be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets and the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic, which may reduce our ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the global effort to control COVID-19 infections could materially and adversely affect our business and the value of our common stock.

The ultimate impact of the COVID-19 pandemic, or any other health epidemic, is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material adverse impact on our operations, and we will continue to monitor the situation closely. To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this "Risk Factors" section.

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

We may experience difficulties in patient enrollment in clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including, but not limited to:

- the number and size of clinical trials for other product candidates in the same therapeutic area that are currently in clinical development, and our ability to compete with such trials for patients and clinical trial sites;
- the patient eligibility criteria defined in the protocols;
- the size of the specific patient populations such as those whose tumors harbor the applicable genetic mutations, if required or other defined subsets of a larger patient population;
- the risk that disease progression will result in death or clinical deterioration before the patient can enroll in clinical trials or before sufficient data has been collected such that the patient contributes no meaningful information for the clinical trial in which the patient is enrolled;
- the proximity and availability of clinical trial sites for prospective patients;
- the design of the trials, including the inclusion of a placebo or comparator arm in a trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion; and
- delays and difficulties in enrollment or patient retention in the trial due to the COVID-19 pandemic.

Our future clinical trials may compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates. This competition reduces the number and types of patients and qualified clinical investigators available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors or clinical trial sites may not allow us to conduct our clinical trial at such site if competing trials are already being conducted there. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. We may also encounter difficulties finding a clinical trial site at which to conduct our trials. Moreover, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy, radiation and other approved therapies, rather than enroll patients in any one of our clinical trials. Global pandemics, such as COVID-19, have negatively affected site initiation, as well as recruitment and retention, at sites in regions or cities whose health care system have become overwhelmed due to the pandemic. For example, as a result of the COVID-19 pandemic, during our MOMENTUM clinical trial several sites paused enrollment or deprioritized clinical trial activities and enrollment. In the future, we may also experience delays or pauses in the delivery of required site activity equipment.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our planned clinical trials, which could prevent completion of these clinical trials and adversely affect our ability to advance any product candidates we may develop.

We have acquired momelotinib from a third party that had already conducted or was in the process of conducting clinical trials. Our acquisition of momelotinib has resulted in us being required to take over responsibility for conducting ongoing momelotinib trials. We may discover that development efforts of the third parties, including but not limited to historical studies and trials conducted by third parties, did not comply with all applicable rules and regulations. Further development and commercialization of momelotinib will require significant financial and operational resources from us.

Prior to our acquisition of momelotinib, third parties had been responsible for all development activities including, drug process, preclinical and clinical development activities, submission of CTAs and INDs, development of the trial protocols, establishment and management of clinical and safety databases, submission of a pediatric investigation plan (PIP), and other activities. Although we believe the historical development activities were conducted in accordance with applicable rules and regulations in material respects, we cannot assure you that we will not discover inaccuracies or noncompliance in prior development activities that have an adverse effect on the future development of momelotinib. For example, a regulatory authority may choose to inspect an investigational site and/or vendor such as a CRO for a momelotinib study that was previously conducted by Gilead such as the SIMPLIFY-1 or SIMPLIFY-2 studies. Findings from such inspections could have an impact on the review of any future marketing applications by the FDA or foreign regulatory authorities.

In connection with our acquisition of momelotinib, we have assumed the responsibility for ongoing clinical studies with momelotinib, including related expenses and manufacturing and regulatory activities, which were previously managed and funded by Gilead. This includes responsibility for the ongoing extended access study, which provides extended access of momelotinib to certain patients previously enrolled in Gilead-sponsored studies, who are currently receiving treatment with momelotinib and have not experienced progression of disease. Further, extended access programs provide supportive safety information for regulatory review. Any adverse events or reactions experienced by subjects in the extended access program may be attributed to momelotinib and may limit our ability to obtain regulatory approval with labeling that we consider desirable, or at all.

We plan to develop product candidates in combination with momelotinib, which can expose us to additional risks.

We plan to develop product candidates in combination with momelotinib or other approved or unapproved therapies. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or comparable foreign regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials prior to approval of the combination therapy. The occurrence of any of these risks could result in our own products, if approved, being removed from the market, require significantly limiting label changes or being less successful commercially.

We also may choose to evaluate product candidates in combination with one or more therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved therapies used in combination face the same regulatory and clinical risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval. If the FDA or comparable foreign regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with our product candidate we develop, we may be unable to obtain approval of or market such combination therapy.

From time to time we may amend the clinical protocols for our product candidates to include additional objectives that could yield important scientific information critical to our overall development strategy. The protocol amendment process requires review and approval by several review bodies, including regulatory agencies and scientific, regulatory and ethics boards. These protocol amendments may not be accepted by the review bodies in the form submitted, or at all, which may delay our planned enhancements to the clinical development program and/or limit or change the type of information we may gather from those studies.

Regulatory, scientific, ethics committee, and possibly other reviews will be required during the activation process for our any product candidates before the protocol is active at any particular site. It is possible that these reviews could require changes to the design of the study. If the FDA, EMA, MHRA, an ethics committee or scientific review board, or another regulatory authority objects to or otherwise does not accept or approve any future protocols or protocol amendments or requires us to further modify trial protocols, our related planned clinical development program may be delayed or suspended and/or we may not be able to gather information we think would be useful to advance development of our product candidates, and our development programs may be adversely affected.

We may expend our limited resources to pursue a particular product candidate, such as momelotinib, and fail to capitalize on product candidates that may later prove to be more profitable or for which there is a greater likelihood of success. In addition, we may intentionally halt or terminate programs in order to conserve capital and focus on our remaining program or programs, which may increase our reliance on those programs to be successful.

Because we have limited financial and managerial resources, we focus our resources on our product candidate, momelotinib. As a result, we may advertently or inadvertently forgo or delay pursuit of opportunities with other product candidates, including SRA737, that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. In addition, if we halt or terminate programs in order to conserve capital and focus on our remaining program or programs, it may increase our reliance on the success of such programs and raise our exposure to the risk of failure among any of our programs.

While we have currently deprioritized development of SRA737, we are exploring options for future development of this product candidate, if any. However, there can be no assurance that we will successfully obtain development support or the funding, through partnership or collaborations, necessary to advance SRA737 on commercially reasonable terms, or at all.

If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, our stock price may decline.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory, product development and commercialization goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, our stock price may decline.

We may form or seek strategic alliances, licensing arrangements or other collaborations in the future or enter into a strategic transaction. We may be unable to form or enter into such alliances or arrangements, and we may not realize the expected benefits of any such transaction.

We evaluate strategic alliances or licensing arrangements, joint ventures or collaborations with third parties and other strategic transactions from time to time including those that will complement or augment our development and commercialization efforts with respect to momelotinib and any future product candidates that we may acquire or develop, or that may provide for other economic value.

For example, in August 2021, we entered into a license agreement with AstraZeneca for an exclusive global license for SRA515 and related compounds. Such license agreement imposes specified diligence, milestone payment, royalty, commercialization, development and other obligations on us and require us to meet development timelines, or to exercise diligent or commercially reasonable efforts to develop and commercialize licensed products, in order to maintain the license. AstraZeneca has the right to terminate a license if we materially breach the agreement and fail to cure such breach within a specified period, in the event of certain patent challenges or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements. If our license agreements are terminated, we may lose our rights to develop and commercialize product candidates and technology, lose patent protection, experience significant delays in the development and commercialization of our product candidates and technology, and incur liability for damages. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, our competitors or other third parties could have the freedom to seek regulatory approval of, and to market, products and technologies identical or competitive to ours and we may be required to cease our development and commercialization of certain of our product candidates and technology. In addition, we may seek to obtain additional licenses from our licensors and, in connection with obtaining such licenses, we may agree to amend our existing licenses in a manner that may be more favorable to the licensors, including by agreeing to terms that could enable third parties, including our competitors, to receive licenses to a portion of the intellectual property that is subject to our existing licenses and to compete with any product candidates we may develop and our technology. Any of the foregoing could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects. Disputes may arise between us and our licensors regarding intellectual property rights subject to a license agreement, including:

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

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensor fail to adequately protect this intellectual property, our ability to develop, manufacture or commercialize products could suffer.

If disputes over intellectual property rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, our business, results of operations, financial condition, and prospects may be adversely affected.

In June 2020, we licensed SRA141 back to Carna Biosciences, the original licensor. We may be entitled to certain profit share on royalty and non-royalty income and royalties on product sales. If Carna Biosciences or its collaborators fail to successfully develop and commercialize SRA141, we will receive limited to no value from this transaction. In September 2016, we entered into an exclusive license agreement with CRT Pioneer Fund LP (CPF) for worldwide rights, know-how and materials to develop SRA737, a small molecule inhibitor targeting Chk1, a promising therapeutic target to treat cancer. If we fail to meet our diligence and other obligations under the license agreement, we could lose our rights to this technology. These licensing agreements or any future strategic transactions and relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, disrupt our management and business, forego potential future economic value or result in the loss of strategic value. These transactions and relationships also may result in a delay in the development of momelotinib or any future product candidates if we become dependent upon the other party and such other party does not prioritize the development of such product candidates relative to its other development activities.

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for momelotinib because it may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view momelotinib as having the requisite potential to demonstrate safety and efficacy. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that would justify such transaction.

Past and future acquisitions could disrupt our business and harm our financial condition and operating results.

We evaluate additional businesses or product candidates from third parties that we believe will complement or augment our existing momelotinib program. For example, in August 2018, we entered into an Asset Purchase Agreement with Gilead whereby we acquired worldwide rights to the pharmaceutical product momelotinib, an investigational orally bioavailable JAK1, JAK2 and ACVR1/ALK2 inhibitor together with all related intellectual property rights and certain other related assets. Even if the assets we acquire have promising markets or technologies, we may not be able to realize the benefit of acquiring such assets if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new product candidates resulting from an acquisition, including momelotinib, which may delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies or benefits from the asset to justify the transaction. The risks we face in connection with strategic transactions, including our acquisition of momelotinib, include, but are not limited to:

- diversion of management time and focus from operating our business to addressing acquisition integration challenges;
- integration of research and development efforts;
- hiring or training of key employees with knowledge regarding the acquired asset;
- changes in relationships with strategic partners as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees, knowledge and processes related to the acquired asset into our organization;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired asset.

Our failure to address these risks or other problems encountered in connection with acquisitions could cause us to fail to realize the anticipated benefits of these transactions, cause us to incur unanticipated liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm our financial condition or operating results.

Provisions of any debt instruments, including the Loan and Security Agreement, may restrict our ability to pursue our business strategies.

In January 2022, we entered into a Loan Agreement with Oxford Finance, LLC pursuant to which we may obtain a loan up to an aggregate principal amount of $125.0 million (of which $50.0 million is subject to the lender’s sole discretion) in four tranches based on certain pre-determined milestones. The Loan and Security Agreement requires us, and any debt instruments we may enter into in the future may require us, to comply with various covenants that limit our ability to, among other things:

- dispose of assets;
- complete mergers or acquisitions;
- incur indebtedness;

- encumber assets;
- pay dividends or make other distributions to holders of our capital stock;
- make specified investments;
- change certain key management personnel; and
- engage in transactions with our affiliates.

These restrictions could inhibit our ability to pursue our business strategies. The Loan and Security Agreement includes customary events of default, including, among others, payment defaults, breach of representations and warrants, covenant defaults, cross-defaults to other debt, judgment defaults, insolvency and bankruptcy defaults, a material adverse change default and delisting of our common stock. If we default under the Loan and Security Agreement, and such event of default was not cured or waived, the lenders could terminate commitments to lend and cause all amounts then outstanding with respect to the debt to be due and payable immediately, which in turn could result in cross defaults under any other debt instruments then outstanding. Our assets and cash flow may not be sufficient to fully repay borrowings under all of our outstanding debt instruments if some or all of these instruments are accelerated upon a default.

We may incur additional indebtedness in the future. The debt instruments governing such indebtedness could contain provisions that are as, or more, restrictive than our existing debt instruments. The credit facility under the Loan and Security Agreement is secured by a lien covering substantially all of our assets, excluding our intellectual property, until the first date on which the aggregate outstanding principal amount of the term loans equals or exceeds $50.0 million, at which time we agree to grant a security interest in our intellectual property. If we are unable to repay, refinance or restructure our indebtedness when payment is due, the lenders could proceed against the collateral granted to them to secure such indebtedness or force us into bankruptcy or liquidation.

The manufacturing of our product candidates may require outsourced, custom manufacturing and we may encounter difficulties in production, particularly with respect to formulation, process development or scaling up of our manufacturing capabilities. If our third-party manufacturers or suppliers encounter such difficulties, our ability to provide supply of our product candidates for preclinical studies, clinical trials or our products for patients, if approved, could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.

As product candidates are developed, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned preclinical studies or future clinical trials.

Due to the COVID-19 pandemic we have recently begun to experience some supply chain delays including resourcing constraints by some of our manufacturing partners. There is a risk that if our supply chain is further interrupted, it would limit our ability to source drug substance and drug product for our clinical trials and may result in delays to the timing of our commercialization plans and could potentially increase our costs which would materially harm our business.

Although we are working to develop commercially viable manufacturing processes, doing so is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, potential problems with process scale up or formulation, process reproducibility, stability issues, lot consistency and timely availability of reagents or raw materials.

Any of these challenges could delay completion of preclinical studies or clinical trials, require bridging studies or trials, or the repetition of one or more studies or trials, increase development costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods and have an adverse effect on our business, financial condition, results of operations and growth prospects.

Our reliance on third-party manufacturing partners or suppliers may cause our supply of research and development, preclinical and clinical development materials as well as future commercial product to become limited or interrupted or fail to be of satisfactory quantity or quality.

We do not have any manufacturing facilities or personnel. We have relied on third parties for the manufacture and supply of preclinical and clinical trial materials in relation to momelotinib and SRA515, including materials for any combination therapy trials that we may undertake, and any future potential product candidates that we may develop for preclinical and clinical testing, as well as for commercial manufacture if momelotinib receives marketing approval. We have engaged, or expect to engage, third-party manufacturers to obtain materials and consumables necessary for the manufacture of momelotinib.

We may be unable to establish further agreements with third-party manufacturers and suppliers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers and suppliers entails additional risks, including, but not limited to:

- reliance on the third party for sufficient quantity and quality;
- the possible breach of the manufacturing or supply agreement by the third party;
- failure to manufacture or supply the product according to our specifications;
- failure to manufacture or supply the product according to our schedule or at all;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or comparator not being properly identified;
- misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions; and
- the reliance on the third party for regulatory compliance, quality assurance and safety reporting.

While we require our third-party manufacturers and suppliers to comply with cGMPs in the manufacture of clinical trial materials and commercial supply, should we obtain approval of momelotinib, these third-party manufacturers and suppliers may cease to continue to comply with cGMPs—which are FDA requirements for ensuring product quality control—or similar regulatory requirements outside the United States. Our contract manufacturers and suppliers are subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, although we are not involved in the day-to-day operations of our contract manufacturers or suppliers, we are ultimately responsible for ensuring that our products and product candidates, and any other materials that may be used in our preclinical studies or clinical trials, are manufactured or supplied in accordance with cGMPs. Therefore, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, quality control and quality assurance. Our failure, or the failure of our third-party manufacturers or suppliers, to comply with applicable regulations could result in momelotinib not being approved or sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of momelotinib or approved products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

Additionally, our third-party manufacturers have experienced and may continue to experience manufacturing difficulties due to resource constraints or as a result of labor disputes, or unstable political environments, or medical pandemics such as the COVID-19 outbreak. For example, many of our raw materials for manufacture of momelotinib are produced in Asia which could impact our ability to manufacture and supply material for clinical and commercial supply. If our contract manufacturers were to encounter any manufacturing difficulties or delays due to these factors, our ability to provide product candidates to patients in clinical trials, or to provide product for treatment of patients once approved, would be jeopardized.

We rely on third-party suppliers for the supply of the raw materials required for the production of our product candidates, and we expect to some extent continue to rely on third-party manufacturers for the commercial supply of any of our product candidates for which we obtain marketing approval. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality, and delivery schedules and non-exclusivity. As a small company, our negotiation leverage is limited, and we are likely to get lower priority than our competitors who are larger than we are. We do not have long-term supply agreements, and we purchase our required supplies on a development manufacturing services agreement or purchase order basis. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require to satisfy our anticipated specifications and quality requirements. Any supply interruption in limited or sole sourced raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supply channel in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would have a material adverse effect on our business.

Any performance failure on the part of our existing or future manufacturers or suppliers, any interruption or poor yield or quality of manufactured or supplied materials, or any interruption or delay caused by a third party being subject to governmental regulations or moratoriums could result in additional costs, not having sufficient quantities or sufficient quality and may delay, prevent or impair our development, commercialization or marketing efforts. We do not currently have arrangements in place for redundant supply. If any one of our current contract manufacturers or suppliers cannot perform as agreed, we may be required to replace that manufacturer or supplier. Although we believe that there are several potential alternative manufacturers or suppliers who could manufacture or supply momelotinib or the materials for trials relating to our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

If our third-party manufacturers or suppliers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages. Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers or suppliers. Our manufacturers and suppliers are subject to federal, state and local laws and regulations in the United States governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' and our suppliers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources.

We do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

Thus, our current and anticipated future dependence upon others for the manufacture or supply of momelotinib or other product candidates and related medicines and materials may adversely affect our development timeline, our future profit margins or our ability to commercialize momelotinib or any future product candidates that receive marketing approval on a timely and competitive basis.

Our product candidates may cause undesirable side effects or have other properties that could halt their development, prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

It is possible that the FDA or foreign regulatory authorities may not agree with any assessment of the safety profile of momelotinib. Undesirable side effects caused by our product candidates could cause us, IRBs, our CROs, the FDA or foreign regulatory authorities to interrupt, delay or discontinue development and could result in a clinical hold on any clinical trial, or the denial of regulatory approval by the FDA or foreign regulatory authorities for any or

all targeted indications. This, in turn, could prevent us from commercializing product candidates and generating revenues from their sale. In addition, if any of our products cause serious or unexpected side effects or are associated with other safety risks after receiving marketing approval, a number of potential significant negative consequences could result, including, but not limited to:

- regulatory authorities may withdraw their approval of this product;
- we may be required to recall the product, change the way it is administered, conduct additional clinical trials or change the labeling of the product;
- the product may be rendered less competitive and sales may decrease;
- our reputation may suffer generally both among clinicians and patients;
- we may be exposed to potential lawsuits and associated legal expenses, including costs of resolving claims;
- regulatory authorities may require certain labeling statements, such as warnings or contraindications or limitations on the indications for use, or impose restrictions on distribution in the form of a Risk Evaluation and Mitigation Strategy (REMS) in connection with approval, if any;
- we may be required to change the way the product is administered or conduct additional preclinical studies or clinical trials; or
- we may be required to change or stop other ongoing clinical trials that may negatively impact the development of the agent for other indications.

If our clinical data demonstrates that momelotinib has an unfavorable safety profile and is unlikely to receive regulatory approval or be successfully commercialized, we may voluntarily suspend or terminate future development of momelotinib.

Any one or a combination of these events could prevent us from obtaining approval and achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing momelotinib, which in turn could delay or prevent us from generating significant revenues from the sale of the product.

We may need to obtain additional capital to complete the potential commercialization of momelotinib and the development and potential commercialization of any future product candidates.

We had cash and cash equivalents of $104.7 million as of December 31, 2021. See Note 11 to our Consolidated Financial Statements under Item 8 of this Form 10-K for additional proceeds received by us during the first quarter of 2022.

We expect to spend substantial capital to advance momelotinib or any future product candidates, in preclinical and clinical development, seek regulatory approvals for such product candidates, establish a commercial sales force to market and manufacture products, if any, that are approved for commercial sale. We also incur significant compliance and administrative costs as a result of operating as a public company.

Our future capital requirements will depend on many factors, including, but not limited to:

- the results of our planned preclinical studies and clinical trials;
- the scope, progress, results and costs of product candidate discovery, preclinical development, laboratory testing and clinical trials for our current and future product candidates;
- the costs, timing and outcome of regulatory review of momelotinib and any other future product candidates;
- the costs of medical affairs and pre-commercialization activities, including regulatory and reimbursement analysis and market research;

- the costs of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for momelotinib or any future product candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator;
- the extent to which we acquire or in-license other drugs and technologies, or to which we out-license our own products and technologies;
- the extent to which we acquire or invest in business, products or technologies, although we currently have no commitments or agreements relating to any of these types of transactions;
- the extent to which we are able to enter into strategic partnerships, collaborations and alliances or licensing arrangements with third parties including for the commercialization of momelotinib in certain global regions;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the success of any collaborations that we may enter into with third parties;
- the timing and amount of milestone and royalty payments;
- the amount of revenue, if any, received from commercial sales of momelotinib or any future product candidates, should any such product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- the compliance and administrative costs associated with being a public company.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, momelotinib, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of momelotinib, if approved, which we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we require but are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the commercialization of momelotinib or other research and development initiatives. In particular, we do not have sufficient funds on hand to adequately prepare for future momelotinib commercialization, if approved. We could also be required to seek collaborators for momelotinib, at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to such product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves. We also may be unable to acquire additional promising product candidates.

We do not have our own laboratory facilities. We rely on third parties to conduct our preclinical studies 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 of or commercialize momelotinib.

We do not have our own laboratory facilities. We depend upon independent investigators and collaborators, such as universities, medical institutions, CROs and strategic partners to conduct our preclinical studies and clinical trials. We expect to have to negotiate budgets and contracts with CROs and trial sites, which may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our preclinical studies and clinical trials, and we control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with GCPs and GLPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for clinical and non-clinical research

intended to support a submission or application to FDA or the comparable foreign authority. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable requirements, the data generated in our studies and trials may be deemed unreliable and the FDA or foreign regulatory authorities may require us to perform additional studies or trials before approving our marketing applications. We cannot assure you that, upon inspection, such regulatory authorities will determine that any of our studies or trials comply with the GCP or GLP requirements. In addition, our studies and trials must be conducted with drug product produced under cGMPs. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat studies or trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

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

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

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

- deficiencies in the conduct of the clinical trials, including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols or to obtain or maintain clinical trial data in accordance with applicable regulatory requirements;
- deficiencies in the clinical trial operations or trial sites;
- the product candidate may have unforeseen adverse side effects;
- deficiencies in the trial designs necessary to demonstrate efficacy;
- fatalities or other adverse events (AEs) arising during a clinical trial due to medical problems that may or may not be related to clinical trial treatments;
- the product candidates may not appear to be more effective than current therapies;
- the quality or stability of the product candidates may fall below acceptable standards; or
- failure to adequately demonstrate study conduct oversight, ensure data integrity, and that clinical trial sites complied with the principles of GCPs.

Although we have never been asked by a regulatory agency, IRB or data safety monitoring board to temporarily or permanently discontinue a clinical trial, if we elect or are forced to suspend or terminate a clinical trial of any

product candidates, the commercial prospects for that product will be harmed and our ability to generate product revenue from that product may be delayed or eliminated. For example, in June 2016, we decided to suspend the development of our former lead product candidate PNT2258 after an interim analysis of data from a Phase 2 clinical trial on PNT2258 indicated only modest efficacy. Furthermore, any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing momelotinib and impair our ability to generate revenue from the commercialization of these products either by us or by our collaboration partners.

Even if we receive regulatory approval to market momelotinib, the market may not be receptive to our product.

Even if we obtain regulatory approval for momelotinib, it may not gain market acceptance among physicians, patients, healthcare payors and/or the medical community. We believe that the degree of market acceptance will depend on a number of factors, including, but not limited to:

- timing of market introduction of momelotinib and competitive products;
- safety and efficacy of our product;
- prevalence and severity of any side effects;
- potential advantages or disadvantages over alternative treatments;
- strength of marketing and distribution support;
- price of our products, both in absolute terms and relative to alternative treatments;
- availability of coverage and reimbursement from government and other third-party payors and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement; and
- sequencing of available products.

If momelotinib is approved for commercial sale and fails to achieve market acceptance, we may not be able to generate significant revenue or achieve or sustain profitability.

We may be subject to requests for access to momelotinib. Demand for compassionate use of our unapproved therapies could strain our resources, delay our drug development activities, negatively impact our regulatory approval or commercial activities, and result in losses.

We are developing momelotinib to treat a life-threatening illness for which there are currently limited therapeutic options. Other companies in our field have been the target of campaigns requesting access to unapproved drugs. If we experience similar request for access campaigns, we may experience significant disruption to our business which could result in losses. We are a small company with limited resources, and any unanticipated trials or access programs resulting from requests for access could deplete our drug supply, increase our capital expenditures, reduce the availability of potentially eligible clinical trial participants, and otherwise divert our resources from our primary goals.

In addition, legislation referred to as "Right to Try" laws have been introduced at the local and national levels, which are intended to give patients access to unapproved therapies. New and emerging legislation regarding expanded access to unapproved drugs for life-threatening illnesses could negatively impact our business in the future. Either activism or legislation related to requests for access may require us to initiate an unanticipated expanded access program or to make momelotinib more widely available sooner than anticipated.

Patients who receive access to unapproved drugs through compassionate use or expanded access programs have life-threatening illnesses and generally have exhausted all other available therapies. The risk for serious adverse events, including those which may be unrelated to momelotinib, in this patient population is high and could have a negative impact on the safety profile of momelotinib, which could cause significant delays or an inability to successfully commercialize momelotinib and could materially harm our business. In addition, in order to perform the controlled clinical trials required for regulatory approval and successful commercialization of momelotinib, we may receive

adverse publicity or experience other disruptions if we do not provide compassionate use access or expanded access programs in response to requests for access from patients in the US or elsewhere in the world. Should we agree to provide compassionate use access or decide to initiate an expanded access program, we could experience adverse publicity or other disruptions related to current or potential participants in such programs. Similarly, we could experience adverse publicity or other disruptions if we were to restructure or pause any compassionate use and/or expanded access program after initiating such a program or after the provision of our product through compassionate access to an individual patient or patients.

We do not have our own laboratory facilities or the ability to discover product candidates. We rely on licensing, acquisition and other forms of strategic relationship to grow our pipeline. Our efforts to acquire additional product candidates and grow our pipeline may be unsuccessful.

We do not have our own laboratory facilities or the ability to discover product candidates. We rely on licensing, acquisition and other forms of strategic relationships to grow our pipeline. We may acquire, or enter into strategic relationships to identify, license and develop, one or more additional product candidates to grow our pipeline. In addition, we may desire to renegotiate our currently existing licensing or asset purchase agreements for any of our product candidates. The identification, evaluation, development and potential acquisition or licensing of additional product candidates is expensive and time-consuming, and our efforts may not lead to the acquisition or licensing of any additional product candidates, that can be successfully developed and commercialized. Competition for viable product candidates is intense, and the acquisition or licensing of product candidates may be more expensive than we are able to afford or may require us to seek additional financing. If our efforts do not lead to the acquisition or successful identification, development and licensing of suitable product candidates, we may be unable to grow our pipeline. In addition, if our efforts to grow our pipeline require us to pursue additional dilutive capital or debt financing strategies, we may experience harm to our financial position and stability.

Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development. For example, they may be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

We face significant competition from other hematology and oncology companies, and our operating results will suffer if we fail to compete effectively.

The hematology and oncology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We may face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies that are available for the indication or indications for which they are approved and new therapies that may become available in the future.

To our knowledge, there are currently three approved myelofibrosis drugs that specifically rely on JAK inhibition. Ruxolitinib, marketed by Incyte Corporation as Jakafi® in the United States and by Novartis as Jakavi in the rest of the world and fedratinib, marketed by Celgene Corporation (now part of Bristol Meyers Squibb (BMS)) as Inrebic® in the United States and Europe. Both of these are approved for intermediate and high-risk myelofibrosis. Recently, pacritinib, marketed by CTI Biopharma Corp as Vonjo® was approved for a subset of myelofibrosis patients with platelet counts less than 50,000/uL. However, to our knowledge, there are no drugs that target JAK1, JAK2 and ACVR1/ALK2 on the market, nor in development. Other competitors developing myelofibrosis therapeutics include BMS, Morphosys (formerly Constellation Pharma), AbbVie, Kartos, Incyte and Geron. BMS is developing luspatercept in a Phase 3 clinical trial for myelofibrosis. Morphosys is developing pelabresib (CPI-0610), a BET inhibitor in Phase 3 clinical trial in combiniation with ruxolitinib. AbbVie is currently conducting two Phase 3 clinical trials in combination with ruxolitinib for JAKi naïve and previously JAKi treated patients. Kartos announced clinical trial plans for KRT-232, a MDM2 inhibitor for JAKi relapsed or refractory myelofibrosis patients. Incyte is conducting Phase 3 clinical trials to evaluate parsaclisib, in combination with ruxolitinib. Geron is conducting a Phase 3 trial for imetelstat for relapsed and refractory myelofibrosis. In addition, there are several Phase 1 and

Phase 2 clinical trials being conducted in myelofibrosis by various companies, including a Phase 2 study of a deuterated form of momelotinib being run by Zelgen Biopharmaceuticals in China. Several additional companies are advancing assets in the early stages of development potentially for the myelofibrosis market. If momelotinib is approved, it will compete with existing therapies for the indication or indications for which it is approved. While we believe that momelotinib may have the ability to provide an anemia benefit in addition to treating the other manifestations of myelofibrosis, which we believe is unique within the JAK inhibitor class of agents, the market for momelotinib is competitive, and physicians and other prescribers may not recommend or prescribe momelotinib over competing products.

To our knowledge, there are no approved drugs that specifically target BET inhibitors. BMS, Incyte, Morphosys and AbbVie are all developing BET inhibitors as monotherapy or in combination with approved JAK inhibitors, across various stages of clinical development. Plexxicon and Zenith Epigenetics are also developing BET inhibitors in combination for solid and hematological malignancies. To our knowledge, SRA515 is the only bivalent, BRD4 specific inhibitor in clinical development. If SRA515 is approved, it will compete with existing therapies and currently marketed drugs for the indication or indications for which it is approved.

To our knowledge, there are no approved drugs that specifically target Chk1 on the market, but there are a number of competitors in clinical development, at a similar stage of development or more advanced than us. To our knowledge, Esperas Pharma is conducting a Phase 1/2 clinical trial of an oral Chk1 inhibitor as monotherapy and in combination with gemcitabine in patients with advanced or metastatic cancer. Acrivon Therapeutics recently in-licensed the Chk1/Chk2 inhibitor ACR-368 (formally prexasertib) from Eli Lilly and intends to develop in various solid tumors. There are also preclinical programs focused on developing Chk1 inhibitors. If SRA737 is approved, it will compete with existing therapies and currently marketed drugs for the indication or indications for which it is approved.

Many of the companies against which we may compete have significantly greater financial and other resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the hematology and oncology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our momelotinib program. Development efforts and clinical results of other companies may be unsuccessful or terminated, which could result in a negative perception of momelotinib, decreases in our stock price and adverse regulatory impacts, which could have a material and adverse effect on our ongoing development programs and our business.

Our commercial opportunity could be reduced or eliminated if any competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain FDA or foreign regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors who may place restrictions on patient access to our drugs in seeking to encourage the use of generic or cheaper drugs. If we fail to compete effectively, our business and operating results would be harmed.

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

Our ability to compete in the highly competitive oncology industry depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We have in the past and may in the future continue to experience changes in our executive management team resulting from the departure of executives or subsequent hiring of new executives, which may be disruptive to our business. Any changes in business strategies can create uncertainty, may negatively impact our ability to execute our business strategy and advance development, and may ultimately be unsuccessful. The impact of hiring new executives may not be immediately realized. We are substantially dependent on the continued service of our existing management, scientific and medical personnel,

including Dr. Stephen Dilly, our President and Chief Executive Officer and Dr. Barbara Klencke, our Chief Medical Officer, because of their familiarity with momelotinib and our development efforts. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, including due to illness resulting from COVID-19, and our inability to find suitable replacements, could result in delays in product development and harm our business.

Our operations are conducted in regions where significant competition exists for key personnel and employees. Many other oncology companies and academic and research institutions are located in these regions. Competition for skilled personnel in these markets is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees.

Should momelotinib receive marketing approval in the United States, Canada, or elsewhere in the world, we would need to hire a substantial number of specialized personnel, including field-based personnel, unless we were to collaborate with a third party to commercialize momelotinib. If we are responsible for commercializing momelotinib, we would need to increase our administrative headcount to support such expanded development and commercialization operations with respect to momelotinib. Our ability to attract and retain qualified personnel in the future is subject to intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses and our current financial position. The loss of the services of any of our senior management could delay or prevent the development and commercialization of momelotinib or have other adverse effects on our business for an indefinite term. In particular, if we lose any members of our current senior management team, we may not be able to find suitable replacements in a timely fashion, if at all, and our business may be harmed as a result.

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

Prior to acquiring momelotinib, our most advanced product candidate was in Phase 1/2 development. Advancing momelotinib, if approved, through commercialization will require us to develop or expand our regulatory, manufacturing, medical affairs, marketing and sales capabilities or contract with third parties to provide these capabilities for us. If approved, we must also successfully integrate the employees and operations related to the commercialization of momelotinib. Maintaining additional relationships and managing our future growth will impose significant added responsibilities on members of our management. We must be able to manage our development efforts effectively, manage our clinical trials effectively, hire, train and integrate additional management, development, medical affairs, administrative and sales and marketing personnel, improve our managerial, development, operational and finance systems, and expand our facilities, all of which may impose a strain on our administrative and operational infrastructure. Our future financial performance will depend, in part, on our ability to manage this growth effectively. Even after regulatory approval, we may not be able to accomplish these tasks, failure of which could prevent us from successfully commercializing momelotinib.

If we are unable to adequately prepare the market for the potential future commercialization of a product, we may not be able to generate product revenue once marketing authorization is obtained. We are currently establishing our marketing and sales organization and have limited experience in marketing products. If we are unable to successfully establish marketing and sales capabilities or enter into agreements with third parties to market and sell momelotinib or any future product candidates, we may not be able to generate product revenue.

We have substantial preparations remaining to be ready for potential future commercialization, and currently have limited commercialization expertise, including no sales, marketing or distribution capabilities and no experience in marketing products. Advancing momelotinib to potential approval will require us to begin commercialization

preparation activities and incur related expenses before we obtain final trial results and know whether MOMENTUM will support regulatory approval. These activities will include, among other things, the development of an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other companies to recruit, hire, train and retain qualified marketing and sales personnel. If we are unable to adequately prepare the market for the potential future commercialization of a product, we may not be able to generate product revenue once marketing authorization is obtained.

Additionally, if we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue collaborative arrangements regarding the sales and marketing of our products, however, there can be no assurance that we will be able to establish or maintain such collaborative arrangements on commercially reasonable terms, or if we are able to do so, that they will have effective sales forces. Any revenue we receive will depend upon the efforts of such third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of such third parties and our revenue from product sales may be lower than if we had commercialized momelotinib or any future product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of momelotinib.

We cannot guarantee that we will be able to develop in-house commercialization expertise, including sales and distribution capabilities, or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

We depend on our information technology and infrastructure.

We rely on the efficient and uninterrupted operation of information technology systems, including mobile technologies, to manage our operations, to process, transmit and store financial and non-financial information, and to comply with regulatory, legal and tax requirements. We also depend on our information technology infrastructure for communications among our personnel, contractors, consultants and vendors. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud based systems during the COVID-19 situation, could compromise our ability to perform these functions in a timely manner, which could harm our ability to conduct business or delay our financial reporting. Such failures could materially adversely affect our operating results and financial condition.

In addition, we depend on third parties to operate and support our information technology systems. These third parties vary from multi-disciplined to boutique providers, and they may have access to our technology infrastructure, systems and our confidential information. Many of these third parties subcontract or outsource some of their responsibilities to other third parties. As a result, our information technology systems, including those functions that are performed by third parties who are involved with or have access to our systems, are very large and complex. Failure by any of these third-party providers to adequately deliver the contracted services, or maintain confidentiality and adequate security controls, could have an adverse effect on our business, which in turn may materially adversely affect our operating results and financial condition. Although we take measures designed to prevent security breaches and cyberattacks, these efforts may not completely eliminate the risk of such incidents and we cannot guarantee security incidents will not impact us in the future. We may need to continuously increase cost and resources to protect security threats and their consequences. If our information technology systems were to fail or be breached, such failure or breach could materially adversely affect our ability to perform critical business functions and sensitive and confidential data could be compromised.

Our internal information technology systems, or those used by our CROs or other contractors or consultants, may fail or suffer security breaches and other security incidents.

Despite our efforts to implement effective administrative, technical, and physical security measures and controls, our internal information technology systems and those of our CROs and other contractors and consultants may become vulnerable to damage and other impacts from security breaches and other incidents and/or unauthorized access, use, and disclosure of protected health information (PHI) and other data. The prevalent use of mobile devices also increases the risk of data security breaches and incidents resulting from lost or stolen devices or compromised security controls. In the ordinary course of our business, we and our CROs and other contractors and consultants collect, store, process and transmit large amounts of sensitive information, including intellectual property,

proprietary business information, personal information, health information, financial information, and other confidential information. It is critical that we and our CROs and other contractors and consultants do so in a secure manner in order to ensure the confidentiality, integrity, and availability of such sensitive information. We and certain of our CROs and other contractors and consultants have in the past experienced, and may in the future experience, a security breach or other security incident. When we have experienced security breaches in the past, we took action designed to prevent additional unauthorized access, put further security controls in place where appropriate and worked with outside counsel for any necessary reporting requirements. Any material system failure or security breach or incident could cause interruptions in our operations and could result in a material disruption of our development programs and our business operations. For example, the loss of data from completed or future preclinical studies or clinical trials could result in significant delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on other third parties for the manufacture of momelotinib and to conduct studies and trials, and similar events relating to their information technology systems could also have a material adverse effect on our business. To the extent that any disruption or security breach or incident were to result in a loss of, or damage to, our data or applications, or inappropriate access to, or use, acquisition, or disclosure of confidential or proprietary information, including personal and sensitive information, we could incur liability and the commercialization of momelotinib could be significantly delayed.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. We cannot assure you that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy and stock price may be adversely affected by any such economic downturn, volatile business environment or large-scale unpredictable or unstable market conditions, including a prolonged government shutdown, conflict between Russia and Ukraine or as a result of a global pandemic such as the COVID-19 pandemic. While the potential economic impact brought by and the duration of the pandemic may be difficult to assess or predict, it has already caused and could result in further, significant disruption of global financial markets, which may reduce our ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of COVID-19 could materially and adversely affect our business and the value of our common stock.

If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

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

We are exposed to the risk of fraud or other illegal activity by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by such individuals could include intentional failures to comply with FDA or international regulations, provide accurate information to the FDA or foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data timely, completely and accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by third parties could also involve the improper use of information obtained in the course of clinical trials.

We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct 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. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of momelotinib outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Even if approved, our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, healthcare payors and others in the medical community. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which the product candidate is approved;
- restrictions on the use of our product candidates, such as boxed warnings or contraindications in labeling, or a REMS, if any, which may not be required of alternative treatments and competitor products;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- pricing and the availability of coverage and adequate reimbursement by third-party payors, including government authorities and patients' willingness to pay out-of-pocket in the absence of such coverage and adequate reimbursement;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the effectiveness of sales and marketing efforts;
- unfavorable publicity relating to our products or product candidates or similar approved products or product candidates in development by third parties; and
- the approval of other new therapies for the same indications.

If any of our product candidates is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted.

We have never commercialized a product candidate before and may lack the necessary expertise, personnel and resources to successfully commercialize any products on our own or together with suitable collaborators.

We have never commercialized a product candidate. We may license certain rights with respect to our product candidates to collaborators, and, if so, we will rely on the assistance and guidance of those collaborators. For product candidates for which we retain commercialization rights and marketing approval, we will have to develop our own sales, marketing and supply organization or outsource these activities to a third party.

Factors that may affect our ability to commercialize our product candidates, if approved, on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, developing adequate educational and marketing programs to increase public acceptance of our approved product candidates, ensuring regulatory compliance of our company, employees and third parties under applicable healthcare laws, and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization will be expensive and time-consuming and could delay the launch of our product candidates upon approval. We may not be able to build an effective sales and marketing organization. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may not generate revenues from them or be able to reach or sustain profitability.

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

We intend to initially focus our product candidate development on treatments for various oncology indications, including myelofibrosis. The addressable patient populations that may benefit from treatment with our product candidates, if approved, are based on our estimates. These estimates, which have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations and market research, may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. Any regulatory approval of our product candidates would be limited to the therapeutic indications examined in our clinical trials and as determined by the FDA, which would not permit us to market our products for any other therapeutic indications not expressly approved by the FDA. Additionally, the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. Even if we receive regulatory approval for any of our product candidates, such approval could be conditioned upon label restrictions that materially limit the addressable patient population. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates prove to be inaccurate, the market opportunity for any product candidate that we or our strategic partners develop could be significantly diminished and have an adverse material impact on our business.

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

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

- decreased demand for momelotinib;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;

- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources;
- the inability to commercialize momelotinib; and
- a decline in our stock price.

We currently hold liability insurance coverage, but that coverage may not be adequate to cover any and all liabilities that we may incur. We would need to increase our insurance coverage when we begin the commercialization of momelotinib, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

A variety of risks associated with marketing our product candidates internationally may materially adversely affect our business.

We plan to eventually seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries, such as the lack of pathways for accelerated drug approval, may result in foreign regulatory approvals taking longer and being more costly than obtaining approval in the United States;
- foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials or our interpretation of data from nonclinical studies or clinical trials;
- approval policies or regulations of foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval;
- impact of the COVID-19 pandemic on our ability to produce our product candidates and conduct clinical trials in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets including as a result of the conflict between Russia and Ukraine;
- compliance with legal requirements applicable to privacy, data protection, information security and other matters;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes and government payors in foreign countries;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;

- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism including the conflict between Russia and Ukraine.

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

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be significantly limited, or entirely restricted.

As of December 31, 2021, we had gross U.S. federal operating loss carryforwards of $52.7 million that are eligible for an indefinite carryforward, and gross state operating loss carryforwards of $51.8 million, expiring in years ranging from 2022 to 2041. We also had U.S. net tax credit carryforwards of $11.2 million which begin to expire in 2039 and net tax credit carryforwards in a foreign jurisdiction of $0.8 million which begin to expire in 2039. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes, such as research tax credits, to offset its post-change income and taxes may be limited. In general, an "ownership change" generally occurs if there is a cumulative change in our ownership by "5% stockholders" that exceeds 50 percentage points over a rolling three-year period. Similar rules may apply under state tax laws.

We have experienced ownership changes in the past, including in 2017 and 2019, and as a result of common stock issuances and changes in the stock ownership that occurred subsequent to 2019, an ownership change under Section 382 is deemed to have occurred during the first quarter of 2022. As such, certain tax attributes existing as of the date of the ownership changes may not be available for future use. The loss or ultimate limitation of these attributes will not have any impact on the financial statements since our net U.S. deferred tax assets are offset by a full valuation allowance. We may experience additional ownership changes in the future as a result of future transactions in our stock, some of which may be outside our control. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards, or other pre-change tax attributes, to offset U.S. federal and state taxable income and taxes may be subject to limitations. We may have exposure to greater than anticipated tax liabilities, which could adversely impact our operating results.

Under the Tax Cuts and Jobs Act as modified by the Coronavirus Aid Relief and Economic Security Act, or the Tax Act, U.S. federal net operating losses arising in tax years beginning after December 31, 2017 can be carried forward indefinitely, but the deductibility of such U.S. federal net operating losses in any particular taxable years beginning after December 31, 2020 is limited to 80% of that years taxable income.

Changes in U.S. and foreign tax laws, as well as the application of such laws, could adversely impact our financial position and operating results.

We are a U.S.-based multinational company subject to tax in certain U.S. and foreign tax jurisdictions. All of these jurisdictions have in the past and may in the future make changes to their corporate income tax rates and other income tax laws which could adversely affect our future income tax provision. For example, our future income tax obligations could be adversely affected by changes in the valuation of our deferred tax assets and liabilities, by changes in the amount of unrecognized tax benefits, or by changes in tax laws, regulations, accounting principles, or interpretations thereof, including changes with possible retroactive application or effect. Further, U.S. federal, state and local, as well as international tax laws and regulations are extremely complex and subject to varying interpretations. Although we believe that our tax estimates and tax positions are reasonable, there can be no assurance that our tax positions will not be challenged by relevant tax authorities or that we would be successful in any such challenge. If we are unsuccessful in such a challenge, the relevant tax authorities may assess additional

taxes, which could result in adjustments to, or impact the timing or amount of, taxable income, deductions or other tax allocations, which may adversely affect our results of operations and financial position.

Our quarterly operating results may fluctuate significantly, which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including, but not limited to:

- variations in the level of expense related to development programs;
- results of preclinical studies and clinical trials, or the addition or termination of preclinical studies, clinical trials or funding support;
- the timing of the release of results from any preclinical studies and clinical trials;
- the timing and amount of milestone and royalty payments;
- changes in the competitive landscape or market opportunity for momelotinib;
- our execution of any new collaboration, licensing or similar arrangement, and the timing of payments we may make or receive under such existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- any securities or other litigation in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures,
- strategic investments or changes in business strategy;
- the receipt of regulatory approval for momelotinib, and market acceptance and demand for momelotinib;
- regulatory developments affecting momelotinib or those of our competitors; and
- changes in general market and economic conditions, including global pandemics such as COVID-19.

If our quarterly operating results or expected results from development of momelotinib fall outside the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Risks Related to Government Regulation

We may be unable to obtain U.S. or foreign regulatory approval of momelotinib, and, as a result, we may be unable to commercialize momelotinib. Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Momelotinib is, and any future product candidates that we may develop will be, subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, import, export, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing, distribution, import and export of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed before a new drug can be marketed in the United States and in many foreign jurisdictions. Satisfaction of these and other regulatory requirements is costly,

time-consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us or our collaborators to begin selling them.

As a company, we have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA or foreign regulatory authorities, and, as a company, we have no experience in obtaining approval of any product candidates. The time required to obtain FDA and other approvals is unpredictable but typically takes many years following the initiation of clinical trials, depending upon the type, complexity and novelty of the product candidate. We may encounter delays or rejections during any stage of the regulatory review and approval process based upon the failure of clinical or laboratory data to demonstrate compliance with, or upon the failure of the product candidates to meet, the FDA's or foreign regulatory authorities' requirements for safety, efficacy and quality.

The standards that the FDA and foreign regulatory authorities use when regulating us are not always applied predictably or uniformly and can change. Because the product candidates we are developing or may develop may represent a new class of drug, the FDA and foreign regulatory authorities have not yet established any definitive policies, practices or guidelines in relation to these drugs. The lack of policies, practices or guidelines may hinder or slow review by the FDA or foreign regulatory authorities of any regulatory filings that we may submit. Moreover, the FDA or foreign regulatory authorities may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the development of any product candidates.

Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA or foreign regulatory authority policy during the period of product development, clinical trials and regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulatory authority, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

In addition, the FDA and/or foreign regulatory authorities may delay, limit, or deny approval of a product candidate for many reasons, including, but not limited to:

- the FDA or foreign regulatory authorities may disagree with the design or implementation of our clinical trials, including our statistical plan;
- we may be unable to demonstrate to the satisfaction of the FDA or foreign regulatory authorities that a product candidate is safe and effective for any indication;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the results of our clinical trials may not demonstrate the safety or efficacy required by the FDA or foreign regulatory authorities for approval;
- we may be unable to demonstrate the integrity of the clinical trial data to the satisfaction of the FDA or foreign regulatory authorities;
- we may be unable to demonstrate the proper conduct of the clinical trial at all clinical trial sites, by our vendors, and by the Sponsor to the satisfaction of the FDA or foreign regulatory authorities;
- we may encounter difficulties coming to agreement with the FDA or foreign regulatory authorities on a pediatric investigation or study plan or may encounter difficulties meeting the terms of the plan, once agreed;
- the FDA or foreign regulatory authorities may find deficiencies in our manufacturing processes or facilities;

- the FDA or foreign regulatory authorities may lack resources or are delayed in conduct pre-approval inspections due to reasons related to COVID-19; and
- the FDA's or foreign regulatory authorities' approval policies or regulations may significantly change in a manner rendering our clinical data insufficient for approval.
- the FDA or foreign regulatory authorities may differ on the appropriate indication for commercial use of current drugs under investigation.

Even if we comply with all of the regulatory requirements of the FDA and foreign regulatory authorities, we may not obtain regulatory approval for momelotinib. If we fail to obtain regulatory approval for momelotinib, we will have no commercialized products and correspondingly no revenue.

In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs, and the FDA's standards, especially regarding drug safety, appear to have become more stringent.

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular product candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. In addition, the FDA has the authority to require a REMS plan as part of or after approval, which may impose further requirements or restrictions on the distribution or use of an approved product, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the product and affect reimbursement by third-party payors.

If we or any collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;
- warning letters;
- voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;
- restrictions on, or prohibitions against, marketing our products;
- restrictions on, or prohibitions against, importation or exportation of our products;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our products;
- suspension or withdrawal of product approvals;
- product seizures;
- injunctions; and
- civil and criminal penalties and fines.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the United States and vice versa.

In Europe, the implementation of the Clinical Trials Regulation depends on confirmation of full functionality of the Clinical Trials Information System (CTIS) through an independent audit, which commenced in September 2020. The system is currently planned to go live in December 2021. The new clinical trial portal and database will be maintained by the EMA in collaboration with the European Commission and the European Union Member States. The objectives of the new regulation include consistent rules for conducting trials throughout the European Union, consistent data standards and adverse events listing, and consistent information on the authorization status. Information on the conduct and results of each clinical trial carried out in the European Union will be made publicly available.

In addition, a new pan-European clinical trial data information database has been created that will be complementary to the database established for pharmacovigilance (Regulation (EC) No 726/2004 with respect to centrally authorized medicinal products). In addition, Commission Implementing Regulation (EU) No 520/2012 outlines the practical implications for marketing authorization holders, national competent authorities, and the EMA. Also, Commission Delegated Regulation (EU) No 357/2014 on post-authorization efficacy studies specifies the situations in which such studies may be required. Post-authorization efficacy studies may be required where concerns relating to some aspects of efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed, or where the understanding of the disease, the clinical methodology or the use of the medicinal product under real-life conditions indicate that previous efficacy evaluations might have to be revised significantly.

Brexit is also expected to disrupt the operation of pre- and post-authorization clinical trial infrastructure. The rules around GMP and pharmacovigilance in the UK currently remain similar to the EU requirements. However, the Falsified Medicines Directive will not apply in Great Britain though it is likely that the UK will implement a procedure to minimize the risk of falsified medicines.

Uncertainty in the regulatory framework and future legislation can lead to disruption in the execution of international multi-center clinical trials, the monitoring of adverse events in through pharmacovigilance programs, the evaluation of the benefit-risk profiles of new medicinal products, and determination of marketing authorization across different jurisdictions. There could also be disruption to the supply and distribution as well as the import/export both of active pharmaceutical ingredients (API) and finished product. Such a disruption could create supply difficulties for ongoing clinical trials and may damage the integrity of the pharmacovigilance database for the safety of new products.

The cumulative effects of the disruption to the regulatory framework, uncertainty in future regulation, and changes to existing regulations may add considerably to the development lead time to marketing authorization and commercialization of products in the European Union and/or the United Kingdom and increase our costs. We cannot predict the impact of such changes and future regulation on our business or the results of our operations.

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

Any regulatory approvals that we receive for any product candidates we may develop will require surveillance to monitor the safety and efficacy of the product candidate, and may require us to conduct post-approval clinical studies. The FDA may also require a REMS in order to approve momelotinib or any future product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a foreign regulatory authority approves momelotinib, the manufacturing processes, labeling,

packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for momelotinib will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval.

Moreover, if we obtain regulatory approval for momelotinib, we will only be permitted to market our products for the indication approved by FDA or foreign regulatory authority, and such approval may involve limitations on the indicated uses or promotional claims we may make for our products, or otherwise not permit labeling that sufficiently differentiates momelotinib from competitive products with comparable therapeutic profiles. For example, we will not be able to claim that our products have fewer side effects, or improve compliance or efficacy unless we can demonstrate those attributes to FDA or foreign regulatory authority in comparative clinical trials. Communications that occur prior to obtaining regulatory approval for momelotinib could also be considered promotional and thus may also be subject to certain FDA or foreign regulatory authority requirements.

Later discovery of previously unknown problems with momelotinib, including adverse effects of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

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

The FDA's and foreign regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

A Fast Track designation by the FDA, as granted for momelotinib or if granted for any future product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that such product candidates will receive marketing approval.

If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation for a particular indication. Marketing applications filed by sponsors of products in Fast Track development may qualify for priority review under the policies and procedures offered by the FDA, but the Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. We previously announced that the FDA had granted Fast Track designation to momelotinib for the treatment of patients with intermediate/high-risk myelofibrosis who have previously received a JAK inhibitor. Receipt of Fast Track designation may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures. In addition, the FDA may withdraw any Fast Track designation at any time if it believes that the designation is no longer supported by data from our clinical development program. We may seek Fast Track designation for any future product candidates, but there is no assurance that the FDA will grant this status to any future proposed product candidates.

If we or any of our independent contractors, consultants, collaborators, manufacturers, vendors or service providers fail to comply with healthcare, privacy and data security laws and regulations, we or they could be subject to enforcement actions, which could result in significant penalties and affect our ability to develop, market and sell momelotinib or any future product candidates and may harm our reputation.

We are or may in the future be subject to federal, state, and foreign healthcare, privacy and data security laws and regulations pertaining to, among other things, fraud and abuse, data protection and patients' rights. These laws and regulations include, but are not limited to:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid;
- the U.S. federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government funded programs such as Medicare or Medicaid that are false or fraudulent, and which may apply to us by virtue of statements and representations made to customers or third parties;
- the U.S. federal Health Insurance Portability and Accountability Act (HIPAA), which created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud healthcare programs;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), which imposes requirements on certain types of people and entities relating to the privacy, security, and transmission of individually identifiable PHI, and requires notification to affected individuals and regulatory authorities of certain breaches of security of PHI;
- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, to report annually to the Centers for Medicare & Medicaid Services (CMS) information related to payments and other transfers of value to covered recipients, including physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare providers (such as physician assistants and nurse practitioners) and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members, which is published in a searchable form on an annual basis; and
- state laws comparable to each of the above federal laws, such as, for example, anti-kickback and false claims laws that may be broader in scope and also apply to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance programs, and laws relating to

patient data privacy and security. Other state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

In the European Union (EU), the General Data Protection Regulation (GDPR) established new and expanded operational requirements for entities that process, or control personal data generated in the EU, including consent requirements for disclosing the way personal information will be used, information retention requirements, notification requirements in the event of a data breach, and other requirements. In addition, the GDPR imposes strict rules on the transfer of personal data out of the European Economic Area (EEA) and Switzerland to the United States. These obligations may be interpreted and applied in a manner that is inconsistent from one jurisdiction to another and may conflict with other requirements or our practices. Recent developments have also created uncertainty regarding the rules around such data transfers.

Any actual or alleged violation of the GDPR could result in regulatory investigations and other proceedings, reputational damage, orders to cease or change our processing of our data, enforcement notices, or assessment notices (for a compulsory audit). We may also face civil claims including representative actions and other class action type litigation (where individuals have suffered harm), potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm. Additionally, following the United Kingdom's exit from the European Union, the UK is a "third country" under the GDPR. In particular, we face exposure in the European Economic Area and the United Kingdom under two parallel regimes, each with the power to impose fines up to the greater of either 4% of total global annual revenue, or €20 million (for the EU) or £17.5 million (for the United Kingdom). We may incur liabilities, expenses, costs, and other operational losses under the GDPR, and applicable laws and regulations relating to privacy and data protection of EU member states and the United Kingdom, in connection with any measures we take to comply with them.

In July 2020, the Court of Justice of the EU (CJEU) invalidated the EU-U.S. Privacy Shield as a mechanism for managing personal data transfers between the EU and the U.S. and onward to other countries. Additionally, in September 2020, the Federal Data Protection and Information Commissioner of Switzerland opined that the Swiss-U.S. Privacy Shield did not provide an adequate level of protection for data transfers from Switzerland to the U.S. pursuant to Swiss data protection law. While the CJEU upheld the adequacy of EU-specified standard contractual clauses (SCCs), a form of contract approved by the European Commission as an adequate data transfer mechanism, the CJEU made clear that reliance on them alone may not necessarily be sufficient in all circumstances and that their use must be assessed on a case-by-case basis taking into account the surveillance laws and right of individuals in the U.S and other onward countries. EU regulators released new SCCs in June 2021 that are required to be implemented over time. Data protection authorities may require measures to be put in place in addition to the SCCs for transfers to countries outside of the EEA, as well as Switzerland and the United Kingdom.

We are currently certified under the EU-U.S. Privacy Shield and the Swiss-U.S. Privacy Shield with respect to our transfer of certain personal data from the EEA to the U.S. We are, however, in the process of updating the mechanisms we currently use to transfer personal data from the EEA and the United Kingdom to the U.S., and any additional mechanisms that may be required to maintain adequate safeguards for personal data transfer, including in light of the new SCCs issued by the European Commission on June 4, 2021. As a result, we may be unsuccessful in maintaining appropriate compliance mechanisms for our transfer and receipt of personal data from the EEA or the United Kingdom and to the U.S. and may be at risk of experiencing reluctance or refusal of European or multi-national partners, clinical trial sites or other third parties with whom we do business and incurring potential regulatory penalties, which may have an adverse effect on our reputation and business.

As developments continue with respect to personal data transfers, we could suffer additional costs, complaints, or regulatory fines, investigations, or other proceedings, and if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect

our financial results. We also may be required to engage in new contract negotiations with third parties that aid in processing data on our behalf.

In the United States, state and federal lawmakers and regulatory authorities have increased their attention on the collection and use of personal information. In the United States, non-sensitive personal information generally may be used under current rules and regulations, subject to certain restrictions, so long as the person does not affirmatively "opt-out" of the collection or use of such data. If an "opt-in" model or additional required "opt-outs", were to be adopted in the United States, less data would be available, and the cost of data would be higher. For example, California enacted the CCPA, which gives California residents new rights to access and require deletion of their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is collected, used, and shared. Further, in November 2020, California voters passed the California Privacy Rights Act (CPRA). The CPRA, which will take effect on January 1, 2023 and creates obligations with respect to certain data relating to consumers as of January 1, 2022, significantly expands the CCPA, including by introducing additional obligations such as data minimization and storage limitations, granting additional rights to consumers, such as correction of personal information and additional opt-out rights, and creates a new entity, the California Privacy Protection Agency, to implement and enforce the law. The CCPA and CPRA present many unresolved compliance complexities. The CCPA and CPRA may increase our compliance costs and potential liability. In addition to the CCPA, numerous other states' legislatures are considering similar laws that will require ongoing compliance efforts and investment. For example, in March 2021, Virginia enacted a Consumer Data Protection Act that will go into effect on January 1, 2023 and in June 2021, Colorado enacted a Colorado Privacy Act that will go into effect on July 1, 2023, both of which share similarities with the CCPA, CPRA, and legislation proposed in other states.

Additionally, if our operations are found to be in violation of any such health care, privacy and data security laws and regulations, we may be subject to significant penalties, including administrative, civil and criminal penalties, monetary damages, disgorgement, imprisonment, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA or foreign regulatory authorities, fees from regulators, fines, significant settlements or judgments resulting from the CCPA's private right of action, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely impact our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation by a private party or governmental agency could cause us to incur significant legal expenses, adversely impact our reputation, and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

The insurance coverage and reimbursement status of newly approved products is uncertain. Any products we develop may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices or healthcare reform initiatives, thereby harming our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Many countries require approval of the sale price of a drug before it can be marketed. The pricing review period begins after marketing or product licensing approval is granted in most cases. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we intend to monitor these regulations, we are currently unable to assess the full impact of such price regulations on our momelotinib program. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other third-party payors. In many jurisdictions, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to the payor supporting scientific, clinical and cost-

effectiveness data for the use of our products. If we are not currently capturing the scientific and clinical data that will be required for reimbursement approval, we may be required to conduct additional trials, which may delay or suspend reimbursement approval. Additionally, in the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of momelotinib to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

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

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are still in clinical development, we are unable at this time to determine their cost effectiveness or the likely level or method of reimbursement. Increasingly, the third-party payors, such as government and private insurance plans, who reimburse patients or healthcare providers, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for pharmaceutical products. If the level of reimbursement provided for any products we develop is inadequate in light of our development and other costs, our return on investment could be adversely affected.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), established the Medicare Part D program to provide a voluntary prescription drug benefit to patients with disabilities and seniors. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that will provide coverage of outpatient prescription drugs, such as momelotinib, if approved. Medicare Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee.

We may face difficulties from changes to current regulations and future legislation. Healthcare legislative measures aimed at reducing healthcare costs may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example:

- changes to our manufacturing arrangements;
- additions or modifications to product labeling;
- the recall or discontinuation of our products; or

- additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

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

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

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

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

Further, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the PPACA) substantially changed the way healthcare is financed by both governmental and private insurers, and continues to significantly impact the pharmaceutical industry in the United States. There have been executive, judicial and Congressional challenges to certain aspects of the PPACA. For example, On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the PPACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the PPACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the PPACA. It is possible that the PPACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and the healthcare reform measures of the Biden administration will impact the PPACA and our business.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. For example, the Bipartisan Budget Act of 2018 also amended the PPACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The American Taxpayer Relief Act of 2012, or ATRA, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Other legislative changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments, including the Infrastructure Investment and Jobs Act, will remain in effect through 2031 with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester.

There has also been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Presidential executive orders, Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, in 2020, under the Trump administration, the U.S. Department of Health and Human Services (HHS) and CMS issued various rules that were expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, importation of prescription drugs from Canada and other countries, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of these new rules. As a result, the Biden administration and HHS have delayed the implementation or published rules rescinding some of these Trump-era policies. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. Pursuant to the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of approved products, which could have a material impact on our business. Further, Congress is considering legislation that, if passed, could have significant impact on prices of prescription drugs covered by Medicare, including limitations on drug price increases and allowing Medicare to negotiate pricing for certain covered drugs. The impact of these and future reform measures on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

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

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure to what extent these and future legislative and regulatory efforts, whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization if we obtain regulatory approval for any of our products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand or additional pricing pressures on any of our products that may receive regulatory approval.

Disruptions at the FDA, the Securities and Exchange Commission and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the Securities and Exchange Commission, or the SEC, and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. Separately, in response to the COVID-19 pandemic, since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. In 2020 and 2021, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA Good Manufacturing Practices. However, the FDA may not be able to continue its current inspection pace, and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. We cannot ensure that FDA or any other regulatory authority will conduct a timely pre-approval inspection of our manufacturing sites or clinical trial sites, which could significantly delay approval of our product candidates. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. In the event of any prolonged government shutdown or other disruption, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities on a timely basis, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns, disruptions or delays could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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

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

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

If we or our third-party manufacturers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

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

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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

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

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

The Tax Cuts and Jobs Act could increase our tax burden and adversely affect our business and financial condition.

In December 2017, the U.S. government enacted comprehensive tax legislation referred to as the Tax Act that includes significant changes to the taxation of business entities. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) revisions to uses and limitations of net operating loss carryforwards, (iii) a partial limitation on the deductibility of business interest expense, and (iv) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a participation exemption system (along with certain rules designed to prevent erosion of the U.S. income tax base).

In addition, beginning in 2022, the tax act will require U.S. research and experimental expenditures to be capitalized and amortized ratably over a five-year period. Any such expenditures attributable to research conducted outside the U.S. must be capitalized and amortized over a 15-year period. Further, the Tax Act, among other things, reduces the orphan drug credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this amortization of research and experimental expenditures and reduction in orphan drug tax credits may result in an increased federal income tax burden, as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability.

Risks Related to Our Intellectual Property

If we are not able to obtain and enforce patent protection for our technologies or momelotinib, development and commercialization of our product candidates may be adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, methods used to manufacture momelotinib and methods for treating patients using momelotinib, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others.

We and our future licensors and licensees may not be able to apply for or prosecute patents on certain aspects of momelotinib or our technologies at a reasonable cost in a timely fashion or at all. It is also possible that we or our current licensors, or any future licensors or licensees, will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If our current licensors, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised and we might not be able to prevent third parties from making, using, and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods, and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial condition and operating results.

There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover momelotinib, methods for treating patients using momelotinib or our technologies for manufacturing momelotinib or to provide meaningful protection from our competitors. Moreover, the patent position of oncology companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and momelotinib are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely impact our position in the market.

The U.S. Patent and Trademark Office (USPTO) and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in oncology patents. Moreover, changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. While we will endeavor to try to protect momelotinib with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time-consuming, expensive and sometimes unpredictable.

Further, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed (or 20 years after the filing date of the first non-provisional US patent application to which it claims priority). Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for momelotinib, we may be open to competition from generic versions of momelotinib. Further, the extensive period of time between patent filing and regulatory approval for a product candidate limits the time during which we can market a product candidate under patent protection, which may particularly affect the profitability of momelotinib.

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

In addition to seeking patent protection for certain aspects of momelotinib and our technologies, we also consider trade secrets, including confidential and unpatented know-how important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us.

Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We are also subject both in the United States and outside the United States to various regulatory schemes regarding requests for the information we provide to regulatory authorities, which may include, in whole or in part, trade secrets or confidential commercial information. While we are likely to be notified in advance of any disclosure of such information and would likely object to such disclosure, there can be no assurance our challenge to the request would be successful.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect momelotinib.

Numerous recent changes to the patent laws and proposed changes to the rules of the USPTO may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the Leahy-Smith America Invents Act (AIA) enacted in 2011 involves significant changes in patent legislation. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but

before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application.

Further, the Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. These changes have led to increasing uncertainty with regard to the scope and value of our issued patents and to our ability to obtain patents in the future.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal court necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that may weaken our and our licensors' ability to obtain new patents or to enforce existing patents we and our licensors or partners may obtain in the future.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification derivation and opposition proceedings in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether.

If we do not obtain patent term extension and data exclusivity for any therapeutic candidate or product we may develop, our business may be materially harmed.

Depending upon the timing, duration, and specifics of any FDA marketing approval of any therapeutic candidate or product we may develop, one or more of our patents for momelotinib or our or in-licensed U.S. patents for our technologies may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act). The Hatch-Waxman Act permits a patent term extension of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar extensions as compensation for patent term lost during regulatory review processes are also available in certain foreign countries and territories, such as in Europe under a Supplementary Patent Certificate. However, we may not be granted an extension in the United States and/or foreign countries and territories because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to list eligible patents in the OrangeBook with the FDA within applicable deadlines, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is shorter than what we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations, and growth prospects could be materially harmed.

We or any future strategic partners may become subject to third-party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights.

We or any future strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights that prevent us from developing and commercializing our products. If we, our licensors or any future strategic partners are found to infringe a third-party patent or other intellectual property rights, we could be required to pay substantial damages, potentially including treble damages and attorneys' fees, if we are found to have willfully infringed. In addition, we or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material adverse impact on our business. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

In addition, in an infringement proceeding, a court may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Interference proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could result in a loss of our current patent rights and could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Litigation or interference proceedings may result in a decision adverse to our interests and, even if we are successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of

our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States.

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. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

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

We have limited foreign intellectual property rights and may not be able to protect our intellectual property rights throughout the world.

We and our licensors or future licensors and licensees have limited intellectual property rights outside the United States. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to oncology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we fail to comply with our obligations under our strategic agreements, we may be required to pay damages.

In connection with our acquisition of momelotinib from Gilead, we are required to make aggregate milestone payments of up to $190.0 million to Gilead upon the achievement of certain regulatory and commercial milestones, including a milestone payment of $25.0 million due upon the approval of momelotinib from the FDA, as well as low double-digit to high-teens percent tiered combined royalties based upon net sales and additional tiered milestone payments upon reaching certain sales milestones. If we breach any of these obligations, we may be required to indemnify the Seller, subject to certain limitations set forth in the momelotinib purchase.

Under our license agreement with AstraZeneca for SRA515 (formerly AZD5153) and related compounds, the Company has agreed to pay AstraZeneca up to $208.0 million upon the achievement of certain development, regulatory and commercial milestones, and a tiered royalty on worldwide net sales ranging from high single-digits to low double-digits. If we breach any of our obligations under this agreement, we may be subject to damages.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other oncology companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

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

Our trademarks or trade names may be challenged, infringed, circumvented, or declared generic or determined to be infringing on other marks. Any trademark litigation could be expensive. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively, and our business may be materially and adversely affected.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been and may continue to be volatile, and you may be unable to sell your shares at or above the price at which you purchased them.

The market price of our common stock has been and may continue to be subject to wide fluctuations. For example, we experienced a significant decrease in our stock price after we announced the suspension of the development of our former lead product candidate PNT2258 and the DNAi platform in June 2016 and after we announced the preliminary clinical data from our two Phase 1/2 studies of SRA737 in June 2019. In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. Factors affecting the market price of our common stock include, but are not limited to:

- the success of existing or new competitive products;
- the timing and results of development activities related to our product candidates;
- our capital requirements, financings and the related dilution;
- the commencement, enrollment or results of future clinical trials we may conduct, or changes in the development status of our product candidates;
- any delay in our regulatory filings for our product candidates including momelotinib and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- any disputes with Gilead regarding our acquisition of momelotinib and assumption of the related clinical trials;
- announcements of significant acquisitions, strategic partnerships, collaborations, joint ventures or capital commitments by us or our competitors;
- our ability to acquire or in-license new product candidates to grow our pipeline;
- adverse results or delays in preclinical studies or clinical trials;
- changes in laws or regulations applicable to our product candidates including momelotinib, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers;

- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations if needed, or to out-license our product candidates including momelotinib or technologies on favorable terms or at all;
- our failure to commercialize our product candidates including momelotinib;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates including momelotinib;
- the size and growth of our initial target markets;
- our ability to successfully treat additional types of cancers or at different stages;
- actual or anticipated variations in quarterly operating results;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or immunotherapy in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- the low trading volume and limited public market for our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- actions instituted by activist shareholders or others;
- general political and economic conditions, including global pandemics such as COVID-19 or the conflict between Russia and Ukraine;
- fiscal and monetary stimulus measures to counteract the impact of the COVID-19 pandemic; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and oncology 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. Securities class action litigation is often instituted against companies following periods of volatility in the market price of a company's securities. For example, we have previously vigorously defended purported securities class action lawsuits against us and certain of our executive officers. This type of litigation could result in substantial costs and a diversion of management's attention and resources, which could harm our business, operating results or financial condition.

Market volatility arising from the COVID-19 pandemic may lead to increased shareholder activism if we experience a market valuation that they believe are not reflective of their intrinsic value. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition.

The issuance or sale of shares of our common stock, or rights to acquire shares of our common stock could depress the trading price of our common stock.

We may conduct future offerings of our common stock, preferred stock or other securities that are convertible into or exercisable for our common stock to finance our operations or fund acquisitions, or for other purposes. For example, in November 2019, we conducted a public equity offering where we raised net proceeds of approximately $97.7 million in a substantially dilutive transaction to our pre-existing investors. In August 2020, we filed a prospectus supplement pursuant to which we issued and sold $20.0 million of our common stock in ATM offerings. In February 2021, we filed a prospectus supplement pursuant to which we can issue and sell an aggregate of up to an additional $30.0 million of our common stock from time to time in ATM offerings. In addition, on May 7, 2021, we filed a prospectus supplement, pursuant to which we can issue and sell an aggregate of up to an additional $50.0 million of our common stock from time to time in ATM offerings. Also, on November 5, 2021, we filed a prospectus supplement, pursuant to which we can issue and sell an aggregate of up to an additional $50.0 million of our common stock from time to time in the ATM offerings. As of December 31, 2021, we sold 5,049,720 shares under the ATM Program (including the amounts sold under the prospectus supplement filed in August 2020) for net proceeds of $87.1 million, net of commissions and offering expenses. As of December 31, 2021, there was $59.6 million under the ATM program. In addition, in January 2022, we completed an underwritten public offering of 4,074,075 shares of our common stock and pre-funded warrants to purchase up to 925,925 shares of our common stock. As part of the underwritten public offering, in February 2022, we issued an additional 750,000 shares of common stock representing the underwriters' full exercise of their over-allotment option. If we issue additional shares of our common stock or rights to acquire shares of our common stock, if any of our existing stockholders sells a substantial amount of our common stock, or if the market perceives that such issuances or sales may occur, then the trading price of our common stock, and, accordingly, the trading price of our common stock may significantly decrease. In addition, our issuance of additional shares of common stock, including upon exercise of our outstanding warrants, will dilute the ownership interests of our existing common stockholders.

We have a significant number of outstanding warrants which may cause significant dilution to our stockholders, have a material adverse impact on the market price of our common stock, make it more difficult for us to raise funds through future equity offerings and discourage an acquisition of us by a third party.

As more fully described in Note 8 in the Notes to the Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K under the subheading "Common Stock Warrants," we issued Series A warrants and Series B warrants in connection with our November 2019 public offering of Series A Preferred Stock and warrants to Gilead pursuant to the amendment to the Asset Purchase Agreement.

Although certain of the warrants have been exercised as detailed in Note 11 of the Notes to the Consolidated Financial Statements included in Part II, Item 8 of this Annual Report on Form 10-K, to the extent additional warrants are exercised, additional shares of common stock will be issued and such issuance may dilute existing stockholders and increase the number of shares eligible for resale in the public market. Sales of substantial numbers of such shares in the public market could adversely affect the market price of our shares. In addition, the perceived risk of dilution as a result of the significant number of outstanding warrants may cause our common stockholders to be more inclined to sell their shares, which would contribute to a downward movement in the price of our common stock. Moreover, the perceived risk of dilution and the resulting downward pressure on our common stock price could encourage investors to engage in short sales of our common stock, which could further contribute to price declines in our common stock. The fact that our warrant holders can sell substantial amounts of our common stock in the public market could make it more difficult for us to raise additional funds through the sale of equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate, or at all.

To the extent we issue shares of common stock to effect a business combination, the potential for the issuance of a substantial number of additional shares upon exercise of our warrants could make us a less attractive acquisition vehicle in the eyes of a target business since the exercise of warrants could reduce the value of the shares issued to complete the business combination. Accordingly, our warrants may make it more difficult to effectuate a business combination or increase the cost of acquiring the target business.

Further, our warrants could make the structuring of any strategic transaction more complex and affect the terms of any such strategic transaction. In connection with certain "fundamental transactions" involving a change in control

of our company, the surviving entity is required to either (1) assume all of our obligations under the warrants or (2) deliver in connection with the closing of a fundamental transaction in exchange for the cancellation of the warrants, consideration equal in value to the Black-Scholes value of the remaining unexercised portion of the warrants, with an assumed volatility of 100%. These provisions could deter a third party from acquiring us even where the acquisition could be beneficial to you. Any negotiated alternative to such treatment of the warrants would require the approval of the holders of warrants exercisable for the majority of the shares underlying the warrants. Three of our ten directors are affiliated with investors that hold a majority-in-interest of the Series A warrants. The holders of warrants could exercise their rights under the warrants in a manner that benefits their interests relative to the holders of common stock generally.

We incur significantly increased costs and devote substantial management time as a result of operating as a public company.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the stock exchange upon which our common stock is listed and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain a non-accelerated filer, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404.

We have in the past and may in the future identify material weaknesses or significant deficiencies in internal control over financial reporting. Under standards established by the Public Company Accounting Oversight Board, a deficiency in internal control over financial reporting exists when the design or operation of a control does not allow management or personnel, in the normal course of performing their assigned functions, to prevent or detect misstatements on a timely basis. A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected and corrected on a timely basis. We cannot assure you that there will not be additional material weaknesses or significant deficiencies that our independent registered public accounting firm or we will identify. If we identify such issues or if we are unable to produce accurate and timely financial statements, our stock price may be adversely affected and we may be unable to maintain compliance with the Nasdaq Stock Market listing requirements.

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

Our restated certificate of incorporation and restated bylaws contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions, among other things:

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

In addition, Section 203 of the Delaware General Corporation Law may discourage, delay or prevent a change in control of our company. Section 203 imposes certain restrictions on mergers, business combinations and other transactions between us and holders of 15% or more of our common stock.

Section 22 of the Securities Act of 1933, as amended (the Securities Act), creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. In April 2020, we amended and restated our restated bylaws to provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act (a Federal Forum Provision). Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law. While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.

Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. In addition, neither the exclusive forum provision nor the Federal Forum Provision applies to suits brought to enforce any duty or liability created by the Exchange Act. Accordingly, actions by our stockholders to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder must be brought in federal court.

Our stockholders will not be deemed to have waived our compliance with the federal securities laws and the regulations promulgated thereunder.

Any person or entity purchasing or otherwise acquiring or holding any interest in any of our securities shall be deemed to have notice of and consented to our exclusive forum provisions, including the Federal Forum Provision. These provisions may limit a stockholders' ability to bring a claim in a judicial forum of their choosing for disputes

with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees.

Certain of our 5% stockholders in the aggregate hold a majority of the voting power and may therefore, in effect, be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2021, our executive officers, directors and 5% stockholders collectively beneficially owned a majority of our outstanding voting shares. Four of our current directors are each affiliates of certain 5% stockholders. As of December 31, 2021, these 5% stockholders beneficially own 84.6% of the voting power of our company. Therefore, if such holders acted in concert, these holders may have the ability to influence us through their ownership position and through representation on our board of directors. For example, numerically, these holders may be able to determine the outcome of votes with respect to elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. They also have contractual rights under the warrants that they may exercise in a manner that adversely impacts the interest of holders of capital stock that do not hold warrants. This concentrated ownership may prevent or discourage unsolicited acquisition proposals or offers for our common stock.

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

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. In November 2019 we conducted a public equity offering where we raised net proceeds of approximately $97.7 million in a substantially dilutive transaction to our pre-existing investors. In August 2020, we filed a prospectus supplement pursuant to which we issued and sold $20.0 million of our common stock. In February 2021, we filed a prospectus supplement pursuant to which we can issue and sell an aggregate of up to $30.0 million of our common stock from time to time in ATM offerings. In addition, on May 7, 2021, we filed a prospectus supplement, pursuant to which we can issue and sell an aggregate of up to an additional $50.0 million of our common stock from time to time in the ATM offerings. Also, on November 5, 2021, we filed a prospectus supplement, pursuant to which we can issue and sell an aggregate of up to an additional $50.0 million of our common stock from time to time in the ATM offerings. As of December 31, 2021, we sold 5,049,720 shares under the ATM Program (including the amounts sold under the prospectus supplement filed in August 2020) for net proceeds of $87.1 million, net of commissions and offering expenses. As of December 31, 2021, there was $59.6 million under the ATM program. In addition, in January 2022, we completed an underwritten public offering of 4,074,075 shares of our common stock and pre-funded warrants to purchase up to 925,925 shares of our common stock. As part of the underwritten public offering, in February 2022, we issued an additional 750,000 shares of common stock representing the underwriters' full exercise of their over-allotment option. The shares of common stock and the pre-funded warrants were offered at a price of $27.00 and $26.999 per shares, respectively. The aggregate net proceeds from the offering were $145.6 million, after deducting underwriting discounts and commissions and other estimated offering expenses. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders will be further diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could involve certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or momelotinib or grant licenses on terms unfavorable to us.

Sales of a substantial number of shares of our common stock in the public market could cause the market price of our common stock to decline. These sales, or the perception in the market that our officers, directors or the holders of a large number of shares of our common stock intend to sell shares, could reduce the market price of our common stock. Our directors, executive officers and certain stockholders affiliated with our directors entered into lock-up agreements in connection with the recent underwritten offering. However, we cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, however, could adversely

affect the market price of our common stock and also could adversely affect our future ability to raise capital through the sale of our common stock or other equity-related securities of ours at times and prices we believe appropriate. Additionally, our stockholders may be further diluted by the exercise of the pre-funded warrants we issued earlier this year.

Shares of our common stock are subordinate to any preferred stock we may issue and to any current and future indebtedness.

Shares of our common stock rank junior to any shares of our preferred stock that we may issue in the future and to any future indebtedness we may incur, as well as to all creditor claims and other non-equity claims against us and our assets available to satisfy claims on us, including claims in a bankruptcy or similar proceeding. Any future indebtedness and preferred stock may restrict, payment of dividends on our common stock.

Furthermore, unlike indebtedness, where principal and interest customarily are payable on specified due dates, in the case of our common stock, (i) dividends are payable only when and if declared by our board of directors or a duly authorized committee of our board of directors, and (ii) as a corporation, we are restricted to making dividend payments and redemption payments out of legally available assets. We have never paid a dividend on our common stock and have no current intention to pay dividends in the future. Furthermore, our common stock places no restrictions on our business or operations or on our ability to incur indebtedness or engage in any transactions, subject only to the voting rights available to our shareholders generally.

General Risks

We may be unable to adequately protect our information technology systems from cyberattacks and other security breaches or incidents, which could result in the disclosure of confidential information, damage our reputation, and subject us to significant financial and legal exposure.

Maintaining the security of our computer information systems and communication systems is a critical issue and we devote considerable internal and external resources to maintaining the security and protection of our systems, but no security measures can provide absolute security. The complexity of our computer systems may make them vulnerable to service interruption, breaches of security, disruption of data integrity, inadvertent errors that expose our data or systems, malicious intrusion, or random attacks. Likewise, privacy or data security incidents or intentional or non-malicious breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information we maintain may be exposed to unauthorized persons or to the public, or that risk of loss or misuse of this information could occur, resulting in litigation and potential liability for us, damage our brand and reputation, or otherwise materially adversely affect our business, results of operations, and financial condition.

Cyberattacks upon systems, across industries, are increasing in their frequency, persistence, and sophistication, and are being conducted by sophisticated, well-funded, and organized groups and individuals. These cyberattacks may occur on our systems or those of our CROs or other third-party providers or partners. Additionally, certain threats are designed to remain dormant or undetectable until launched against a target and we may not be able to implement adequate preventative measures. Such cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, the deployment of harmful malware, ransomware attacks, denial-of-service, and/or other means to threaten data confidentiality, integrity and availability. Those engaging in attacks may implement social engineering techniques to induce our employees or contractors to disclose passwords or other sensitive information or take other actions to gain improper access to data or systems. Further, we engage third-party service providers to store and otherwise process sensitive and personal information, including our CROs. Our CROs and other service providers and partners face substantial risks of security breaches and incidents. Security breaches and other security incidents may result from malfeasance, error or negligence of our employees, contractors, CROs or other service providers or partners. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the loss or misappropriation of confidential business information and trade secrets, unauthorized access to or other compromise of personal information or other sensitive information, and the disclosure of corporate strategic plans. We have in the past experienced, and may in the future experience, a compromise of our data or information technology systems, or one or more other events, including employee or contractor error or malfeasance, that results in unauthorized access to, or acquisition, use, or disclosure of,

confidential or proprietary information about our company or sensitive information about individuals, such as employees or clinical trial participants, including PHI and other types of personal information. There can be no assurance that our cybersecurity protection efforts will prevent information security breaches or incidents we or those who maintain or process data on our behalf, including CROs and other contractors and consultants, may suffer that would result in business, legal or reputational harm to us, or would have a material adverse effect on our operating results and financial condition. We also may be required to incur significant costs in an effort to detect and prevent security breaches and other security-related incidents. Confidential information obtained by third parties in connection with past or future attacks could be used in ways that adversely affect our company or our stockholders.

Also, the majority of our workforce works remotely rather than in our offices, and we may be more susceptible to security breaches and incidents as a result. Our service providers may be more susceptible to security breaches and other security incidents while social distancing measures restrict the ability of their employees to work at offices to combat the COVID-19 pandemic. Depending on the nature of any information compromised, in the event of a data breach or other unauthorized access to our sensitive information, we may also have obligations to notify affected individuals and regulators about the incident, and we may be required or find it appropriate to provide some form of remedy, such as a subscription to credit monitoring services, pay significant fines to one or more regulators, or pay compensation in connection with a class-action settlement.

While our insurance policies include liability coverage for certain of these matters, subject to applicable deductibles, our insurance coverage might not be adequate for data handling or data security liabilities actually incurred, such insurance may not continue to be available to us in the future on economically reasonable terms, or at all, and insurers may deny us coverage as to any future claim. The successful assertion of one or more large claims against us that exceed available insurance coverage, or the occurrence of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could have a material adverse effect on our business, including our financial condition, operating results, and reputation.

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

Our operations, and those of our CROs and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemic, such as the COVID-19 pandemic, and other natural or man-made disasters or business interruptions, for which we may not have insurance coverage. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. In particular, the potential effects on our business due to the COVID-19 pandemic may be significant and could materially harm our business, operating results and financial condition. We rely on third-party manufacturers to produce and process momelotinib. Our ability to obtain supplies of momelotinib could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our corporate headquarters are located in San Mateo, California, which is near a major earthquake fault. Our operations and financial condition could suffer in the event of a major earthquake or other natural disaster near any of our locations.

We face risks related to securities litigation that could result in significant legal expenses and settlement or damage awards.

We have in the past and may in the future become subject to claims and litigation alleging violations of the securities laws or other related claims, which could harm our business and require us to incur significant costs. Any future litigation may require significant attention from management and could result in significant legal expenses, settlement costs or damage awards that could have a material impact on our financial position, results of operations and cash flows.

Changes in interpretation or application of generally accepted accounting principles may adversely affect our operating results.

We prepare our financial statements to conform to United States Generally Accepted Accounting Principles. These principles are subject to interpretation by the Financial Accounting Standards Board, American Institute of Certified Public Accountants, the Public Company Accounting Oversight Board, the Securities and Exchange Commission

and various other regulatory or accounting bodies. A change in interpretations of, or our application of, these principles can have a significant effect on our reported results and may even affect our reporting of transactions completed before a change is announced. Additionally, as we are required to adopt new accounting standards, our methods of accounting for certain items may change, which could cause our results of operations to fluctuate from period to period.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the securities or industry analysts who publish research about us downgrade our stock or publish inaccurate or unfavorable evaluations of our company or our stock, the price of our stock could decline. If one or more of these analysts cease coverage of our company, our stock may lose visibility in the market, which in turn could cause our stock price to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are located in San Mateo, California, where we occupy approximately 3,800 square feet of office space under a lease that expires on April 30, 2025. We believe that this facility is sufficient to meet our current needs.

Item 3. Legal Proceedings.

From time to time, we may become subject to other legal proceedings, claims and litigation arising in the ordinary course of business. In addition, we may receive letters alleging infringement of patents or other intellectual property rights. We are not currently a party to any other material legal proceedings, nor are we aware of any pending or threatened litigation that, in the opinion of our management, would have a material adverse effect on our business, operating results, cash flows or financial conditions should such litigation be resolved unfavorably. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Our common stock is listed on the Nasdaq Global Market. Our stock trades under the symbol "SRRA". As of March 7, 2022, there were 50 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

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. In addition, our ability to pay cash dividends is currently prohibited by the terms of our Loan and Security Agreement with Oxford Finance, LLC.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Securities Authorized for Issuance under Equity Compensation Plans

The information called for by this item is incorporated by reference to our Proxy Statement for the 2022 Annual Meeting of Stockholders. See Part III, Item 12 "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters."

Item 6. [Reserved].

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

The following discussion contains management's discussion and analysis of our financial condition and results of operations and should be read together with the historical consolidated financial statements and the notes thereto included in Part II, Item 8 "Consolidated Financial Statements and Supplementary Data." A discussion regarding our financial condition and results of operations for the year ended December 31, 2020 compared to the year ended December 31, 2019 is included in Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 11, 2021. This discussion and other parts of this Annual Report contain forward-looking statements that reflect our plans, objectives, expectations, intentions and beliefs and involve numerous risks and uncertainties, including but not limited to those described in the "Risk Factors" section of this Annual Report. Actual results may differ materially from those contained in any forward-looking statements. You should carefully read "Special Note Regarding Forward-Looking Statements" and Part I, Item 1A, "Risk Factors."

Overview

We are a late-stage biopharmaceutical company on a mission to deliver targeted therapies that treat rare forms of cancer. Our main focus is the development and potential commercialization of momelotinib, an investigational agent for the treatment of myelofibrosis. In January 2022, we announced positive topline results from our global Phase 3 clinical trial for patients with myelofibrosis who are symptomatic and anemic and previously treated with an approved JAK inhibitor, called MOMENTUM. Approximately 1,000 myelofibrosis patients have received momelotinib through clinical trials at different stages of clinical development, and several of our clinical trial patients have remained on treatment more than 11 years later.

In the fourth quarter of 2019, we launched MOMENTUM, a randomized double-blind Phase 3 trial designed to enroll 180 myelofibrosis patients who were symptomatic and anemic and had been treated previously with a JAK inhibitor. The Primary Endpoint of the trial is the Total Symptom Score (TSS) response rate of momelotinib compared to danazol at Week 24. Danazol has been selected as an appropriate treatment comparator given its use to ameliorate anemia in myelofibrosis patients, as recommended by National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) guidelines. Patients were randomized 2:1 to receive either momelotinib or danazol. After 24 weeks of treatment, patients on danazol were allowed to crossover to receive momelotinib.

During 2020 and 2021, we operationalized the MOMENTUM trial on a global basis despite the ongoing COVID-19 pandemic. In June 2021, we announced that the MOMENTUM Phase 3 clinical trial enrollment was completed, enrolling 195 patients based on a planned 180 patients. We recently announced that the MOMENTUM Phase 3 clinical trial met all of its primary and key secondary endpoints. We expect to submit a new drug application (NDA) to the U.S. Food and Drug Administration (FDA) for regulatory approval in the second quarter of 2022, and if approved, we could anticipate a commercial launch early in the first half of 2023. There are 15,000 prevalent myelofibrosis patients with anemia in the United States, which represents a potential addressable market for anemic myelofibrosis patients of $3.0 billion. We continue to explore opportunities to expand our pipeline via potential combination therapy studies involving momelotinib in combination with other therapeutic candidate(s), including with our newly in-licensed compound SRA515.

SRA515 (formerly AZD5153), is a potent and selective bromodomain-containing protein 4 (BRD4) bromodomain and extraterminal (BET) inhibitor with a novel bivalent binding mode that we acquired in August 2021 via an exclusive global licensing agreement with AstraZeneca AB (AstraZeneca). We plan to initiate a Phase 2 study examining momelotinib in combination with SRA515 for the treatment of myelofibrosis in the first half of 2022.

Our portfolio also includes SRA737, a selective, orally bioavailable small molecule inhibitor of Checkpoint kinase 1 (Chk1), an emerging target for the treatment of cancer which has a key role in the DNA Damage Response (DDR). In November 2020, we entered into an amendment to the License Agreement with CRT Pioneer Fund (CPF) to allow for the potential future clinical development of SRA737. We continue to evaluate several options for combination studies with momelotinib, SRA515 and SRA737 and hope to initiate one or more of them in 2022.

We wholly own momelotinib, subject to future milestone payments and royalties, and retain the global commercialization rights to SRA515 and SRA737.

COVID-19

The extent of the impact of COVID-19 on our operational and financial performance will depend on certain developments, including the duration and spread of the outbreak and any variants which have resulted in increased cases and has led to the reimplementation of restrictions in many areas, impact on our clinical studies, employee or industry events, and effect on our suppliers and manufacturers, all of which are uncertain and cannot be predicted. Due to the COVID-19 pandemic, we have recently begun to experience some supply chain delays including resourcing constraints by some of our manufacturing partners. There is a risk that if our supply chain is further interrupted, it would limit our ability to source drug substance and drug product for our clinical trials and may result in delays to the timing of our commercialization plans and could potentially increase our costs which would materially harm our business. We may experience constrained supply of momelotinib, SRA515 or, with respect to our planned clinical trials, we could again experience delays in planned site initiations and activations, or experience delays in enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis that could materially adversely impact our business, results of operations and overall financial performance in future periods. Specifically, we may experience impact from changes in how we and companies worldwide conduct business due to the COVID-19 pandemic, including but not limited to restrictions on travel and in-person meetings, prioritization of hospital resources toward pandemic effort, delays in review by the FDA and comparable foreign regulatory agencies, and further disruptions in our supply chain for momelotinib or SRA515. Any such delays to our planned development timelines and pre-commercialization efforts could also impact the use and sufficiency of our existing cash reserves, and we may be required to raise additional capital. We may be unable to raise additional capital if and when needed, which may result in delays or suspension of our development and potential commercial launch plans. As of the filing date of this Annual Report on Form 10-K, the extent to which COVID-19 may impact our financial condition, results of operations or guidance is uncertain. The effect of the COVID-19 pandemic will not be fully reflected in our results of operations and overall financial performance until future periods. See the section entitled “Risk Factors” included elsewhere in this report for further discussion of the possible impact of the COVID-19 pandemic on our business.

Components of Statements of Operations

Collaboration Revenue

Collaboration revenue consists of upfront license fees recognized under a collaboration agreement with Carna Biosciences, Inc.

Operating Expenses

Research and Development

Research and development expenses consist primarily of the following:

- fees, milestone payments or other expenses incurred in connection with license and asset purchase agreements and their related amendments;
- personnel-related costs, which include salaries, benefits, stock-based compensation, recruitment fees and travel costs;
- costs associated with research and preclinical studies, clinical trials, regulatory activities and manufacturing activities to support clinical activities and commercial product supply as we approach potential regulatory approval of momelotinib;
- fees paid to external service providers that conduct certain research and development, clinical and manufacturing activities on our behalf; and

- facility-related costs, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expenses and other supplies.

The largest recurring component of our total operating expenses has historically been our investment in research and development activities, including the development of momelotinib. We expect our research and development expenses will increase over the next few years as we continue to advance momelotinib, pursue regulatory approval of momelotinib in the United States and other jurisdictions, prepare for potential commercialization, including further significant investment in areas related to contract manufacturing and inventory buildup, achieve regulatory milestones that trigger payments due under our Asset Purchase Agreement with Gilead, including a milestone payment of $25.0 million due upon the approval of momelotinib from the FDA, develop SRA515, including a combination study examining momelotinib with SRA515, achieve certain milestones that trigger payments due under our license agreement with AstraZeneca, and expand our portfolio of product candidates.

The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for our lead product candidate, momelotinib. The probability of success of our product candidates may be affected by numerous factors, including clinical data, regulatory developments, competition, manufacturing capability and commercial viability. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization of momelotinib.

General and Administrative

General and administrative expenses consist of personnel-related costs, facility-related costs, business insurance, allocated expenses and professional fees for services, including legal, activities in preparation for potential commercialization, patent prosecution and maintenance, human resources, audit and accounting services. Personnel-related costs consist of salaries, benefits, stock-based compensation, recruitment fees, severance costs and travel costs.

We expect to incur additional expenses associated with supporting our growing research and development activities, preparing for potential commercialization, continuing to operate as a public company and other administration and professional services.

Other Expense (Income), net

Changes in Fair Value of Warrant Liabilities

Our common stock warrants issued in connection with our November 2019 financing were classified as liabilities on our consolidated balance sheets and, as such, were re-measured to fair value until January 2020, when they were no longer considered derivative instruments. Changes in fair value, which were directly attributable to changes in the fair value of the underlying stock and discount for lack of marketability, were recorded as an expense in the consolidated statement of operations.

Other Expense (Income), net

Other expense (income), net primarily consists of interest earned on our cash and cash equivalents and foreign currency exchange gains and losses related to transactions and monetary asset and liability balances denominated in currencies other than the U.S. dollar. Foreign currency exchange gains and losses may fluctuate in the future due to changes in foreign currency exchange rates.

Provision for (Benefit from) Income Taxes, net

Provision for (benefit from) income taxes, net consists of federal and state income taxes in the United States, income tax benefit resulting from research and development tax credits in Canada, income taxes in Canada and Australia, as well as deferred income taxes reflecting the net tax effects of temporary differences between the carrying amounts of

assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, and changes in related valuation allowance.

We did not record a provision for U.S. federal income taxes for the years ended December 31, 2021 and 2020. Our income tax provision relates to income taxes in Canada and Australia and our tax benefit relates to research and development tax credits in Canada. Our net U.S. deferred tax assets continue to be offset by a full valuation allowance.

Results of Operations

Year Ended December 31, 2021 Compared to Year Ended December 31, 2020

	Year Ended December 31,		Change	
	2021	2020	$	%
	(in thousands, except percentages)			
Collaboration revenue	$ —	$ 300	$ (300)	(100%)
Operating expenses:				
Research and development	67,150	45,118	22,032	49%
General and administrative	27,435	20,123	7,312	36%
Total operating expenses	94,585	65,241	29,344	45%
Loss from operations	(94,585)	(64,941)	(29,644)	46%
Other expense (income), net:				
Changes in fair value of warrant liabilities	—	16,240	(16,240)	(100%)
Other expense (income), net	77	(421)	498	(118%)
Total other expense (income), net	77	15,819	(15,742)	(100%)
Loss before provision for (benefit from) income taxes, net	(94,662)	(80,760)	(13,902)	17%
Provision for (benefit from) income taxes, net	(3)	142	(145)	(102%)
Net loss	$ (94,659)	$ (80,902)	$ (13,757)	17%

Collaboration Revenue

Collaboration revenue of $0.3 million was recognized during the year ended December 31, 2020 pursuant to the upfront fee received from a collaboration agreement (see Note 7 in the Notes to Consolidated Financial Statements). No collaboration revenue was recognized during the year ended December 31, 2021.

Research and Development

Research and development expenses increased $22.0 million, from $45.1 million in 2020 to $67.2 million in 2021. The increase was attributable to a $9.1 million increase in personnel-related and allocated overhead costs, including $2.9 million that pertained to an increase in non-cash stock-based compensation, primarily due to headcount additions to support the continued development and preparation for the regulatory submission of momelotinib. Also attributing to the increase was an upfront cash payment of $8.0 million that was made to AstraZeneca for the exclusive global license of SRA515, and external costs for momelotinib, including a $4.4 million increase in third-party manufacturing costs primarily pertaining to the production of pre-approval inventory and a $2.2 million increase in clinical trial and development costs primarily pertaining to the MOMEMENTUM clinical trial and the related preparation for regulatory submission. These increases were partially offset by a $1.5 million non-cash charge during the year ended December 31, 2020 to recognize the change in fair value of the securities until their issuance in January 2020 and a $0.2 million decrease in costs for SRA737.

General and Administrative

General and administrative expenses increased $7.3 million, from $20.1 million in 2020 to $27.4 million in 2021. The increase was attributable to a $4.9 million increase in personnel-related and allocated overhead costs, including a $0.5 million increase in non-cash stock-based compensation, primarily due to headcount additions for the expansion and continued buildout of our infrastructure to support our potential commercialization efforts, including the establishment of key commercial functions such as marketing and market access. Also attributing to the increase was an increase of $2.4 million in professional fees primarily relating to pre-commercial costs for momelotinib for the year ended December 31, 2021.

Changes in Fair Value of Warrant Liabilities

Our common stock warrants issued in connection with our November 2019 financing were classified as liabilities on our consolidated balance sheets and, as such, were re-measured to fair value until January 2020, when they were no longer considered derivative instruments. Changes in fair value, which were directly attributable to changes in the fair value of the underlying stock and discount for lack of marketability, were recorded as an expense in 2020. No such expense was recorded in 2021.

Other Expense (Income), net

Other expense (income), net increased $0.5 million, from $0.4 million of other income, net in 2020 to $0.1 million of other expense, net in 2021. This change primarily attributable to a $0.5 million decrease in interest income, due to lower interest rates for the year ended December 31, 2021.

Provision for (Benefit from) Income Taxes, net

Net provision for (benefit from) income taxes in 2021 and 2020 represented benefit from foreign research and development tax credits and foreign income taxes.

Liquidity and Capital Resources

Since our inception, we have never generated product revenue and have incurred significant net losses. We have funded our operations to date primarily from the issuance and sale of our common stock, pre-funded warrants, and convertible voting preferred stock and accompanying warrants through public offerings (including ATM equity offerings), our convertible and redeemable convertible preferred stock in private financings and, to a lesser extent, through exercises of our stock options and warrants. Our net losses for the year ended December 31, 2021 and 2020 were $94.7 million and $80.9 million, respectively. As of December 31, 2021, we had an accumulated deficit of $941.2 million, of which approximately $428.0 million pertained to the revaluation and conversion of redeemable convertible preferred stock upon our initial public offering in July 2015, $37.2 million related to changes in fair value of our Series A and Series B warrant liabilities until their reclassification to equity, and $12.0 million pertained to a securities issuance obligation settled in the first quarter of 2020. Our principal sources of liquidity as of December 31, 2021 were cash and cash equivalents of $104.7 million.

In March 2022, we issued 725,283 shares of common stock pertaining to the exercise of the warrant that was previously issued to Gilead pursuant to the securities purchase agreement. The warrant exercise provided $9.6 million of proceeds to us.

In January 2022, we completed an underwritten public offering of 4,074,075 shares of our common stock and pre-funded warrants to purchase up to 925,925 shares of our common stock. As part of the underwritten public offering, in February 2022, we issued an additional 750,000 shares of common stock representing the underwriters' full exercise of their over-allotment option. The shares of common stock and the pre-funded warrants were offered at a price of $27.00 and $26.999 per shares, respectively. The aggregate net proceeds from the offering were $145.6 million, after deducting underwriting discounts and commissions and estimated offering expenses.

In January 2022, we entered into a Loan and Security Agreement (Loan Agreement) with Oxford Finance, LLC (Oxford), pursuant to which we may obtain a loan up to an aggregate principal amount of $125.0 million (of which $50.0 million is subject to the lender's sole discretion) in four tranches based on certain pre-determined milestones. Contemporaneously with executing the Loan Agreement, we drew down the first $5.0 million tranche, which bears interest at a floating per year rate equal to the prime rate, plus a margin of 5.25%, subject to a floor of 8.50% and matures on January 1, 2027.

In August 2020, we filed a prospectus supplement, pursuant to which we issued and sold $20.0 million of our common stock from time to time in ATM offerings. In February, May and November 2021, we filed prospectus supplements pursuant to which we can issue and sell an aggregate of up to an additional $130.0 million from time to time in ATM offerings. During the second half of 2020, we sold 732,752 shares under the ATM program for proceeds of $8.9 million, net of commissions and offering expenses. During the year ended December 31, 2021, we sold 4,316,968 shares under the ATM program for proceeds of $78.2 million, net of commissions and offering expenses. As of December 31, 2021, there was $59.6 million remaining under the ATM program.

In November 2019, we completed an underwritten public offering of an aggregate of (i) 103,000 shares of Series A Preferred Stock, that all converted into 7,803,273 shares of common stock in January 2020, (ii) Series A warrants to purchase up to an aggregate of 7,802,241 shares of our common stock at an exercise price equal to $13.20, and (iii) Series B warrants to purchase up to an aggregate of 2,574,727 shares of common stock at an exercise price equal to $13.20. Each share of Series A Preferred Stock and the accompanying Series A and Series B warrants were issued at a combined price to the public of $1,000. The aggregate net proceeds from the offering were $97.7 million, net of underwriting discounts and commissions and offering expenses. The Series A warrants contain a cash and/or cashless exercise provision and expire on January 22, 2025. The Series B warrants may only be exercised by paying the exercise price in cash and expire on April 10, 2022. Subsequent to December 31, 2021, we issued 18,937 and 2,312,257 shares of common stock pertaining to the cash exercise of Series A and Series B warrants, respectively, providing proceeds of $30.8 million to us. The remaining outstanding Series B warrants, if fully exercised, would provide $2.8 million in proceeds.

We expect to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- hire additional personnel to support potential commercialization efforts, and additional clinical, regulatory, scientific, drug development and management personnel;
- invest to further develop our product candidates, potentially including combination studies as the field of myelofibrosis evolves;
- establish a sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval;
- invest in scaling our manufacturing capacity to support development and our global commercialization strategy;
- seek regulatory and marketing approvals for any product candidates that we may develop;
- achieve regulatory milestones that trigger payments due under our Asset Purchase Agreement with Gilead, including a milestone payment of $25.0 million due upon the approval of momelotinib from the FDA;
- achieve certain milestones that trigger payments due under our license agreement with AstraZeneca;
- acquire or in-license additional product candidates and technologies;
- develop additional product candidates;
- defend against potential lawsuits or other legal issues;
- maintain, expand and protect our intellectual property portfolio; and

- add operational, financial and management information systems and personnel to support our growing research and development activities, prepare for potential commercialization and continue to operate as a public company.

Our existing cash and cash equivalents may not be sufficient for us to prepare for the commercialization and the potential launch of momelotinib. Accordingly, we may need additional capital to continue our clinical development programs, fund our pre-commercial, and launch activities, however, we believe that our existing cash and cash equivalents will be sufficient to fund our current operating plans for at least the next twelve months. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities. Our forecast for the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. The amount and timing of the potential need for future funding requirements will depend on many factors, including costs related to our pre-commercialization, potential launch, and clinical development efforts including combination studies, the potential impacts of the COVID-19 pandemic on these efforts, or costs to develop additional product candidates.

We evaluate opportunities for strategic transactions, such as collaborations, strategic partnerships and alliances or licensing arrangements from time to time. To the extent that we raise additional capital through future equity financings, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. If we raise additional funds through strategic partnerships and alliances with third parties, we may have to relinquish valuable rights to our technologies or momelotinib or grant licenses on terms unfavorable to us. There can be no assurance that such additional financing, if available, can be obtained on terms acceptable to us. If we are to need but be unable to obtain additional financing, we would need to reevaluate our future operating plans.

Operating Expenditure Requirements and Contractual Obligations

We believe that our existing cash and cash equivalents will be sufficient to fund our current operating plans for at least the next twelve months.

We have contracted with various vendors and consultants to assist us in research and development activities for our product candidates, including agreements with contract research organizations and contract manufacturing organizations, potential commercialization efforts for momelotinib and operating as a public company. These contracts can be terminated at any time, subject to certain termination provisions.

We have operating lease obligations related to our office space in San Mateo, California and Vancouver, Canada. See Note 6 to our Consolidated Financial Statements under Item 8 of this Form 10-K.

We have entered into an asset purchase and license agreements that obligate us to make potential payments in the future if certain developmental, regulatory and commercial milestones are achieved. The milestones are accrued once they are considered probable of occurring. Additionally, we may be required to pay future royalties based upon net sales of a successfully developed product under these agreements. See Note 7 to our Consolidated Financial Statements under Item 8 of this Form 10-K.

In January 2022, we entered into a Loan Agreement with Oxford, pursuant to which we may obtain a loan up to an aggregate principal amount of $125.0 million (of which $50.0 million is subject to the lender's sole discretion) in four tranches based on certain pre-determined milestones. Contemporaneously with executing the Loan Agreement, we drew down the first $5.0 million tranche, which bears interest at a floating per year rate equal to the prime rate, plus a margin of 5.25%, subject to a floor of 8.50% and matures on January 1, 2027. In addition, a final payment fee of 6.0% of the principal amount of the loan will be payable upon repayment of the loan. See Note 11 to our Consolidated Financial Statements under Item 8 of this Form 10K.

Cash Flows

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Cash used in operating activities	$ (78,964)	$ (52,367)
Cash used in investing activities	(72)	(12)
Cash provided by financing activities	79,808	8,901
Effect of foreign exchange rate changes on cash, cash equivalents and restricted cash	(78)	5
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 694	$ (43,473)

Cash Flows from Operating Activities

In 2021, cash used in operating activities of $79.0 million was attributable to a net loss of $94.7 million, partially offset by $13.2 million in non-cash and other adjustments and a net change of $2.5 million in our net operating assets and liabilities. The non-cash charges consisted primarily of $12.9 million of non-cash stock-based compensation. The change in net operating assets and liabilities was primarily attributable to timing of payment of our operating expenses.

In 2020, cash used in operating activities of $52.4 million was attributable to a net loss of $80.9 million, partially offset by $27.7 million in non-cash and other adjustments and a net change of $0.8 million in our net operating assets and liabilities. The non-cash charges consisted primarily of a $16.2 million change in fair value of our warrant liabilities, a $1.5 million non-cash charge relating to the securities issuable to Gilead in connection with the amendment to the Asset Purchase Agreement, and $9.5 million of non-cash stock-based compensation. The change in net operating assets and liabilities was primarily attributable to timing of payment of our operating expenses.

Cash Flows from Investing Activities

Cash used in investing activities for each of December 31, 2021 and 2020 was primarily attributable to the purchase of property and equipment.

Cash Flows from Financing Activities

In 2021, cash provided by financing activities of $79.8 million consisted of $78.2 million net proceeds (gross proceeds of $81.1 million) from the sale of 4,316,968 shares under the ATM program, $0.8 million from the exercise of warrants to purchase common stock and $0.8 million from the exercise of stock options to purchase common stock.

In 2020, cash provided by financing activities was $8.9 million of net proceeds (gross proceeds of $9.3 million) from the sale of 732,752 shares under the ATM program.

Critical Accounting Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP). The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the

reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Research and Development Expenses

As part of the process of preparing financial statements, we are required to estimate and accrue expenses, a significant portion of which are research and development expenses. Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites. This process involves the following:

- reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost;
- estimating and accruing expenses in our financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with selected service providers and making adjustments, if necessary.

Estimated research and development expenses that we recognize include clinical trial costs under arrangements with third parties, such as contract research organizations (CROs), manufacturing costs under agreements with contract manufacturing organizations (CMOs), external research and development expenses incurred under arrangement with third parties and consultants, and license fees for technology that has not reached technological feasibility and does not have an alternative future use.

We recognize our expense related to clinical trials based on estimated cost of services provided by CROs and efforts expended pursuant to contracts with multiple research institutions that conduct and manage clinical trials on our behalf. Manufacturing costs are accrued based on our estimates of costs associated with various manufacturing stages and the estimated progress made by CMOs. The financial terms of these agreements vary for each contract and may result in uneven payment flows. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

To date, we have not experienced significant changes in our estimates of research and development expenses after a reporting period. However, due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research and development activities.

Stock-Based Compensation

Stock-based compensation costs related to stock options granted to employees are measured at the date of grant based on the estimated fair value of the award. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the estimated fair value of stock-based awards. See Note 9 to our Consolidated Financial Statements under Item 8 of this Form 10-K for detailed description of the assumptions we use. We will continue to use judgment in evaluating the expected volatility and expected terms utilized for our stock-based compensation calculations on a prospective basis.

For stock-based awards subject to the satisfaction of a service requirement and performance component, we exercise judgment in determining the probability of achieving the performance component and estimating the service periods required to achieve those performance components. Due to the nature of estimates, we cannot assure you that we will not make changes to our estimates in the future as we become aware of additional information.

Warrant Liabilities

Prior to the reclassification to equity on January 22, 2020, warrants for the purchase of shares of our common stock issued in connection with our November 2019 financing were classified as derivative liabilities on our consolidated balance sheets at their fair value. We estimated the fair value of these liabilities using assumptions that were based on the individual characteristics of the warrants on the valuation dates using the Black-Scholes option-pricing model. The valuation model was based on inputs, some of which were unobservable, as of the valuation dates, including the estimated volatility of our stock, the remaining contractual term of the warrants and the risk-free interest rates. An estimated non-marketable discount was also applied if applicable. These estimates affected the fair value of the warrant liabilities and the resulting expense recorded in our consolidated statement of operations. See Note 4 to our Consolidated Financial Statements under Item 8 of this Form 10-K for detailed description of the assumptions used.

Securities Issuance Obligation

The obligation to issue shares of our common stock and a warrant to purchase the same number of shares of common stock pursuant to the amendment to the Asset Purchase Agreement with Gilead was classified as a liability on our consolidated balance sheet at their fair values until its settlement on January 31, 2020. We estimated the fair values of these obligations using assumptions that were based on the individual characteristics of the securities to be issued. We used the fair value of the underlying stock and estimated non-marketable discount to determine the common stock issuance obligation, and the Black-Scholes option-pricing model and the fair value of the underlying stock to determine the fair value of the warrant issuance obligation. The valuation model was based on inputs, some of which were unobservable, as of the valuation dates, including the estimated volatility of our stock, the remaining contractual term of the warrants and the risk-free interest rates. An estimated non-marketable discount was also applied if applicable. These estimates affected the fair value of the securities issuance obligation and the resulting expense recorded in our consolidated statement of operations. See Note 4 to our Consolidated Financial Statements under Item 8 of this Form 10-K for detailed description of the assumptions used.

Off-Balance Sheet Arrangements

As of December 31, 2021, we did not have any off-balance sheet financing arrangements or any interest in entities referred to as variable interest entities, which includes special purpose entities and other structured finance entities.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities, foreign currency risk and inflation risk.

Interest Rate Sensitivity

We had cash and cash equivalents of $104.7 million as of December 31, 2021, which consisted primarily of bank deposits and money market funds. See Note 11 to our Consolidated Financial Statements under Item 8 of this Form 10-K for additional proceeds received by us during the first quarter of 2022. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. While the instruments in our portfolio are of short-term nature and a sudden change in market interest rates would not be expected to have a material impact, a zero-rate environment for an extended period of time could adversely affect our results of operations. We do not believe that our cash or cash equivalents have significant risk of default or illiquidity.

Foreign Currency Risk

Our consolidated results of operations and cash flows are subject to fluctuations due to changes in foreign currency exchange rates. A substantial majority of our expenses are denominated in U.S. Dollars, with the remainder in Canadian Dollars, Swiss Franc, Australian Dollars and British Pounds. Our consolidated results of operations and cash flow are, therefore, subject to fluctuations due to changes in foreign currency exchange rates and may be adversely affected in the future due to changes in foreign exchange rates. To date, we have not entered into any hedging arrangements with respect to foreign currency risk or other derivative instruments. The effect of a hypothetical 10% change in foreign currency exchanges rates applicable to our business would not have a material impact on our operating loss.

Inflation Risk

Inflation generally may affect us by increasing our cost of labor and operating costs. Inflation has not had a material effect on our business, financial condition or results of operations.

Item 8. Consolidated Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of Sierra Oncology, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Sierra Oncology Inc. and subsidiaries (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, shareholders' equity, and cash flows, for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

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 critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued Liabilities and Prepaid Expenses – Management’s Estimates of Accrued and Prepaid Research and Development Costs Associated with Clinical Trials - Refer to Notes 2 and 5 to the Financial Statements

Critical Audit Matter Description

The Company recognizes research and development costs for clinical trials based on an evaluation of the progress to completion of specific tasks using information and data provided by contract research organizations (CROs) and other third parties. Depending on the timing of payments to providers of research and development services, the Company recognizes prepaid expenses or accrued expenses related to these costs. These prepaid or accrued expenses are based on management’s estimates of the work performed under service agreements and milestones achieved.

We identified accrued and prepaid research and development costs related to clinical trials as a critical audit matter because of the judgments necessary for management to estimate the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of actual cost. The volume and complexity of the service agreements required a high degree of auditor judgment and an increased extent of effort when performing audit procedures to audit management's estimates of services performed and costs incurred and evaluating the results of those procedures.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to accrued and prepaid research and development costs associated with clinical trials include the following, among others:

- We evaluated publicly available information (such as press releases and investor presentations) and board of directors' materials regarding the status of clinical trial activities.
- We made selections of specific amounts recognized as research and development expense as well as those recognized as accrued and prepaid expenses to evaluate management's estimates of the services performed and costs incurred and performed the following procedures:
    - Obtained and read the related service agreements, amendments thereto, purchase orders, invoices, or other supporting documentation (such as communications between the Company and CROs).
    - Performed corroborating inquiries with Company management and clinical operations personnel.
    - Evaluated management's judgments compared to the evidence obtained.

/s/ Deloitte & Touche LLP

Grand Rapids, Michigan
March 10, 2022

We have served as the Company's auditor since 2014.

SIERRA ONCOLOGY, INC.

Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2021	December 31, 2020
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 104,749	$ 104,055
Prepaid expenses and other current assets	2,644	2,415
Total current assets	107,393	106,470
Property and equipment, net	141	52
Operating lease right-of-use assets	788	318
Other assets	1,045	647
TOTAL ASSETS	$ 109,367	$ 107,487
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accrued and other liabilities	$ 10,726	$ 7,148
Accounts payable	2,158	2,205
Total current liabilities	12,884	9,353
Operating lease liabilities	485	175
TOTAL LIABILITIES	13,369	9,528
Commitments and Contingencies (Note 7)		
STOCKHOLDERS' EQUITY:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized as of December 31, 2021 and December 31, 2020; nil shares issued and outstanding as of December 31, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value; 500,000,000 shares authorized as of December 31, 2021 and December 31, 2020; 15,571,656 and 11,128,484 shares issued and outstanding as of December 31, 2021 and 2020	16	11
Additional paid-in capital	1,037,230	944,537
Accumulated deficit	(941,248)	(846,589)
TOTAL STOCKHOLDERS' EQUITY	95,998	97,959
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 109,367	$ 107,487

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

SIERRA ONCOLOGY, INC.

Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,		
	2021	**2020**	**2019**
Collaboration revenue	$ —	$ 300	$ —
Operating expenses:			
Research and development	67,150	45,118	53,249
General and administrative	27,435	20,123	13,743
Total operating expenses	94,585	65,241	66,992
Loss from operations	(94,585)	(64,941)	(66,992)
Other expense (income), net:			
Changes in fair value of warrant liabilities	—	16,240	20,926
Other expense (income), net	77	(421)	517
Total other expense (income), net	77	15,819	21,443
Loss before provision for (benefit from) income taxes, net	(94,662)	(80,760)	(88,435)
Provision for (benefit from) income taxes, net	(3)	142	(160)
Net loss and comprehensive loss	$ (94,659)	$ (80,902)	$ (88,275)
Net loss per common share, basic and diluted	$ (7.14)	$ (7.70)	$ (30.30)
Weighted-average shares used in computing net loss per common share, basic and diluted	13,252,605	10,506,739	2,913,487

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

SIERRA ONCOLOGY, INC.
Consolidated Statements of Stockholders' Equity
(in thousands, except share data)

	Series A Convertible Voting Preferred Stock		Common Stock		Additional Paid-In	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Equity
Balance—December 31, 2018	—	$ —	1,859,120	$ 74	$ 771,817	$ (677,412)	$ 94,479
Issuance of common stock for exercise of common stock options	—	—	8,056	—	445	—	445
Stock-based compensation	—	—	—	—	5,695	—	5,695
Issuance of convertible voting preferred stock, net of offering costs of $4.0 million	103,000	1	—	—	74,000	—	74,001
Net loss	—	—	—	—	—	(88,275)	(88,275)
Balance—December 31, 2019	103,000	1	1,867,176	74	851,957	(765,687)	86,345
Conversion of Series A convertible voting preferred stock to common stock	(103,000)	(1)	7,803,273	8	(7)	—	—
Reclassification of warrant liabilities to equity	—	—	—	—	62,175	—	62,175
Issuance of common stock in connection with an amendment to the asset purchase agreement	—	—	725,283	1	8,781	—	8,782
Issuance of warrant in connection with an amendment to the asset purchase agreement	—	—	—	—	3,188	—	3,188
Reverse stock split adjustment	—	—	—	(73)	73	—	—
Stock-based compensation	—	—	—	—	9,470	—	9,470
Issuance of common stock from an At-The-Market equity offering, net of offering costs of $0.4 million	—	—	732,752	1	8,900	—	8,901
Net loss	—	—	—	—	—	(80,902)	(80,902)
Balance—December 31, 2020	—	—	11,128,484	11	944,537	(846,589)	97,959
Issuance of common stock from an At-The-Market equity offering, net of offering costs of $2.9 million	—	—	4,316,968	5	78,146	—	78,151
Issuance of common stock for exercise of common stock warrants	—	—	61,357	—	810	—	810
Issuance of common stock for exercise of common stock options	—	—	64,847	—	847	—	847
Stock-based compensation	—	—	—	—	12,890	—	12,890
Net loss	—	—	—	—	—	(94,659)	(94,659)
Balance—December 31, 2021	—	$ —	15,571,656	$ 16	$ 1,037,230	$ (941,248)	$ 95,998

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

SIERRA ONCOLOGY, INC.

Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2021	**2020**	**2019**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (94,659)	$ (80,902)	$ (88,275)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	12,890	9,470	5,695
Depreciation and amortization	305	238	83
Changes in fair value of warrant liabilities	—	16,240	20,926
Securities issuance obligation	—	1,485	10,485
Asset impairment	—	106	—
Warrant issuance costs	—	—	1,279
Term loan repayment fee	—	—	438
Other	(39)	201	161
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(622)	(33)	336
Accrued, other and operating lease liabilities	3,270	(366)	(2,034)
Accounts payable	(109)	1,194	(277)
Net cash used in operating activities	(78,964)	(52,367)	(51,183)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	(72)	(12)	(39)
Net cash used in investing activities	(72)	(12)	(39)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock from At-The-Market equity offering, net of offering costs	78,151	8,901	—
Proceeds from exercise of common stock options	847	—	445
Proceeds from exercise of common stock warrants	810	—	—
Proceeds from public offering, net of offering costs	—	—	97,731
Payment of term loan and repayment fee	—	—	(5,438)
Net cash provided by financing activities	79,808	8,901	92,738
Effect of foreign exchange rate changes on cash, cash equivalents and restricted cash	(78)	5	(34)
NET INCREASE (DECREASE) IN CASH, CASH EQUIVALENTS AND RESTRICTED CASH	694	(43,473)	41,482
CASH, CASH EQUIVALENTS AND RESTRICTED CASH — Beginning of period	104,355	147,828	106,346
CASH, CASH EQUIVALENTS AND RESTRICTED CASH — End of period	$ 105,049	$ 104,355	$ 147,828
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Cash paid for (refund of) income taxes, net	$ 66	$ 28	$ (69)
Cash paid for interest	$ —	$ —	$ 336
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING INFORMATION:			
Right-of-use asset obtained in exchange for operating lease obligation	$ 730	$ —	$ 771
Property and equipment purchases included in accounts payable	$ 62	$ —	$ —
Offering costs not yet paid	$ 54	$ 10	$ —
Issuance of common stock and common stock warrant in connection with an amendment to the asset purchase agreement	$ —	$ 11,970	$ —
Reclassification of warrant liabilities to equity	$ —	$ 62,175	$ —
Issuance costs of convertible voting preferred stock and warrants included in accrued and other liabilities	$ —	$ —	$ 268

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

1. Organization

Description of Business

Sierra Oncology, Inc. (together with its subsidiaries, collectively referred to as the "Company"), a Delaware corporation, is a late-stage biopharmaceutical company focused on development and potential commercialization of momelotinib, an investigational agent for the treatment in myelofibrosis. Momelotinib is a selective and orally bioavailable JAK1 (Janus kinase 1), JAK2 (Janus kinase 2) and ACVR1 (Activin A receptor type 1) / activin receptor-like kinase-2 (ALK2) inhibitor with a differentiated mechanism of action. In January 2022, the Company announced positive topline results from its global Phase 3 clinical trial, called MOMENTUM, for patients with myelofibrosis who are symptomatic and anemic and previously treated with an approved JAK inhibitior. Momelotinib achieved a statistically significant benefit on symptoms, anemia and splenic size. The MOMENTUNM data, combined with data from earlier clinical trials, will be the basis for a New Drug Application (NDA) that the Company plans to submit in the second quarter of 2022. Approximately 1,000 myelofibrosis patients have received momelotinib through clinical trials at different stages of clinical development, and several of these patients remain on treatment more than 11 years later.

In August 2021, the Company acquired an exclusive global license from AstraZeneca AB (AstraZeneca) for SRA515 (formerly AZD5153), a potent and selective bromodomain-containing protein 4 (BRD4) bromodomain and extraterminal (BET) inhibitor with a novel bivalent binding mode (See Note 7).

The Company's portfolio also includes SRA737, a selective, orally bioavailable small molecule inhibitor of Checkpoint kinase 1 (Chk1), an emerging target for the treatment of cancer which has a key role in the DNA Damage Response (DDR).

The Company's primary activities since inception have been conducting research and development activities, conducting preclinical and clinical testing, recruiting personnel, preparing for potential commercialization, performing business and financial planning, identifying and evaluating additional drug candidates for potential in-licensing or acquisition, and raising capital to support development activities.

The Company has not generated any product revenue related to its primary business purpose to date, nor has it generated any net income, and is subject to a number of risks and uncertainties, which include dependence on key individuals, the need to identify and successfully develop commercially viable products, the need to obtain regulatory approval for its products and commercialize them, and the potential need to obtain additional financing to continue the Company's clinical development programs and fund pre-commercial and launch activities.

As of December 31, 2021, the Company had $104.7 million of cash and cash equivalents. The Company believes that its balance of cash and cash equivalents as of the date of the issuance of these consolidated financial statements is sufficient to fund its current operational plan for at least the next twelve months.

Reverse Stock Split

On January 21, 2020, the Company's shareholders approved an amendment to the Company's certificate of incorporation to effect a reverse split of the Company's common stock (Reverse Stock Split). On January 21, 2020, the Company's board of directors approved the specific ratio for the Reverse Stock Split, which became effective on January 22, 2020, at 1-for-40. The authorized shares and par value of the common and preferred stock were not adjusted as a result of the Reverse Stock Split. All issued and outstanding common stock, warrants for common stock, options for common stock and per share amounts contained in the consolidated financial statements have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America (U.S. GAAP). The accompanying consolidated financial statements include the accounts of Sierra Oncology, Inc. and its wholly-owned subsidiaries. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of the consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of consolidated financial statements and the reported amounts of expense during the reporting period. Significant estimates and assumptions made in the accompanying consolidated financial statements include, but are not limited to, the fair values of stock options and warrants issued, the fair value of the securities issuance obligation, the probability of achieving performance-based milestones of stock options, accruals such as research and development costs, and recoverability of the Company's net deferred tax assets, and related valuation allowance. The Company evaluates its estimates and assumptions on an ongoing basis using historical experience and other factors and adjusts those estimates and assumptions when facts and circumstances dictate. Actual results could materially differ from those estimates.

Foreign Currency

The functional currency of the Company's foreign subsidiaries is the U.S. Dollar. Transactions denominated in currencies other than the functional currency are recorded at prevailing exchange rates during the period. At the end of each reporting period, monetary assets and liabilities are remeasured to the functional currency using exchange rates in effect at the balance sheet date. Non-monetary assets and liabilities are recorded at historical exchange rates. Gains and losses related to remeasurement are recorded in other expense (income), net in the consolidated statements of operations. The net foreign exchange transaction losses (gains) included in other expense (income), net in the accompanying consolidated statements of operations were insignificant for the years ended December 31, 2021, 2020 and 2019.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents consist primarily of funds invested in readily available checking and savings accounts and highly liquid investments in money market funds.

Restricted Cash

Restricted cash, which consists of funds held in a savings account, represents collateral for a corporate credit card facility and is included in other assets in the accompanying consolidated balance sheets. See also Note 5.

Concentrations of Credit Risk

Financial instruments that subject the Company to significant concentrations of credit risk consist of cash, cash equivalents and restricted cash. All of the Company's cash, cash equivalents and restricted cash are held at financial institutions in the United States and Canada that management believes to be of high credit quality. Deposits held in the United States and Canada with these financial institutions exceed federally insured limits.

The primary focus of the Company's investment strategy is to preserve capital and meet liquidity requirements. The Company's investment policy addresses the level of credit exposure by limiting the concentration in any one corporate issuer and establishing a minimum allowable credit rating.

Fair Value of Financial Instruments

The Company's cash and cash equivalents, restricted cash, other current assets, accounts payable and accrued and other liabilities approximate their fair values at December 31, 2021 and 2020, due to their short duration. The warrant liabilities and securities issuance obligation contained unobservable inputs that reflected the

Company's own assumptions in which there was little, if any, market activity at the measurement date, thus the Company's warrant liabilities and securities issuance obligation were measured at their fair values on a recurring basis using unobservable inputs until such time the warrants were no longer considered derivative instruments and the securities issuance obligation was settled.

The Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible. The Company determines the fair value of its financial instruments based on assumptions that market participants would use in pricing an asset or liability in the principal or most advantageous market. When considering market participant assumptions in fair value measurements, the following fair value hierarchy distinguishes between observable and unobservable inputs, which are categorized in one of the following levels:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level 3—Unobservable inputs that are significant to the measurement of the fair value of the assets or liabilities that are supported by little or no market data.

Property and Equipment, Net

Property and equipment, net are stated at cost, less accumulated depreciation. Depreciation on property and equipment, excluding leasehold improvements, is computed using the straight-line method over the estimated useful lives of the respective assets, generally three to five years. Leasehold improvements are amortized on a straight-line basis over the shorter of the estimated useful lives of the assets or the remaining lease term. Depreciation begins at the time the asset is placed in service. Maintenance and repairs are charged to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the consolidated balance sheet and the resulting gain or loss is reflected in the consolidated statement of operations.

Other Assets

Other assets consist primarily of restricted cash pledged as collateral for a corporate credit card facility, deferred income tax assets in foreign jurisdictions, noncurrent portion of implementation costs related to cloud-computing arrangements and deferred financing costs.

Operating Lease Right-of-Use Assets and Lease Liabilities

The Company recognizes operating leases with terms greater than one year as right-of-use (ROU) assets and lease liabilities on its consolidated balance sheet using the portfolio approach. Lease liabilities and ROU assets are recorded based on the present value of future lease payments over the contractual terms of the operating leases. The Company utilizes its incremental borrowing rate from information available as at the date of initial adoption or inception of the lease in determining the present value of the future lease payments. The lease liabilities and ROU assets are amortized over the terms of the leases.

Research and Development Costs

Research and development costs are expensed as incurred. The Company accounts for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the goods have been received or when the service has been performed rather than when the payment is made. Depending on the timing of payments to service providers of research and development costs, the Company recognizes prepaid expenses or accrued expenses related to these costs. These prepaid or accrued expenses are based on management's estimates of the work performed under service agreements and milestones achieved.

Upfront payments made in connection with asset purchase and license agreements are expensed as research and developments costs, as the assets acquired do not have alternative future use. Contingent milestone payment obligations due to third parties under license and asset purchase agreements are expensed when the milestones are considered probable of occurring. To the extent an obligation is to be settled by future issuance of securities, the fair value of these instruments is recorded in research and development expense until the securities are issued.

Research and development costs include fees incurred in connection with asset purchase and license agreements and their related amendments, compensation and other related costs for employees engaged in research and development, costs associated with research and preclinical studies, clinical trials, regulatory activities, manufacturing activities to support clinical activities and commercial product supply as the Company approaches potential regulatory approval of momelotinib, fees paid to external service providers that conduct certain research and development, clinical, and manufacturing activities on behalf of the Company and an allocation of overhead expenses.

Stock-Based Compensation

The Company accounts for stock-based payments at fair value, which is measured using the Black-Scholes option-pricing model. For stock-based awards that vest subject to the satisfaction of a service requirement, the fair value measurement date for stock-based compensation awards is the date of grant and the expense is recognized on a straight-line basis over the vesting period, which is generally the service period. For stock-based awards that vest subject to the satisfaction of a service requirement and a performance component, the fair value measurement date is the date of grant and the expense is recognized over the requisite service period as achievement of the performance objective becomes probable. The Company accounts for forfeitures as they occur.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Management makes an assessment of the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to the Company's historical operating performance and the recorded cumulative net losses in prior fiscal periods, the net U.S. deferred tax assets have been offset by a full valuation allowance.

The Company recognizes uncertain income tax positions at the largest amount that is more likely than not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained. Changes in recognition or measurement are reflected in the period in which judgment occurs. The Company recognizes interest and penalties related to the underpayment of income taxes as a component of provision for (benefit from) income taxes, net.

Segment Information

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by the Company's chief operating decision maker in deciding how to allocate resources and assessing performance. The Company's chief operating decision maker is its Chief Executive Officer.

The Company's Chief Executive Officer views the Company's operations and manages its business in one operating segment, which is the business of researching, developing and commercializing therapies for the treatment of patients with hematology and oncology needs. Accordingly, the Company has a single reporting segment.

3. Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common stock outstanding during the period without consideration for common stock equivalents. In 2019, preferred stock with characteristics of common stock was also included in the determination of the weighted average. Diluted net loss per share is computed by dividing net loss by the weighted-average number of common stock equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, stock options and warrants for common stock are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following shares of common stock equivalents were excluded from the calculation of diluted net loss per share for the periods presented because including them would have been antidilutive:

	As of December 31,		
	2021	2020	2019
Series A warrants for common stock	7,790,879	7,802,241	7,802,241
Series B warrants for common stock	2,524,732	2,574,727	2,574,727
Options to purchase common stock	4,937,189	4,146,928	326,023
Warrants for common stock	727,122	727,122	1,839
Total potential dilutive shares	15,979,922	15,251,018	10,704,830

Also excluded from the calculation of diluted net loss per share are 4,824,075 shares of common stock and pre-funded warrants to purchase up to 925,925 common stock issued subsequent to December 31, 2021 (see Note 11).

4. Fair Value Measurements

The Company measures and reports its cash equivalents at fair value. The following table sets forth the fair value of the Company's financial assets measured on a recurring basis by level within the fair value hierarchy:

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial Assets				
Money market funds	$ 102,526	$ —	$ —	$ 102,526

	December 31, 2020			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial Assets				
Money market funds	$ 101,919	$ —	$ —	$ 101,919

Money market funds are measured at fair value on a recurring basis using quoted prices and are classified as a Level 1 input.

Prior to reclassification into equity in January 2020, the Company's warrant liabilities and securities issuance obligation contained unobservable inputs that reflected the Company's own assumptions in which there was little, if any, market activity at the measurement date. Accordingly, the Company's warrant liabilities and

securities issuance obligation were measured at fair value on a recurring basis using unobservable inputs and were classified as Level 3 inputs.

The fair values of the Series A and Series B warrants (see Note 8) were estimated using the Black-Scholes option-pricing model. The expected terms represented the periods that the warrants are expected to be outstanding. The risk-free interest rates were based on the U.S. Constant Maturity treasury curve commensurate with the time to expiry. The expected dividend was zero as the Company has not paid nor does it anticipate paying any dividends on its common stock in the foreseeable future. The expected volatilities were estimated by backsolving to volatility implied in the transaction price. Discount for lack of marketability was dependent on the restriction period and the estimated volatility during the period.

The fair value of the warrant issuance obligation (see Note 7) was estimated using the Black-Scholes option-pricing model. The expected term represented the period that the underlying warrant is expected to be outstanding from the time the issuance obligation arose. The risk-free interest rate was based on the U.S. Constant Maturity treasury curve commensurate with the time to expiry. The expected dividend was zero as the Company has not paid nor does it anticipate paying any dividends on its common stock in the foreseeable future. The expected volatility was estimated by backsolving to volatility implied in the transaction price. The fair value of the common stock issuance obligation was estimated based on the fair value of the underlying common stock. Discount for lack of marketability was dependent on the restriction period and the estimated volatility during the period.

The assumptions used in calculating the estimated fair values at the end of the reporting period represent the Company's best estimate. However, inherent uncertainties are involved. If factors or assumptions change, the estimated fair values could be materially different.

At November 13, 2019, upon the issuance of Series A and Series B warrants and when the securities issuance obligation arose, the Company estimated the fair values of the financial liabilities using the following assumptions:

	Series A Warrant	Series B Warrant	Warrant Issuance Obligation	Common Stock Issuance Obligation
Expected term (in years)	5.2	2.3	5.2	N/A
Expected volatility	43%	88%	43%	N/A
Risk-free interest rate	1.70%	1.64%	1.70%	N/A
Expected dividend yield	— %	— %	— %	N/A
Discount for lack of marketability	30%	30%	32%	32%

At December 31, 2019, the Company remeasured these liabilities to their fair values using the following assumptions:

	Series A Warrant	Series B Warrant	Warrant Issuance Obligation	Common Stock Issuance Obligation
Expected term (in years)	5.1	2.2	5.1	N/A
Expected volatility	43%	88%	43%	N/A
Risk-free interest rate	1.69%	1.59%	1.70%	N/A
Expected dividend yield	— %	— %	— %	N/A
Discount for lack of marketability	25%	25%	25%	25%

At January 22, 2020, Series A and Series B warrants were no longer considered to be derivative instruments. The Company remeasured the fair value of the warrant liabilities at the time of reclassification to equity using the following assumptions:

	Series A Warrant	Series B Warrant
Expected term (in years)	5.0	2.1
Expected volatility	43%	88%
Risk-free interest rate	1.57%	1.53%
Expected dividend yield	—%	—%

The fair value of the Series A and Series B warrants at the time of issuance in November 2019, at December 31, 2019 and at the time they ceased to be derivative instruments in January 2020 were estimated to be $25.0 million, $45.9 million and $62.1 million, respectively. The Company recorded a $16.2 million and $20.9 million non-cash expense relating to the change in fair value of warrant liabilities in other expense (income), net in the accompanying consolidated statement of operations for the years ended December 31, 2020 and 2019, respectively.

On September 8, 2021, the Company amended certain terms of Series A warrants and Series B warrants (see Note 8). The amendments did not result in changes to the fair value of these warrants.

At January 31, 2020, the securities issuance obligation was settled by the issuance of common stock and a common stock warrant. The fair value of its common stock issuance obligation was remeasured based on the value of the common stock at the time of issuance. The fair value of the warrant issuance obligation was remeasured using the following assumptions:

	Warrant Issuance Obligation
Expected term (in years)	5.0
Expected volatility	43%
Risk-free interest rate	1.57%
Expected dividend yield	— %

The fair value of the securities issuance obligation when the obligation arose in November 2019, at December 31, 2019 and at the time the obligation was settled in January 2020 were estimated to be $6.4 million, $10.5 million and $12.0 million, respectively. The Company recognized a $10.5 million and $1.5 million non-cash research and development expense for the years ended December 31, 2020 and 2019, respectively, based on the fair value of the securities to be issued, in the consolidated statement of operations.

The following table provides a summary of changes in the estimated fair values of the Company's Level 3 financial liabilities, which were measured at fair value on a recurring basis using unobservable inputs:

	Series A Warrant Liability	Series B Warrant Liability	Warrant Issuance Obligation	Common Stock Issuance Obligation	Total
			(in thousands)		
Balance, December 31, 2019	$ 32,616	$ 13,319	$ 3,036	$ 7,449	$ 56,420
Changes in fair value	11,597	4,643	152	1,333	17,725
Settlement of financial liabilities by securities issuance	—	—	(3,188)	(8,782)	(11,970)
Reclassification to equity	(44,213)	(17,962)	—	—	(62,175)
Balance, December 31, 2020 and 2021	$ —	$ —	$ —	$ —	$ —

Fluctuations in fair values of the financial liabilities were attributable to changes in the fair value of the underlying stock and non-marketable discount.

There were no transfers between Levels 1, 2 or 3 during the years ended December 31, 2021 and 2020.

5. Balance Sheet Components

Cash and Cash Equivalents

Cash and cash equivalents consist of the following:

	December 31, 2021	December 31, 2020
	(in thousands)	
Cash	$ 2,223	$ 2,136
Cash equivalents:		
Money market accounts	102,526	101,919
Total cash and cash equivalents	$ 104,749	$ 104,055

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported in the consolidated balance sheets to the amounts shown in the consolidated statements of cash flows.

	December 31, 2021	December 31, 2020
	(in thousands)	
Cash and cash equivalents	$ 104,749	$ 104,055
Restricted cash included in other assets	300	300
Total cash, cash equivalents and restricted cash shown in the consolidated statement of cash flows	$ 105,049	$ 104,355

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31, 2021	December 31, 2020
	(in thousands)	
Prepaid insurance	$ 1,029	$ 991
Prepaid software and subscription fees	536	376
Prepaid research and development project costs	290	321
Other receivables	147	311
Other	642	416
Total prepaid expenses and other current assets	$ 2,644	$ 2,415

Property and Equipment, net

Property and equipment, net consists of the following:

	December 31, 2021	December 31, 2020
	(in thousands)	
Software	$ 456	$ 361
Leasehold improvements	35	—
Computer equipment	5	—
Property and equipment, gross	496	361
Less: accumulated depreciation	(355)	(309)
Total property and equipment, net	$ 141	$ 52

Depreciation related to the Company's property and equipment for the year ended December 31, 2021 was $45,000. Depreciation for each of the years ended December 31, 2020 and 2019 was $0.1 million.

Accrued and Other Liabilities

Accrued and other liabilities consist of the following:

	December 31, 2021	December 31, 2020
	(in thousands)	
Accrued employee related costs	$ 6,725	$ 4,359
Accrued research and development costs	2,727	1,715
Accrued professional fees	739	774
Operating lease liabilities	368	207
Other	167	93
Total accrued and other liabilities	$ 10,726	$ 7,148

6. Leases

In December 2020, the Company entered into a 48-month operating lease agreement to lease office space in San Mateo, California. The lease commenced on April 30, 2021 and expires on April 30, 2025.

The Company also has an operating lease agreement to lease office space in Vancouver, Canada that expires on February 28, 2023. In December 2020, the Company entered into an agreement to sublet the entire office premises to a third party until February 27, 2023. Pursuant to the sublease agreement, the subtenant will pay base rent of $0.2 million per annum to the Company and all operating costs related to the office space. The Company recorded an impairment charge of $0.1 million during the year ended December 31, 2020.

The components of lease expense and related cash flows for the years ended December 31, 2021, 2020 and 2019 were as follows:

	Year ended December 31,		
	2021	2020	2019
	(in thousands)		
Operating lease cost	$ 299	$ 195	$ 203
Short-term lease cost	27	42	117
	326	237	320
Operating cash flows used for operating leases	$ 286	$ 212	$ 198

As of December 31, 2021, the weighted average remaining lease term and discount rate for the operating leases are 2.9 years and 4.7%, respectively.

As of December 31, 2021, maturities of lease liability due under the lease agreement are as follows:

Years Ending December 31:	Operating Leases (in thousands)
2022	397
2023	223
2024	230
2025	58
Total lease payments	908
Less imputed interest	(55)
Total	$ 853

These amounts have not been reduced by future base rent due under the Vancouver sublease of $0.2 million. In addition to base rent, the Vancouver lease requires payment of operating costs. These costs are also not included in the table above or the sublease amount.

7. Commitments and Contingencies

Asset Purchase Agreement

In August 2018, the Company entered into an Asset Purchase Agreement with Gilead whereby the Company acquired worldwide rights to the pharmaceutical product momelotinib, an investigational orally-bioavailable JAK1, JAK2 and ACVR1/ALK2 inhibitor together with all related intellectual property rights and certain other related assets. Pursuant to the agreement, the Company made a one-time upfront payment of $3.0 million in August 2018. In October 2019, the Company entered into an amendment to the Asset Purchase Agreement in which the Company agreed to issue, subject to certain conditions, shares of common stock and a warrant to purchase common stock to Gilead in consideration for meaningfully reduced royalty rates and elimination of a near term milestone payment in the Asset Purchase Agreement. Pursuant to the amended agreement, milestone payments of up to an aggregate of $190.0 million may become payable to Gilead upon the achievement of certain regulatory and commercial milestone events, including a milestone payment of $25.0 million due upon the approval of momelotinib from the U.S. Food and Drug Administration (FDA). These milestones will be accrued once they are considered probable of occurring. In addition, the Company is now required to pay Gilead low double-digit to high-teens percent tiered combined royalties based upon net sales.

License Agreements

In August 2021, the Company entered into a license agreement with AstraZeneca for an exclusive global license for SRA515 and related compounds, which selectively inhibit BRD4. Under the agreement, the Company has an exclusive license to develop, manufacture and commercialize SRA515 for all therapeutic, prophylactic, palliative and diagnostic uses in humans and animals. The Company made a one-time, non-refundable upfront cash payment of $8.0 million to AstraZeneca, which was expensed as research and development costs during the year ended December 31, 2021. In addition, pursuant to the license agreement, the Company will pay $0.9 million to AstraZeneca for the purchase of drug products and drug substance, which is expected to occur in the first quarter of 2022. Aggregate milestone payments of up to $208.0 million may become payable by the Company upon the achievement of certain development, regulatory and commercial milestones. These milestones will be accrued once they are considered probable of occurring. In addition, the Company is required to pay AstraZeneca a tiered royalty on worldwide net sales ranging from high single-digits to low double-digits.

In September 2016, the Company entered into an exclusive license agreement with CRT Pioneer Fund LP (CPF) for worldwide rights, know-how and materials to develop SRA737, a small molecule inhibitor targeting Chk1, a promising therapeutic target to treat cancer. Pursuant to the agreement, the Company made a one-time upfront payment of $7.0 million to CPF in October 2016 and paid $2.0 million to CPF in January 2017 for the successful transfer of two ongoing Phase 1 clinical trials. Pursuant to the original license agreement, additional milestone payments of up to an aggregate of $319.5 million may have become payable to CPF upon the achievement of certain milestones. In November 2020, the Company entered into an amendment to the license agreement with CPF, which amended the terms and reduced the amounts of certain future milestones. Pursuant to the amended agreement, future milestone payments of up to an aggregate of $290.0 million may become payable to CPF upon the achievement of certain developmental, regulatory and commercial milestones, including a milestone payment of $2.0 million upon the dosing of the first patient of the first trial of SRA737 following the effective date of the amendment. These milestones will be accrued once they are considered probable of occurring. In addition, the Company is required to pay CPF, on a product-by-product and country-by-country basis, tiered high single-digit to low double-digit royalties on the net sales of any product successfully developed.

In May 2016, the Company entered into an exclusive license agreement (Carna License Agreement) with Carna Biosciences, Inc. (Carna) for worldwide rights to develop and commercialize SRA141, a small molecule kinase inhibitor targeting Cdc7. In exchange for this exclusive right, the Company paid Carna an upfront payment of $0.9 million in June 2016. In June 2020, the Company entered into a collaboration agreement (Carna Collaboration Agreement) with Carna, effectively terminating the Carna License Agreement. Pursuant to the Carna Collaboration Agreement, Carna paid an upfront fee of $0.3 million, which was recognized as collaboration revenue during the year ended December 31, 2020 by the Company, for the exclusive worldwide rights for SRA141 and other transition services. In addition, the Company may be entitled to single-digit royalties on product sales, on a product-by-product basis, and low to mid-teen profit share on royalty and non-royalty income.

Legal

From time to time, the Company may become subject to other legal proceedings, claims and litigation arising in the ordinary course of business. In addition, the Company may receive letters alleging infringement of patent or other intellectual property rights. The Company is not currently a party to any other material legal proceedings, nor is it aware of any pending or threatened litigation that, in the Company's opinion, would have a material adverse effect on the business, operating results, cash flows or financial condition should such litigation be resolved unfavorably.

COVID-19

The full extent of the impact of the COVID-19 pandemic on financial markets, economies worldwide and our business continues to be highly uncertain. Research and development expenses and general and administrative expenses may vary significantly if there is an increased impact from COVID-19 on the costs and timing

associated with the conduct of clinical trials and other related business activities. The Company is carefully monitoring the pandemic and the potential length and depth of the resulting economic impact on its financial condition and results of operations. As of December 31, 2021, the Company was not aware of any contingencies and no related estimates were recorded in its financial statements as a result of COVID-19.

8. Stockholders' Equity

At-The-Market Common Stock Offerings

In August 2020, the Company filed a prospectus supplement, pursuant to which it sold $20.0 million of its common stock in At-The-Market (ATM) offerings. In February, May and November 2021, the Company filed prospectus supplements pursuant to which it can issue and sell an aggregate of up to an additional $130.0 million of its common stock from time to time in ATM offerings. During the year ended December 31, 2021 and 2020, the Company sold 4,316,968 and 732,752 shares, respectively, under the ATM program for net proceeds of $78.2 million and $8.9 million, respectively, net of commissions and offering expenses. As of December 31, 2021, there was $59.6 million remaining available under the ATM program.

Common Stock Reserved for Issuance

The Company is required to reserve and keep available out of its authorized but unissued shares of common stock a number of shares sufficient to effect the conversion of all outstanding options granted and available for grant under the incentive plans, shares reserved for issuance under the employee stock purchase plan and issued warrants.

	December 31, 2021	December 31, 2020
Shares reserved under Series A warrant	7,790,879	7,802,241
Shares reserved under Series B warrant	2,524,732	2,574,727
Shares reserved for future option grants under equity plans	1,207,827	1,117,796
Outstanding stock options under equity incentive plans	4,937,189	4,146,928
Outstanding warrants	727,122	727,122
Shares reserved under the 2015 employee stock purchase plan	17,500	17,500
Total common stock reserved for issuance	17,205,249	16,386,314

Preferred Stock

On November 13, 2019, the Company completed an underwritten public offering whereby it issued 103,000 shares of Series A convertible voting preferred stock (Series A Preferred Stock) together with Series A warrants and Series B warrants for a combined purchase price of $1,000. The aggregate net proceeds received by the Company from the offering were $97.7 million, net of underwriting discounts and commissions and offering expenses of $5.3 million. Each share of Series A Preferred Stock was convertible into shares of the Company's common stock equal to the stated value of the Series A Preferred Stock of $1,000 divided by the voting conversion price of $13.20. On January 29, 2020, all shares of Series A Preferred Stock converted into 7,803,273 shares of the Company's common stock.

Common Stock Warrants

In connection with the Company's November 2019 public offering of the Series A Preferred Stock, the Company issued Series A warrants to purchase up to 7,802,241 shares of common stock at an exercise price equal to $13.20, and Series B warrants to purchase up to 2,574,727 shares of common stock at an exercise price equal to $13.20. Both Series A and Series B warrants are exercisable following stockholder approval in January 2020 of an increase in authorized common stock sufficient to allow for the exercise of the warrants, subject to certain beneficial ownership limitations. The Series A warrants will expire five years from the date they first became exercisable or on January 22, 2025 and contain a cash and/or cashless exercise provision. The Series B warrants will expire on the 75th day anniversary following the announcement of top-line data

from the Company's MOMENTUM Phase 3 clinical trial of momelotinib and may only be exercised by paying the exercise price in cash. With the announcement of topline data by the Company on January 25, 2022, the Series B warrants will expire on April 10, 2022 (see Note 11 for information pertaining to the exercise of Series B warrants subsequent to December 31, 2021). During the year ended December 31, 2021, 151,500 Series B warrants to purchase 49,995 shares of common stock and 11,362 Series A warrants to purchase 11,362 shares of common stock were exercised for proceeds of $0.7 million and $0.1 million, respectively. There were no warrants exercised during the year ended December 31, 2020.

On September 8, 2021, the Company entered into Amendment No. 1 to Series A warrants and Amendment No. 1 to Series B warrants. These amendments clarified the methodology by which Series A warrants and Series B warrants would be assumed or settled in the event of a Fundamental Transaction, as defined under the warrant agreements, and provided for greater consistency in the treatment of these warrants by a publicly-traded or private buyer. The amendments did not result in changes to the fair value of these warrants. As such, no expense was recorded during the year ended December 31, 2021 relating to the modifications to the warrants.

In connection with obligations under the amendment to the Asset Purchase Agreement (See Note 7), the Company entered into a securities purchase agreement on January 31, 2020 and issued to Gilead 725,283 shares of the Company's common stock and a warrant to purchase 725,283 shares of common stock at a price per share of $13.20. The warrant is immediately exercisable, will expire on January 31, 2025 and contains a cash and/or cashless exercise provision (see Note 11 for information pertaining to exercise of the warrant subsequent to December 31, 2021).

In August 2018, in connection with a Loan and Security Agreement (Loan Agreement) with Silicon Valley Bank (SVB), the Company issued a warrant to SVB to purchase 1,839 of the Company's common stock at a price per share of $74.80. The warrant is immediately exercisable, will expire on August 21, 2028 and contains a cashless exercise provision.

9. Stock-Based Compensation

In the accompanying consolidated statement of operations, the Company recognized stock-based compensation expense for its employees and non-employees as follows:

	Year ended December 31,		
	2021	2020	2019
	(in thousands)		
Research and development	$ 7,197	$ 4,316	$ 3,873
General and administrative	5,693	5,154	1,822
Total stock-based compensation	$ 12,890	$ 9,470	$ 5,695

Determination of Fair Value

The estimated grant-date fair value of all the Company's stock-based awards was calculated using the Black-Scholes option pricing model, based on the following assumptions:

	Year Ended December 31,		
	2021	2020	2019
Expected term (in years)	5.3 – 7.0	5.3 – 7.0	5.3 – 6.9
Expected volatility	82 – 85%	87 – 90%	89 – 94%
Risk-free interest rate	0.5 – 1.3%	0.3 – 1.2%	1.6 – 2.6%
Expected dividend rate	—%	—%	—%

The fair value of each stock option grant was determined by the Company on the date of grant using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment and estimation by management.

Expected Term—The expected term represents the period that stock-based awards are expected to be outstanding. As the Company's historical share option exercise is limited due to a lack of sufficient data points, and does not provide a reasonable basis upon which to estimate an expected term, the expected term is derived by using the midpoint between the weighted-average vesting term and the contractual expiration period of the stock-based award.

Expected Volatility—The expected volatility is determined based on stock volatilities over a period equivalent to the expected term of the stock-based award. Expected volatility was derived from the trading history of the Company's common stock for the year ended December 31, 2021, a weighted volatility using both the Company's trading history for its common stock and the historical stock volatilities of comparable peer public companies within its industry for the year ended December 31, 2020, a weighted volatility using solely the historical stock volatilities of comparable peer public companies within its industry for the year ended December 31, 2019.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the date of grant for zero-coupon U.S. Treasury notes with maturities approximately equal to the stock-based awards' expected term.

Expected Dividend Rate—The expected dividend is zero as the Company has not paid nor anticipate paying any dividends on its common stock in the foreseeable future.

Forfeiture Rate—The Company accounts for forfeitures when they occur.

Equity Incentive Plans

2018 Equity Inducement Plan

In September 2018, the Company's Compensation Committee approved the 2018 Equity Inducement Plan (2018 Plan). The number of shares available for awards under the 2018 Plan was set to 37,500. In June 2020 and February 2021, amendments to the 2018 Plan were approved by the Company's Board of Directors and Compensation Committee, respectively, each to increase the authorized number of shares available for issuance by 500,000 shares for an aggregate increase of 1,000,000 shares. As of December 31, 2021, 1,037,500 shares were reserved for issuance under the 2018 Plan. On February 8, 2022, the Company's Compensation Committee approved an amendment to the 2018 Plan to increase the authorized number of shares available for issuance by 500,000. The exercise price of each stock-based award issued under the 2018 Plan is required to be no less than the fair value of the Company's common stock. The vesting and exercise provisions of options or restricted awards granted are determined individually with each grant. Stock options have a 10-year life and expire if not exercised within that period or if not exercised within three months of cessation of employment with the Company or such longer period of time as specified in the option agreement.

2015 Plan

The 2015 Equity Incentive Plan (2015 Plan) became effective on July 14, 2015. On January 21, 2020, the Company's stockholders approved the following amendments to the 2015 Plan: (i) increase to the authorized number of shares available for issuance by 4,312,500 shares and proportionately increase the share limit related to incentive stock options, (ii) provide limits on the total value of compensation that may be granted to any non-employee director in each calendar year, and (iii) eliminate the annual individual grant limit to reflect changes to the tax law in 2017 tax legislation.

As of December 31, 2021, 5,123,736 shares were reserved for issuance under the 2015 Plan. The number of shares reserved for issuance under the 2015 Plan will increase automatically on January 1 of each calendar

year 2016 through 2025 by the number of shares equal to 4% of the total outstanding shares of the Company's common stock as of the immediately preceding December 31. The Company's Board of Directors or Compensation Committee may reduce the amount of the increase in any particular year. The exercise price of each stock-based award issued under the 2015 Plan is required to be no less than the fair value of the Company's capital stock. The vesting and exercise provisions of options or restricted awards granted are determined individually with each grant. Stock options have a 10-year life and expire if not exercised within that period or if not exercised within three months of cessation of employment with the Company or such longer period of time as specified in the option agreement, unless modified.

2008 Plan

The Company granted options under the 2008 Stock Plan (2008 Plan) until July 2015 when it was terminated as to future awards, although it continues to govern the terms of options that remain outstanding under the 2008 Plan. The 2008 Plan provided for the granting of Incentive Stock Options (ISO), nonqualified stock options and stock purchase rights. In connection with the Board of Director's approval of the 2015 Plan, all remaining shares available for future award under the 2008 Plan were transferred to the 2015 Plan, and the 2008 Plan was terminated.

A summary of activity under the 2008 Plan, 2015 Plan and 2018 Plan and related information is as follows:

		Options Outstanding			
	Shares Available for Grant	Number of Shares Outstanding	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value of Outstanding Options (in thousands)
Outstanding — December 31, 2020	1,117,796	4,146,928	$ 19.45	8.84	$ 12,227
Awards authorized	945,139				
Options granted	(1,134,860)	1,134,860	17.78		
Options exercised	—	(64,847)	13.06		
Options forfeited/cancelled	279,752	(279,752)	17.99		
Outstanding — December 31, 2021	1,207,827	4,937,189	$ 19.23	8.14	$ 36,080
Exercisable — December 31, 2021		1,421,885	$ 30.98	6.56	$ 9,682
Vested and expected to vest — December 31, 2021		4,422,699	$ 20.06	8.07	$ 31,146

The weighted-average grant date fair values of options granted during the years ended December 31, 2021, 2020 and 2019 was $12.54, $8.81 and $50.40 per share. The aggregate intrinsic value of options exercised was $0.5 million and $0.1 million for the years ended December 31, 2021 and 2019. There were no options exercised for the year ended December 31, 2020. The total grant date fair value of options vested for the years ended December 31, 2021, 2020 and 2019 was $11.3 million, $5.2 million and $6.0 million.

In August 2020, the Company granted executives and employees stock options with performance-based conditions. Vesting is achieved based upon the satisfaction of pre-determined milestones. There were 1,029,000 and 1,104,500 of the performance-based options outstanding and unvested as of December 31, 2021 and 2020. In January 2022, the first performance-based milestone was met, and accordingly 257,255 of the performance-based options vested. For the years ended December 31, 2021 and 2020, the Company recognized $3.0 million and $0.9 million in stock-based compensation expense related to the options with performance-based criteria.

In May 2020, the Company entered into a separation agreement with the Company's former President and Chief Executive Officer, in connection with his resignation. Pursuant to the separation agreement, the former executive's unvested options that would have vested during the one-year period from the date of separation accelerated and vested immediately. The vesting date of all remaining unvested options accelerated by one year and vested in accordance with the accelerated vesting schedule through December 31, 2020. All unvested

options were cancelled on December 31, 2020. Furthermore, the former executive received an extension of the expiration date of his vested stock options to 75 days following the Company's announcement of the top-line data results from its MOMENTUM clinical trial, which was announced by the Company on January 25, 2022, setting the expiration to April 10, 2022. Compensation costs relating to the vesting acceleration and the modifications to option terms was $2.2 million for the year ended December 31, 2020.

As of December 31, 2021, total unrecognized stock-based compensation related to unvested stock options was $25.3 million, which the Company expects to recognize over a remaining weighted-average period of 2.7 years. In addition, as of December 31, 2021, total unrecognized stock-based compensation related to unvested stock options with performance-based conditions was $5.3 million.

2015 Employee Stock Purchase Plan

The Company adopted the 2015 Employee Stock Purchase Plan (ESPP) and initially reserved 17,500 shares of common stock as of its effective date of July 15, 2015. The aggregate number of shares issued over the term of the 2015 Employee Stock Purchase Plan will not exceed 85,000 shares of common stock. The ESPP will not become effective until such time as the Compensation Committee determines in the future, and as of December 31, 2021, the initial offering periods had not commenced. As of December 31, 2021, no shares of common stock have been issued to employees participating in the ESPP and 17,500 shares were available for issuance under the ESPP.

10. Income Taxes

The geographical breakdown of loss before provision for income taxes is as follows:

	Year Ended December 31,		
	2021	2020	2019
	(in thousands)		
United States	$ (95,605)	$ (81,670)	$ (89,459)
International	$ 943	910	1,024
Loss before provision for (benefit from) income taxes, net	$ (94,662)	$ (80,760)	$ (88,435)

The components of the provision for (benefit from) income taxes are as follows:

	Year Ended December 31,		
	2021	2020	2019
	(in thousands)		
Current tax provision (benefit):			
Federal	$ —	$ —	$ —
State	—	—	—
Foreign	38	59	85
Total current tax provision (benefit)	$ 38	$ 59	$ 85
Deferred tax provision (benefit):			
Foreign	(41)	83	(245)
Total deferred tax provision (benefit)	$ (41)	$ 83	$ (245)
Total provision for (benefit from) income taxes	$ (3)	$ 142	$ (160)

The reconciliation between income taxes computed at the federal statutory income tax rate and the provision for (benefit from) income taxes is as follows:

	Year Ended December 31,		
	2021	2020	2019
Federal statutory rate	21.0%	21.0%	21.0%
Effect of:			
Change in valuation allowance	(27.8)	(23.6)	12.4
Federal tax credit	7.4	5.8	1.5
Warrant issuance and remeasurement	—	(4.2)	(5.3)
Effect of ownership change on deferred tax assets	(0.1)	1.3	(29.0)
State income tax benefit, net of federal benefit	—	0.2	0.2
Other permanent items	(0.5)	(0.7)	(0.6)
Total provision for (benefit from) income taxes%	0.0%	(0.2)%	0.2%

The components of the deferred tax assets are as follows:

	December 31,	
	2021	2020
	(in thousands)	
Deferred tax assets:		
59 (e) expenditures and amortization	$ 21,833	$ 6,222
Net operating loss carryforwards	13,546	14,011
Federal R&D and orphan drug credits	11,992	5,107
Stock based compensation	8,806	6,459
License fee	4,691	3,224
Other	1,468	1,024
Gross deferred tax assets	62,336	36,047
Valuation allowance	(61,847)	(35,513)
Total deferred tax assets	489	534
Deferred tax liabilities:		
Lease Asset	19	114
Other	82	73
Total deferred tax liabilities	101	187
Total net deferred tax assets	$ 388	$ 347

Recognition of deferred tax assets is appropriate when realization of these assets is more likely than not. Based upon the weight of available evidence, which includes historical operating performance and the recorded cumulative net losses in prior fiscal periods, the Company recorded a full valuation allowance of $61.4 million and $35.2 million against the net U.S. deferred tax assets as of December 31, 2021 and 2020. The U.S. net valuation allowance increased by $26.2 million and $18.8 million for the year ended December 31, 2021 and 2020, respectively.

Management assesses the available positive and negative evidence to estimate if sufficient future taxable income will be generated to use the existing U.S. deferred tax assets. Based on the weight of all evidence, including a history of operating losses and the uncertainty of the Company's ability to generate future taxable income to realize the assets, management has determined that it is more likely than not that the U.S. deferred tax assets will not be realized.

As of December 31, 2021, the Company had gross U.S. federal tax net operating loss carryforwards of $52.7 million, that are eligible for an indefinite carryforward, and gross state operating loss carryforwards of $51.8 million expiring in years ranging from 2022 to 2041. The Company also had U.S. net tax credit carryforwards

of $11.2 million which begin to expire in 2039 and net tax credit carryforwards in a foreign jurisdiction of $0.8 million which begin to expire in 2039.

Utilization of the Company's net operating loss and U.S. research and development credit carryforwards to offset taxable income are subject to an annual limitation, pursuant to Internal Revenue Code (IRC) Sections 382 and 383. As a result of common stock issuances and changes in the stock ownership that occurred subsequent to 2019, an ownership change under Section 382 is deemed to have occurred during the first quarter of 2022. As such, certain of the Company's tax attributes existing as of the date of the ownership changes may not be available for future use. The loss or ultimate limitation of these attributes will not have any impact on the financial statements since the net U.S. deferred tax assets are offset by a full valuation allowance.

Uncertain Tax Positions

The activity related to the gross amount of unrecognized tax benefits is as follows:

	Year Ended December 31,		
	2021	2020	2019
	(in thousands)		
Beginning balance	$ 621	$ 314	$ 264
Increases based on tax positions related to prior years	39	—	—
Decreases based on tax positions related to prior years	(83)	(54)	(103)
Decreases due to ownership change	—	(207)	—
Increases based on tax positions in current year	780	568	153
Settlement	—	—	—
Lapse of statute of limitations	—	—	—
Ending balance	$ 1,357	$ 621	$ 314

If recognized, gross unrecognized tax benefits would not have a material impact on the Company's effective tax rate due to the Company's full valuation allowance position on the U.S. deferred tax assets. From time to time, the Company is subject to review by tax authorities. It is not possible to estimate the impact of changes, if any, to previously recorded uncertain tax positions. However, the Company does not expect the changes, if any, to be materially different from what is recorded and will adjust its estimate and liability as necessary.

The Company recognizes interest and penalties related to unrecognized tax benefits in the provision for income taxes in the accompanying consolidated statement of operations. Accrued interest and penalties, if applicable, are included in accrued liabilities in the consolidated balance sheet. For the years ended December 31, 2021 and 2020, the Company did not recognize any accrued interest and penalties.

The Company is subject to taxation in the United States, various states, Canada and Australia. Tax years 2018 through 2020 remain open to examination by the United States, various state jurisdictions and Canada. The tax year ended December 31, 2020 remains open to examination in Australia. The Company is not under examination in any tax jurisdiction for any year.

11. Subsequent Event

Loan and Security Agreement

On January 21, 2022 (Effective Date), the Company entered into a Loan and Security Agreement (Loan Agreement) with Oxford Finance, LLC (Oxford), pursuant to which it may obtain a loan up to an aggregate principal amount of $125.0 million (Term Loans) in four tranches. Contemporaneously with executing the Loan Agreement, the Company drew down the first $5.0 million tranche (Term Loan A). The second and third tranche (Term Loan B and Term Loan C, respectively) may be drawn upon the achievement of certain pre-determined milestones. During the first quarter of 2022, the Company met the milestone required to borrow under Term Loan B but has elected to defer the draw and combine with Term Loan C for a total of a $70.0 million, per the terms of the Loan Agreement. Term Loan C must be drawn within 30 days after the completion of the related milestone but no later than December 31, 2023. The $50.0 million under Term Loan D will only be available at the sole discretion of the lender.

The Term Loans will bear interest at a floating per year rate equal to the prime rate, plus a margin of 5.25%, subject to a floor of 8.50%. Interest is payable monthly in arrears on the first calendar day of each calendar month. Beginning (i) March 1, 2025, if either the Term B Loan or the Term C Loan is not made or (ii) September 1, 2025, if both the Term B Loan and the Term C Loan are made, the Company shall repay the Term Loans in consecutive equal monthly payments of principal, together with applicable interest, in arrears. All unpaid principal and accrued and unpaid interest with respect to each Term Loan is due and payable in full on January 1, 2027.

The Company will be required to make a final payment of 6.0% of the original principal amount of the Term Loans, payable at maturity or upon any earlier acceleration or prepayment of the Term Loans. The Company may prepay all, but not less than all, of the Term Loans, subject to a prepayment fee equal to (i) 2.0% of the principal amount of the applicable Term Loan if prepaid on or before the first anniversary date of the Effective Date and (ii) 1.0% of the principal amount of the applicable Term Loan if prepaid after the first and on or before the third anniversary of the Effective Date. All Term Loans will be subject to a facility fee of 0.5% of the principal amount.

Underwritten Public Offering and Common Stock Issuances

On January 31, 2022, the Company completed an underwritten public offering of 4,074,075 shares of common stock and pre-funded warrants to purchase up to 925,925 shares of common stock. As part of the underwritten public offering, on February 3, 2022, the Company issued an additional 750,000 shares of common stock representing the underwriters' full exercise of their over-allotment option. The shares of common stock and the pre-funded warrants were offered by the company at a price to the public of $27.00 and $26.999 per share, respectively. The aggregate net proceeds received by the Company from the offering were $145.6 million, net of underwriting discounts and commissions and estimated offering expenses of $9.7 million.

Subsequent to December 31, 2021, 18,937 and 2,312,257 shares of common stock were issued pertaining to the exercise of Series A and Series B warrants, respectively, providing proceeds of $30.8 million to the Company.

Subsequent to December 31, 2021, 725,283 shares of common stock were issued pertaining to the exercise of the warrant that was previously issued to Gilead pursuant to the securities purchase agreement, providing $9.6 million of proceeds to the Company.

Subsequent to December 31, 2021, 212,892 shares of common stock were issued in connection with the exercise of stock options by former employees and pre-established non-discretionary sales plans, providing proceeds of $2.8 million to the Company.

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

As of December 31, 2021, our management, with the participation of our Chief Executive Officer and Chief Financial Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and the Chief Financial Officer, to allow timely decisions regarding required disclosures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2021, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

As of December 31, 2021, management assessed the effectiveness of our internal control over financial reporting based on the framework established in "Internal Control—Integrated Framework" issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) (2013 Framework). Based on this evaluation, management has determined that our internal control over financial reporting was effective as of December 31, 2021.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Mark Kowalski, M.D., Ph.D., our Chief, Research and Early Development, separated from employment from the Company effective March 10, 2022.

Item 9C. Disclosure Regarding Foreign Jurisdictions That Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 11. Executive Compensation.

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

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

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 14. Principal Accounting Fees and Services.

The information required by this item is incorporated herein by reference to our Proxy Statement with respect to our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

Item 15. Exhibits, Consolidated Financial Statement Schedules.

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

1. Consolidated Financial Statements

See Index to Consolidated Financial Statements at Item 8 herein.

2. Consolidated Financial Statement Schedules

No consolidated financial statement schedules are provided because the information called for is not required or is shown either in the consolidated financial statements or notes thereto.

3. Exhibits

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
2.1+†	Asset Purchase Agreement dated August 20, 2018 by and between the Registrant and YM Biosciences Australia Pty Ltd. and Gilead Sciences, Inc.	10-Q	001-37490	2.1	November 8, 2018	
2.2++	Amendment to Asset Purchase Agreement dated October 28, 2019, by and between the Registrant and YM Biosciences Australia Pty Ltd. and Gilead Sciences, Inc.	10-K	001-37490	2.2	March 3, 2020	
3.1	Restated Certificate of Incorporation.	S-1	333-204921	3.2	June 12, 2015	
3.2	Certificate of Amendment to the Restated Certificate of Incorporation.	8-K	001-37490	3.1	January 22, 2020	
3.3	Amended and Restated Bylaws.	8-K	001-37490	3.1	April 16, 2020	
3.4	Certificate of Designation of Preferences, Rights and Limitations, with respect to the Series A Convertible Voting Preferred Stock.	8-K	001-37490	3.1	November 13, 2019	
4.1	Form of Common Stock Certificate.	S-1	333-204921	4.1	July 6, 2015	
4.2	Third Amended and Restated Investor Rights Agreement, dated April 17, 2014, by and among the Registrant and certain of its stockholders, as amended.	S-1	333-204921	4.2	June 12, 2015	
4.3	Warrant dated August 21, 2018 issued to Silicon Valley Bank	10-Q	001-37490	4.1	November 8, 2018	
4.4	Description of Securities					X
4.5	Form of Series A Warrant	8-K	001-37490	4.1	November 7, 2019	
4.6	Form of Series B Warrant	8-K	001-37490	4.2	November 7, 2019	
4.7	Form of Amendment No. 1 to the Series A Warrant to Purchase Common Stock	8-K	001-37490	4.1	September 13, 2021	
4.8	Form of Amendment No. 1 to the Series B Warrant to Purchase Common Stock	8-K	001-37490	4.1	September 13, 2021	

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
4.9	Securities Purchase Agreement by and between the Company and Gilead Sciences, Inc.	8-K	001-37490	10.1	February 6, 2020	
4.10	Form of Warrant to Gilead Sciences, Inc.	8-K	001-37490	10.2	February 6, 2020	
10.1*	Form of Indemnification Agreement.	S-1	333-204921	10.1	June 12, 2015	
10.2*	2008 Stock Plan, as amended, and forms of award agreements thereunder.	S-1	333-204921	10.2	June 12, 2015	
10.3*	2015 Equity Incentive Plan, as amended, and forms of award agreements thereunder.	10-K	001-37490	10.3	March 11, 2021	
10.4*	2015 Employee Stock Purchase Plan.	S-1	333-204921	10.4	July 6, 2015	
10.5*	2018 Equity Inducement Plan, as amended, and forms of award agreements thereunder.					X
10.6*	Form of Executive Officer Employment Agreement.	S-1	333-204921	10.5	July 6, 2015	
10.7	Form of Amendment to Executive Officer Employment Agreement (other than Chief Executive Officer)	10-Q	001-37490	10.1	May 9, 2017	
10.8*	Employment Agreement between the Registrant and Stephen G. Dilly	10-Q	001-37490	10.1	August 6, 2020	
10.9+	License Agreement dated September 27, 2016 by and between the Registrant and CRT Pioneer Fund LP.	10-Q	001-37490	10.1	November 10, 2016	
10.10+	Amendment No. 1 to the License Agreement dated November 10, 2020 by and between the Registrant and CRT Pioneer Fund LP.	10-K	001-37490	10.12	March 11, 2021	
10.11+	License Agreement dated August 3, 2021 by and between the Registrant and AstraZeneca AB.	10-Q	001-37490	10.1	November 5, 2021	
10.12	Office Lease, dated June 12, 2017, by and between Sierra Oncology Canada ULC and The Cadillac Fairview Corporation Limited, as the duly authorized agent of Ontrea Inc. and Van885 West Georgia GP Ltd., the general partner of Van885 West Georgia LP.	10-Q	001-37490	10.1	August 10, 2017	
10.13	Office Sublease, dated December 1, 2020, by and between Sierra Oncology Canada ULC and Scougall Management (1987) Limited and consented to on December 18, 2020 by Van885 West Georgia GP Ltd. and Ontrea Inc., the general partners of Van885 West Georgia LP.	10-K	001-37490	10.14	March 11, 2021	

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.14	Office Lease, dated December 10, 2020 and effective December 14, 2020, by and between Sierra Oncology, Inc. and KW Fund VI-San Mateo, LLC.	10-K	001-37490	10.15	March 11, 2021	
23.1	Consent of independent registered public accounting firm.					X
24.1	Power of Attorney. Reference is made to the signature page hereto.					X
31.1	Certification of Principal Executive Officer, pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
31.2	Certification of Principal Financial Officer, pursuant to Rule 13a-14(a)/15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X
32.1**	Certification of Chief Executive Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2**	Certification of Chief Financial Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	Inline XBRL Instance Document.					X
101.SCH	Inline XBRL Schema Linkbase Document.					X
101.CAL	Inline XBRL Calculation Linkbase Document.					X
101.DEF	Inline XBRL Definition Linkbase Document.					X
101.EXT	Inline XBRL Extension label Linkbase Document.					X
101.PRE	Inline XBRL Presentation Linkbase Document.					X
104	The cover page from the Company's Annual Report on Form 10-K for the year ended December 31, 2021 has been formatted in Inline XBRL.					X

* Executive compensation plan or agreement.

** This certification is deemed not filed for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act or the Exchange Act.

+ Confidential treatment has been granted for portions of this exhibit under Rule 24b-2 promulgated under the Exchange Act. The Registrant has omitted and filed separately with the SEC the confidential portions of this exhibit.

++ Registrant has omitted portions of the exhibit as permitted under Item 601(b)(10) of Regulation S-K.

† Schedules and similar attachments to the agreement have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company will furnish supplementally a copy of any omitted schedule or similar attachment to the SEC upon request.

Item 16. Form 10-K Summary.

None.

SIGNATURES

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

Date: March 10, 2022

SIERRA ONCOLOGY, INC.

By: /s/ Stephen G. Dilly
Stephen G. Dilly
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Stephen Dilly and Sukhi Jagpal, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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

Signature	Title	Date
/s/ Stephen G. Dilly Stephen G. Dilly	President, Chief Executive Officer and Director (Principal Executive Officer)	March 10, 2022
/s/ Sukhi Jagpal Sukhi Jagpal	Chief Financial Officer (Principal Accounting and Financial Officer)	March 10, 2022
/s/ Robert Pelzer Robert Pelzer	Chairman of the Board	March 10, 2022
/s/ Gaurav Aggarwal Gaurav Aggarwal	Director	March 10, 2022
/s/ Andrew Allen Andrew Allen	Director	March 10, 2022
/s/ Mona Ashiya Mona Ashiya	Director	March 10, 2022
/s/ Craig Collard Craig Collard	Director	March 10, 2022
/s/ Jeffrey H. Cooper Jeffrey H. Cooper	Director	March 10, 2022
/s/ Georgia Erbez Georgia Erbez	Director	March 10, 2022
/s/ Christy Oliger Christy Oliger	Director	March 10, 2022
/s/ Andrew Sinclair Andrew Sinclair	Director	March 10, 2022

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 500,000,000 shares of common stock, $0.001 par value per share, and 10,000,000 shares of undesignated preferred stock, $0.001 par value per share. The following description summarizes the most important terms of our capital stock. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our restated certificate of incorporation and restated bylaws, which are included as exhibits to our most recent Annual Report on Form 10-Kand to the applicable provisions of Delaware law.

Common Stock

Dividend Rights

Subject to preferences that may apply to any shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Voting Rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. We have not provided for cumulative voting for the election of directors in our restated certificate of incorporation. Accordingly, holders of a majority of the shares of our common stock are able to elect all of our directors. Our restated certificate of incorporation establishes a classified board of directors, divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms.

No Preemptive or Similar Rights

Our common stock is not entitled to preemptive rights, and is not subject to conversion, redemption or sinking fund provisions.

Right to Receive Liquidation Distributions

Upon our liquidation, dissolution or winding-up, the assets legally available for distribution to our stockholders would be distributable ratably among the holders of our common stock and any participating preferred stock outstanding at that time, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights of and the payment of liquidation preferences, if any, on any outstanding shares of preferred stock.

Common Stock Warrants

In connection with our November 2019 public offering of the Series A Preferred Stock, we issued Series A warrants to purchase up to 7,802,241 shares of common stock at an exercise price equal to $13.20, and Series B warrants to purchase up to 2,574,727 shares of common stock at an exercise price equal to $13.20. The Series A warrants will expire five years from the date they first became exercisable or on January 22, 2025 and contain a cash and/or cashless exercise provision. The Series B warrants will expire on the 75th day anniversary following the announcement of top-line data from our MOMENTUM Phase 3 clinical trial of momelotinib and may only be exercised by paying the exercise price in cash. With the announcement of topline data on January 25, 2022, the Series B warrants will expire on April 10, 2022. During the year ended December 31, 2021, 151,500 Series B

warrants to purchase 49,995 shares of common stock and 11,362 Series A warrants to purchase 11,362 shares of common stock were exercised. There were no warrants exercised during the year ended December 31, 2020.

On September 8, 2021, we entered into Amendment No. 1 to Series A warrants and Amendment No. 1 to Series B warrants. These amendments clarified the methodology by which Series A warrants and Series B warrants would be assumed or settled in the event of a Fundamental Transaction, as defined under the warrant agreements, and provided for greater consistency in the treatment of these warrants by a publicly-traded or private buyer.

In connection with obligations under the amendment to the Asset Purchase Agreement, we entered into a securities purchase agreement on January 31, 2020 and issued to Gilead Sciences, Inc. 725,283 shares of our common stock and a warrant to purchase 725,283 shares of common stock at a price per share of $13.20. The warrant is immediately exercisable, will expire on January 31, 2025 and contains a cash and/or cashless exercise provision.

In August 2018, in connection with a Loan and Security Agreement (Loan Agreement) with Silicon Valley Bank (SVB), we issued a warrant to SVB to purchase 1,839 of our common stock at a price per share of $74.80. The warrant is immediately exercisable, will expire on August 21, 2028 and contains a cashless exercise provision.

Pre-Funded Warrants

In January 2022, we issued and sold pre-funded warrants to purchase an aggregate of 925,925 shares of our common stock at an offering price of $26.999 per pre-funded warrant in an underwritten public offering pursuant to a shelf registration on Form S-3.

The pre-funded warrants do not expire and may be exercised at any time after their original issuance. The exercise price per whole share of common stock purchasable upon the exercise of the pre-funded warrants is $0.001 per warrant share. The exercise price of the pre-funded warrants is subject to appropriate adjustment upon the occurrence of certain events, including in the event of certain share dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our shares of common stock. The exercise price will not be adjusted below the par value of our common stock. The holder may, in its sole discretion, elect to exercise the warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. Subject to restrictions on transfer set forth in the pre-funded warrants and applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our shares of common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding shares of common stock or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding shares of common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercised contained in the pre-funded warrants.

Except by virtue of such holder’s ownership of our shares of common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our shares of common stock, including any voting rights, until the holder exercises the pre-funded warrant.

Registration Rights

Certain of our common stockholders are entitled to certain registration rights with respect to the sale of such shares under the Securities Act. We refer to these shares as registrable securities. These rights are provided under the terms of an amended and restated investors’ rights agreement between us and the holders of these shares, which was entered into in connection with our preferred stock financings, and include demand registration rights, short-form registration rights and piggyback registration rights. In any registration made pursuant to such amended and restated

investors' rights agreement, all fees, costs and expenses of underwritten registrations, including fees and disbursements of one special counsel to the selling stockholders not to exceed $30,000, will be borne by us and all selling expenses, including estimated underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

The registration rights terminate on July 21, 2020 or, with respect to any particular stockholder, at such time as such stockholder can sell all of its shares in a single transaction pursuant to Rule 144 promulgated under the Securities Act.

Demand Registration Rights

Under the terms of the amended and restated investor rights agreement, if we receive a written request from the holders of at least 25% of the registrable securities then outstanding that we file a registration statement under the Securities Act with an anticipated aggregate price to the public of at least $5.0 million, we will be obligated to notify all holders of registrable securities of the written request and use commercially reasonable efforts to effect the registration of all registrable securities that holders request to be registered. We are required to effect no more than two registration statements that are declared or ordered effective, subject to certain exceptions. We may postpone the filing of a registration statement for up to 90 days once in a 12-month period if in the good-faith judgment of our board of directors such registration would be detrimental to us.

Piggyback Registration Rights

If we register any of our securities for public sale in an offering pursuant to this prospectus, we are required to afford each holder of registrable securities an opportunity to include all or part of the holder's registrable securities in such registration. Each holder desiring to include all or any part of the registrable securities held by it in any such registration statement is required to notify us within 10 business days of being notified by us in writing of the registration. This right does not apply to registration statements relating to demand registrations, for Form S-3 registrations, employee benefit plans, a corporate reorganization or other transaction under Rule 145 of the Securities Act, or stock issued upon conversion of debt securities. The underwriter of any underwritten offering will have the right to limit, due to marketing factors, the number of shares registered by these holders to 30% of the total shares covered by the registration statement. In no event will shares of any other selling stockholder be included in such registration that would reduce the number of shares which may be included by these holders without the consent of the holders of at least two-thirds (66 2/3%) of the registrable securities proposed to be sold in the offering.

Form S-3 Registration Rights

The holders of registrable securities can request that we register all or a portion of their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and the aggregate price to the public of the shares offered is at least $5.0 million. The holders of registrable securities may require us to effect at most two registration statements on Form S-3 in any 12-month period. We may postpone the filing of a registration statement for up to 90 days once in a 12-month period if in the good-faith judgment of our board of directors such registration would be detrimental to us or if we notify holders within 30 days of making the Form S-3 registration request that we intend to make a public offering within 90 days.

Anti-Takeover Provisions

The provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could have the effect of delaying, deferring or discouraging another person from acquiring control of our company. These provisions, which are summarized below, may have the effect of discouraging takeover bids. They are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging a proposal to acquire us because negotiation of these proposals could result in an improvement of their terms.

Delaware Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, regulating corporate takeovers. In general, DGCL Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years following the date on which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

- the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction or series of transactions together resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that DGCL Section 203 may also discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Restated Certificate of Incorporation and Restated Bylaws Provisions

Our restated certificate of incorporation and our restated bylaws include a number of provisions that could deter hostile takeovers or delay or prevent changes in control of our company, including the following:

- ***Board of Directors Vacancies.*** Our restated certificate of incorporation and restated bylaws authorize only our board of directors to fill vacant directorships, including newly created seats. In addition, the number of directors constituting our board of directors is permitted to be set only by a resolution adopted by a majority vote of our entire board of directors. These provisions would prevent a stockholder from increasing the size of our board of directors and then gaining control of our board of directors by filling the resulting vacancies with its own nominees. This makes it more difficult to change the composition of our board of directors but promotes continuity of management.

- ***Classified Board.*** Our restated certificate of incorporation and restated bylaws provide that our board of directors is classified into three classes of directors, each with staggered three-year terms. A third party may be discouraged from making a tender offer or otherwise attempting to obtain control of us as it is more difficult and time consuming for stockholders to replace a majority of the directors on a classified board of directors.

- ***Stockholder Action; Special Meetings of Stockholders.*** Our restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. As a result, a holder controlling a majority of our capital stock would not be able to amend our restated bylaws or remove directors without holding a meeting of our stockholders called in accordance with our restated bylaws. Further, our restated bylaws and restated certificate of incorporation provide that special meetings of our stockholders may be called only by a majority of our board of directors, the chairman of our board of directors, our Chief Executive Officer or our President, thus prohibiting a stockholder from calling a special meeting. These provisions might delay the ability of our stockholders to force consideration of a proposal or for stockholders controlling a majority of our capital stock to take any action, including the removal of directors.

- ***Advance Notice Requirements for Stockholder Proposals and Director Nominations.*** Our restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders or to nominate candidates for election as directors at our annual meeting of stockholders. Our restated bylaws also specify certain requirements regarding the form and content of a stockholder's notice. These provisions might preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed. We expect that these provisions might also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

- ***No Cumulative Voting.*** The DGCL provides that stockholders are not entitled to the right to cumulate votes in the election of directors unless a corporation's certificate of incorporation provides otherwise. Our restated certificate of incorporation and restated bylaws do not provide for cumulative voting.

- ***Directors Removed Only for Cause.*** Our restated certificate of incorporation provides that stockholders may remove directors only for cause and only by the affirmative vote of the holders of at least two-thirds of our outstanding common stock.

- ***Amendment of Charter Provisions.*** Any amendment of the above provisions in our restated certificate of incorporation requires approval by holders of at least two-thirds of our outstanding common stock.

- ***Issuance of Undesignated Preferred Stock.*** Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock would enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or other means.

- ***Choice of Forum.*** Our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the DGCL, restated certificate of incorporation or our restated bylaws; any action to interpret, apply, enforce or determine the validity of our restated certificate of incorporation or our restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable.

Exchange Listing

Our common stock is listed on The Nasdaq Global Market under the symbol "SRRA."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer and Trust Company, LLC.

EXHIBIT 10.5

SIERRA ONCOLOGY, INC.

2018 EQUITY INDUCEMENT PLAN

ADOPTED BY THE COMPENSATION COMMITTEE OF THE BOARD OF DIRECTORS: SEPTEMBER 2018
FIRST AMENDMENT BY THE BOARD OF DIRECTORS: JUNE 2020SECOND AMENDMENT BY THE COMPENSATION COMMITTEE OF THE BOARD OF DIRECTORS: FEBRUARY 2021
THIRD AMENDMENT BY THE COMPENSATION COMMITTEE OF THE BOARD OF DIRECTORS: FEBRUARY 2022

1. **PURPOSE**. The purpose of this Plan is to provide incentives to attract, retain and motivate eligiblepersons whose present and potential contributions are important to the success of the Company, and any Parents and Subsidiaries that exist now or in the future, by offering them an opportunity to participate in the Company's future performance through the grant of Awards. Capitalized terms not defined elsewhere in the text are defined in Section 21.

2. **SHARES SUBJECT TO THE PLAN**.

2.1 Number of Shares Available. Subject to Section 2.4 and any other applicable provisions hereof, the total number of Shares reserved and available for grant and issuance pursuant to this Plan is 1,537,500.

2.2 Lapsed, Returned Awards. Shares subject to Awards, and Shares issued under the Plan under any Award, will again be available for grant and issuance in connection with subsequent Awards under this Plan to the extent such Shares: (a) are subject to issuance upon exercise of an Option granted under this Plan but which cease to be subject to the Option for any reason other than exercise of the Option;
(b) are subject to Awards granted under this Plan that are forfeited or are repurchased by the Company at the original issue price or (c) are subject to Awards granted under this Plan that otherwise terminate withoutsuch Shares being issued. To the extent an Award under the Plan is paid out in cash rather than Shares, suchcash payment will not result in reducing the number of Shares available for issuance under the Plan. Sharesused to pay the exercise price of an Award or withheld to satisfy the tax withholding obligations related toan Award will become available for future grant or sale under the Plan.

2.3 Minimum Share Reserve. At all times the Company shall reserve and keep available a sufficient number of Shares as shall be required to satisfy the requirements of all outstanding Awards granted under this Plan.

2.4 Adjustment of Shares. If the number of outstanding Shares is changed by a stock dividend,extraordinary dividends or distributions (whether in cash, shares or other property, other than a regular cash dividend) recapitalization, stock split, reverse stock split, subdivision, combination, reclassification, spin- off or similar change in the capital structure of the Company, without consideration, then (a) the number ofShares reserved for issuance and future grant under the Plan set forth in Section 2.1, (b) the Exercise Pricesof and number of Shares subject to outstanding Options and (c) the number of Shares subject to other outstanding Awards, shall be proportionately adjusted, subject to any required action by the Board or the stockholders of the Company and in compliance with applicable securities laws; provided that fractions ofa Share will not be issued.

3. **ELIGIBILITY**. Awards may be granted only to a person who, at the time of granting of the Awardby the Committee: (a) has been hired as an Employee by the Company or any Subsidiary and such Awardis a material inducement to such person being hired; (b) has been rehired as an Employee following a bona

fide period of interruption of employment with the Company or any Subsidiary; or (c) has become anEmployee of the Company or any Subsidiary in connection with a merger or acquisition.

4. ADMINISTRATION.

4.1 Committee Composition; Authority. This Plan will be administered by the Committee or by the Board acting as the Committee. Subject to the general purposes, terms and conditions of this Plan, and to the direction of the Board, the Committee will have full power to implement and carry out this Plan.Notwithstanding the foregoing, the grant of any Award will not be effective unless: (i) if the grant is madeby the Board, then it must be approved by a majority of the Outside Directors on the Board; and (ii) if the grant is made by the Committee, then the Committee must be comprised solely of Outside Directors (exceptas otherwise permitted under applicable rules). The Committee will have the authority to:

(a) construe and interpret this Plan, any Award Agreement and any other agreementor document executed pursuant to this Plan;

(b) prescribe, amend and rescind rules and regulations relating to this Plan or any Award;

(c) select persons to receive Awards;

(d) determine the form and terms and conditions, not inconsistent with the terms of the Plan, of any Award granted hereunder. Such terms and conditions include, but are not limited to, the exercise price, the time or times when Awards may vest and be exercised (which may be based on performance criteria) or settled, any vesting acceleration or waiver of forfeiture restrictions, the method to satisfy tax withholding obligations or any other tax liability legally due and any restriction or limitation regarding any Award or the Shares relating thereto, based in each case on such factors as the Committee will determine;

(e) determine the number of Shares or other consideration subject to Awards;

(f) determine the Fair Market Value in good faith and interpret the applicable provisions of this Plan and the definition of Fair Market Value in connection with circumstances that impactthe Fair Market Value, if necessary;

(g) determine whether Awards will be granted singly, in combination with, in tandem with, or as alternatives to, other Awards under this Plan or any other incentive or compensation plan of theCompany or any Parent or Subsidiary of the Company;

(h) grant waivers of Plan or Award conditions;

(i) determine the vesting, exercisability and payment of Awards;

(j) correct any defect, supply any omission or reconcile any inconsistency in this Plan, any Award or any Award Agreement;

(k) determine whether an Award has been earned;

(l) reduce or waive any criteria with respect to Performance Factors;

(m) adjust Performance Factors to take into account changes in law and accounting or tax rules as the Committee deems necessary or appropriate to reflect the impact of extraordinary or unusual items, events or circumstances to avoid windfalls or hardships;

(n) adopt terms and conditions, rules and/or procedures (including the adoption of any subplan under this Plan) relating to the operation and administration of the Plan to accommodate requirements of local law and procedures outside of the United States; and

(o) make all other determinations necessary or advisable for the administration of this Plan.

4.2 Committee Interpretation and Discretion. Any determination made by the Committee with respect to any Award shall be made in its sole discretion at the time of grant of the Award or, unless in contravention of any express term of the Plan or Award, at any later time, and such determination shall be final and binding on the Company and all persons having an interest in any Award under the Plan. Any dispute regarding the interpretation of the Plan or any Award Agreement shall be submitted by the Employee or Company to the Committee for review. The resolution of such a dispute by the Committee shall be final and binding on the Company and the Employee. The Committee may delegate to one or more executive officers the authority to review and resolve disputes with respect to Awards held by Employees who are not Insiders, and such resolution shall be final and binding on the Company and the Employee.

4.3 Section 16 of the Exchange Act. Awards granted to Employees who are subject to Section 16 of the Exchange Act must be approved by two or more "non-employee directors" (as defined in the regulations promulgated under Section 16 of the Exchange Act).

4.4 Documentation. The Award Agreement for a given Award, the Plan and any other documents may be delivered to, and accepted by, an Employee or any other person in any manner (including electronic distribution or posting) that meets applicable legal requirements.

4.5 Foreign Award Recipients. Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws and practices in other countries in which the Company and its Subsidiaries operate or have employees eligible for Awards, the Committee, in its sole discretion, shall have the power and authority to: (a) determine which Subsidiaries and Affiliates shall be covered by the Plan; (b) determine which Employees outside the United States are eligible to participate in the Plan; (c) modify the terms and conditions of any Award granted to individuals outside the United States or foreign nationals to comply with applicable foreign laws, policies, customs and practices; (d) establish subplans and modify exercise procedures and other terms and procedures, to the extent the Committee determines such actions to be necessary or advisable (and such subplans and/or modifications shall be attached to this Plan as appendices); provided, however, that no such subplans and/or modifications shall increase the share limitations contained in the Plan; and (e) take any action, before or after an Award is made, that the Committee determines to be necessary or advisable to obtain approval or comply with any local governmental regulatory exemptions or approvals. Notwithstanding the foregoing, the Committee may not take any actions hereunder, and no Awards shall be granted, that would violate the Exchange Act or any other applicable United States securities law, the Code, or any other applicable United States governing statute or law.

5. **OPTIONS**. An Option is the right but not the obligation to purchase a Share, subject to certain conditions, if applicable. The Committee may grant Options to eligible Employees and will determine the number of Shares subject to the Option, the Exercise Price of the Option, the period during which the Option

may vest and be exercised, and all other terms and conditions of the Option, subject to the following terms of this section.

5.1 Option Grant. Each Option granted under this Plan will be a Nonqualified Stock Option ("***NSO***"). An Option may be, but need not be, awarded upon satisfaction of such Performance Factors during any Performance Period as are set out in advance in the Employee's individual Award Agreement. If the Option is being earned upon the satisfaction of Performance Factors, then the Committee will: (a) determine the nature, length and starting date of any Performance Period for each Option; and (b) select from among the Performance Factors to be used to measure the performance, if any. Performance Periods may overlap and Employees may participate simultaneously with respect to Options that are subject to different performance goals and other criteria.

5.2 Date of Grant. The date of grant of an Option will be the date on which the Committee makes the determination to grant such Option, or a specified future date. The Award Agreement and a copy of this Plan will be delivered to the Employee within a reasonable time after the granting of the Option.

5.3 Exercise Period. Options may be vested and exercisable within the times or upon the conditions as set forth in the Award Agreement governing such Option; provided, however, that no Option will be exercisable after the expiration of ten (10) years from the date the Option is granted. The Committee also may provide for Options to become vested or exercisable at one time or from time to time, periodically or otherwise, in such number of Shares or percentage of Shares as the Committee determines.

5.4 Exercise Price. The Exercise Price of an Option will be determined by the Committee when the Option is granted; provided that: the Exercise Price of an Option will be not less than one hundred percent (100%) of the Fair Market Value of the Shares on the date of grant. Payment for the Shares purchased may be made in accordance with Section 7 and the Award Agreement and in accordance with any procedures established by the Company.

5.5 Method of Exercise. Any Option granted hereunder will be vested and exercisable according to the terms of the Plan and at such times and under such conditions as determined by the Committee and set forth in the Award Agreement. An Option may not be exercised for a fraction of a Share. An Option will be deemed exercised when the Company receives: (a) notice of exercise (in such form as the Committee may specify from time to time) from the person entitled to exercise the Option (and/or via electronic execution through the authorized third party administrator), and (b) full payment for the Shares with respect to which the Option is exercised (together with applicable withholding taxes). Full payment may consist of any consideration and method of payment authorized by the Committee and permitted by the Award Agreement and the Plan. Shares issued upon exercise of an Option will be issued in the name of the Employee. Until the Shares are issued (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to vote or receive dividends or any other rights as a stockholder will exist with respect to the Shares, notwithstanding the exercise of the Option. The Company will issue (or cause to be issued) such Shares promptly after the Option is exercised. No adjustment will be made for a dividend or other right for which the record date is prior to the date the Shares are issued, except as provided in Section 2.4 of the Plan. Exercising an Option in any manner will decrease the number of Shares thereafter available, both for purposes of the Plan and for sale under the Option, by the number of Shares as to which the Option is exercised.

5.6 Termination of Service. If the Employee's Service terminates for any reason except for Cause or the Employee's death or Disability, then the Employee may exercise such Employee's Options (only to the extent that such Options are exercisable by the Employee on the date Employee's Service terminates) during the period ending no later than three (3) months after the date Employee's Service

terminates (or such shorter or longer time period as may be determined by the Committee), but in any event no later than the expiration date of the Options.

(a) Death. If the Employee's Service terminates because of the Employee's death (or the Employee dies within three (3) months after Employee's Service terminates other than for Cause or because of the Employee's Disability), then the Employee's Options may be exercised only to the extent that such Options would have been exercisable by the Employee on the date Employee's Service terminates and must be exercised by the Employee's legal representative, or authorized assignee, no later than twelve (12) months after the date Employee's Service terminates (or such shorter time period or longer time periods as may be determined by the Committee), but in any event no later than the expiration date of the Options.

(b) Disability. If the Employee's Service terminates because of the Employee's Disability, then the Employee's Options may be exercised only to the extent that such Options would have been exercisable by the Employee on the date Employee's Service terminates and must be exercised by the Employee (or the Employee's legal representative or authorized assignee) no later than twelve (12) months after the date Employee's Service terminates (or such shorter or longer time period as may be determined by the Committee, but in any event no later than the expiration date of the Options.

(c) Cause. If the Employee is terminated for Cause, then Employee's Options shall expire on such Employee's date of termination of Service, or at such later time and on such conditions as are determined by the Committee, but in any event no later than the expiration date of the Options. Unless otherwise provided in the Award Agreement or other agreement between the Company and Employee, Cause shall have the meaning set forth in this Plan.

5.7 Limitations on Exercise. The Committee may specify a minimum number of Shares that may be purchased on any exercise of an Option, provided that such minimum number will not prevent any Employee from exercising the Option for the full number of Shares for which it is then exercisable.

5.8 Modification, Extension or Renewal. The Committee may modify, extend or renew outstanding Options and authorize the grant of new Options in substitution therefor, provided that any such action may not, without the written consent of an Employee, impair any of such Employee's rights under any Option previously granted.

6. RESTRICTED STOCK UNITS. A Restricted Stock Unit ("***RSU***") is an award to an eligible Employee covering a number of Shares that may be settled in cash, or by issuance of those Shares. All RSUs shall be made pursuant to an Award Agreement.

6.1 Terms of RSUs. The Committee will determine the terms of an RSU including, without limitation: (a) the number of Shares subject to the RSU; (b) the time or times during which the RSU may be settled; (c) the consideration to be distributed on settlement; and (d) the effect of the Employee's termination of Service on each RSU. An RSU may be awarded upon satisfaction of such performance goals based on Performance Factors during any Performance Period as are set out in advance in the Employee's Award Agreement. If the RSU is being earned upon satisfaction of Performance Factors, then the Committee will: (x) determine the nature, length and starting date of any Performance Period for the RSU; (y) select from among the Performance Factors to be used to measure the performance, if any; and (z) determine the number of Shares deemed subject to the RSU. Performance Periods may overlap and participants may participate simultaneously with respect to RSUs that are subject to different Performance Periods and different performance goals and other criteria.

6.2 Form and Timing of Settlement. Payment of earned RSUs shall be made as soon as practicable after the date(s) determined by the Committee and set forth in the Award Agreement. The

Committee, in its sole discretion, may settle earned RSUs in cash, Shares, or a combination of both. The Committee may also permit a Employee to defer payment under an RSU to a date or dates after the RSU isearned provided that the terms of the RSU and any deferral satisfy the requirements of Section 409A of theCode.

6.3 Termination of Service. Except as may be set forth in the Employee's Award Agreement,vesting ceases on such date Employee's Service terminates (unless determined otherwise by the Committee).

7. PAYMENT FOR SHARE PURCHASES. Payment from an Employee for Shares purchased pursuant to this Plan may be made in cash or by check or, where expressly approved for the Employee by the Committee and where permitted by law (and to the extent not otherwise set forth in the applicable Award Agreement):

(a) by cancellation of indebtedness of the Company to the Employee;

(b) by surrender of shares of the Company held by the Employee that have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which said Award will be exercised or settled;

(c) by waiver of compensation due or accrued to the Employee for services rendered or to be rendered to the Company or a Parent or Subsidiary of the Company;

(d) by consideration received by the Company pursuant to a broker-assisted or other form of cashless exercise program implemented by the Company in connection with the Plan;

(e) by any combination of the foregoing; or

(f) by any other method of payment as is permitted by applicable law.

8. WITHHOLDING TAXES.

8.1 Withholding Generally. Whenever Shares are to be issued in satisfaction of Awards grantedunder this Plan or the applicable tax event occurs, the Company may require the Employee to remit to the Company, or to the Parent or Subsidiary employing the Employee, an amount sufficient to satisfy applicable
U.S. federal, state, local and international withholding tax requirements or any other tax or social insuranceliability legally due from the Employee prior to the delivery of Shares pursuant to exercise or settlement ofany Award. Whenever payments in satisfaction of Awards granted under this Plan are to be made in cash, such payment will be net of an amount sufficient to satisfy applicable U.S. federal, state, local and international withholding tax or social insurance requirements or any other tax liability legally due from the Employee. The Fair Market Value of the Shares will be determined as of the date that the taxes are required to be withheld and such Shares will be valued based on the value of the actual trade or, if there isnone, the Fair Market Value of the Shares as of the previous trading day.

8.2 Stock Withholding. The Committee, in its sole discretion and pursuant to such proceduresas it may specify from time to time and to limitations of local law, may require or permit an Employee to satisfy such tax withholding obligation or any other tax liability legally due from the Employee, in whole or in part by (without limitation) (a) paying cash, (b) electing to have the Company withhold otherwise deliverable cash or Shares having a Fair Market Value equal to up to the maximum statutory amount permitted to be withheld, (c) delivering to the Company already-owned Shares having a Fair Market Value equal to up to the maximum statutory amount permitted to be withheld or (d) withholding from the proceeds

of the sale of otherwise deliverable Shares acquired pursuant to an Award either through a voluntary sale or through a mandatory sale arranged by the Company.

9. **TRANSFERABILITY**. Unless determined otherwise by the Committee, an Award may not be sold, pledged, assigned, hypothecated, transferred, or disposed of in any manner other than by will or by the laws of descent or distribution. If the Committee makes an Award transferable, including, without limitation, by instrument to an inter vivos or testamentary trust in which the Awards are to be passed to beneficiaries upon the death of the trustor (settlor) or by gift or by domestic relations order to a Permitted Transferee, such Award will contain such additional terms and conditions as the Committee deems appropriate. All Awards shall be exercisable: (a) during the Employee's lifetime only by (i) the Employee, or (ii) the Employee's guardian or legal representative; (b) after the Employee's death, by the legal representative of the Employee's heirs or legatees; and (c) by a Permitted Transferee

10. **PRIVILEGES OF STOCK OWNERSHIP; RESTRICTIONS ON SHARES**.

10.1 Voting and Dividends. No Employee will have any of the rights of a stockholder with respect to any Shares until the Shares are issued to the Employee, except for any Dividend Equivalent Rights permitted by an applicable Award Agreement. Any Dividend Equivalent Rights shall be subject to the same vesting or performance conditions as the underlying Award. In addition, the Committee may provide that any Dividend Equivalent Rights permitted by an applicable Award Agreement shall be deemed to have been reinvested in additional Shares or otherwise reinvested. After Shares are issued to the Employee, the Employee will be a stockholder and have all the rights of a stockholder with respect to such Shares, including the right to vote and receive all dividends or other distributions made or paid with respect to such Shares; provided, that if such Shares are Unvested Shares, then any new, additional or different securities the Employee may become entitled to receive with respect to such Shares by virtue of a stock dividend, stock split or any other change in the corporate or capital structure of the Company will be subject to the same restrictions as the Unvested Shares; provided, further, that the Employee will have no right to retain such stock dividends or stock distributions with respect to Shares that are repurchased at the Employee's Exercise Price, pursuant to Section 10.2.

10.2 Restrictions on Shares. At the discretion of the Committee, the Company may reserve to itself and/or its assignee(s) a right to repurchase (a "***Right of Repurchase***") a portion of any or all Unvested Shares held by an Employee following such Employee's termination of Service at any time within ninety
(90) days (or such longer or shorter time determined by the Committee) after the later of the date Employee's Service terminates and the date the Employee purchases Shares under this Plan, for cash and/or cancellation of purchase money indebtedness, at the Employee's Exercise Price.

11. **CERTIFICATES**. All Shares or other securities (whether or not certificated) delivered under this Plan will be subject to such stock transfer orders, legends and other restrictions as the Committee may deem necessary or advisable, including restrictions under any applicable U.S. federal, state or foreign securities law, or any rules, regulations and other requirements of the SEC or any stock exchange or automated quotation system upon which the Shares may be listed or quoted and any non-U.S. exchange controls or securities law restrictions to which the Shares are subject.

12. **ESCROW; PLEDGE OF SHARES**. To enforce any restrictions on an Employee's Shares, the Committee may require the Employee to deposit all certificates representing Shares, together with stock powers or other instruments of transfer approved by the Committee, appropriately endorsed in blank, with the Company or an agent designated by the Company to hold in escrow until such restrictions have lapsed or terminated, and the Committee may cause a legend or legends referencing such restrictions to be placed on the certificates. Any Employee who is permitted to execute a promissory note as partial or full consideration for the purchase of Shares under this Plan will be required to pledge and deposit with the

Company all or part of the Shares so purchased as collateral to secure the payment of the Employee's obligation to the Company under the promissory note; provided, however, that the Committee may requireor accept other or additional forms of collateral to secure the payment of such obligation and, in any event, the Company will have full recourse against the Employee under the promissory note notwithstanding anypledge of the Employee's Shares or other collateral. In connection with any pledge of the Shares, the Employee will be required to execute and deliver a written pledge agreement in such form as the Committeewill from time to time approve. The Shares purchased with the promissory note may be released from the pledge on a pro rata basis as the promissory note is paid.

13. **SECURITIES LAW AND OTHER REGULATORY COMPLIANCE**. An Award will not be effective unless such Award is in compliance with all applicable U.S. and foreign federal and state securities and exchange control laws, rules and regulations of any governmental body, and the requirements of any stock exchange or automated quotation system upon which the Shares may then be listed or quoted, as theyare in effect on the date of grant of the Award and also on the date of exercise or other issuance. Notwithstanding any other provision in this Plan, the Company will have no obligation to issue or deliver certificates for Shares under this Plan prior to: (a) obtaining any approvals from governmental agencies that the Company determines are necessary or advisable; and/or (b) completion of any registration or other qualification of such Shares under any state or federal or foreign law or ruling of any governmental body that the Company determines to be necessary or advisable. The Company will be under no obligation to register the Shares with the SEC or to effect compliance with the registration, qualification or listing requirements of any foreign or state securities laws, exchange control laws, stock exchange or automated quotation system, and the Company will have no liability for any inability or failure to do so.

14. **NO OBLIGATION TO EMPLOY**. The Employee's participation in the Plan is voluntary. Nothing in this Plan or any Award granted under this Plan will confer or be deemed to confer on any Employee any right to continue in the employ of, or to continue any other relationship with, the Companyor any Parent, Subsidiary or Affiliate or limit in any way the right of the Company or any Parent, Subsidiaryor Affiliate to terminate Employee's employment or other relationship at any time.

15. **CORPORATE TRANSACTIONS**. In the event of a Corporate Transaction any or all outstanding Awards may be assumed or replaced by the successor corporation, which assumption or replacement shall be binding on all Employees. In the alternative, the successor corporation may substitute equivalent Awards or provide substantially similar consideration to Employees as was provided to stockholders (after taking into account the existing provisions of the Awards). The successor corporation may also issue, in place of outstanding Shares of the Company held by the Employee, substantially similar shares, cash or other property subject to repurchase restrictions no less favorable to the Employee. In the event such successor or acquiring corporation (if any) refuses to assume, convert, replace or substitute Awards, as provided above, pursuant to a Corporate Transaction, then notwithstanding any other provision in this Plan to the contrary, such Awards shall have their vesting accelerate as to all shares subject to such Award (and any applicable rights of repurchase shall fully lapse) immediately prior to the Corporate Transaction. In addition, in the event such successor or acquiring corporation (if any) refuses to assume, convert, replace or substitute Awards, as provided above, pursuant to a Corporate Transaction, the Committee will (i) notifythe Employee in writing or electronically that such Award will, if applicable, be exercisable for a period oftime determined by the Committee in its sole discretion, and such Award will terminate upon the earlier ofthe expiration of such period or immediately prior to the Corporate Transaction or (ii) provide that each Award shall be cancelled immediately upon the occurrence of the Corporate Transaction in exchange for apayment in cash or securities in an amount equal to (A) the excess of the consideration paid per Share in the Corporate Transaction over the exercise price or purchase price (if any) per Share subject to the Award

multiplied by (B) the number of Shares subject to the Award. Awards need not be treated similarly in a Corporate Transaction

16. **TERM OF PLAN/GOVERNING LAW**. Unless earlier terminated as provided herein, this Plan will become effective on the Effective Date and will terminate on the later of ten (10) years from the date this Plan is adopted by the Committee or the date additional Shares are added to the Plan by the Committee. This Plan and all Awards granted hereunder shall be governed by and construed in accordance with the laws of the State of Delaware (excluding its conflict of law rules).

17. **AMENDMENT OR TERMINATION OF PLAN**. The Board or Committee may at any time terminate or amend this Plan in any respect, including, without limitation, amendment of any form of Award Agreement or instrument to be executed pursuant to this Plan; provided, however, that the Board or Committee will not, without the approval of the stockholders of the Company, amend this Plan in any manner that requires such stockholder approval; provided further, that an Employee's Award shall be governed by the version of this Plan then in effect at the time such Award was granted.

18. **NONEXCLUSIVITY OF THE PLAN**. Neither the adoption of this Plan by the Committee nor any provision of this Plan will be construed as creating any limitations on the power of the Board or the Committee to adopt such additional compensation arrangements as it may deem desirable, including, without limitation, the granting of stock awards and bonuses otherwise than under this Plan, and such arrangements may be either generally applicable or applicable only in specific cases.

19. **INSIDER TRADING POLICY**. Each Employee who receives an Award shall comply with any policy adopted by the Company from time to time covering transactions in the Company's securities by Employees, officers and/or directors of the Company.

20. **ALL AWARDS SUBJECT TO COMPANY CLAWBACK OR RECOUPMENT POLICY**. All Awards, subject to applicable law, shall be subject to clawback or recoupment pursuant to any compensation clawback or recoupment policy adopted by the Board or required by law during the term of Employee's employment or other service with the Company that is applicable to executive officers, employees, directors or other service providers of the Company, and in addition to any other remedies available under such policy and applicable law, may require the cancellation of outstanding Awards and the recoupment of any gains realized with respect to Awards.

21. **DEFINITIONS**. As used in this Plan, and except as elsewhere defined herein, the following terms will have the following meanings:

21.1 "***Affiliate***" means (i) any entity that, directly or indirectly, is controlled by, controls or is under common control with, the Company and (ii) any entity in which the Company has a significant equity interest, in either case as determined by the Committee, whether now or hereafter existing.

21.2 "***Award***" means any award under this Plan, including any Option or Restricted Stock Unit.

21.3 "***Award Agreement***" means, with respect to each Award, the written or electronic agreement between the Company and the Employee setting forth the terms and conditions of the Award, and country-specific appendix thereto for grants to non-U.S. Employees, which shall be in substantially a form (which need not be the same for each Employee) that the Committee (or in the case of Award agreements that are not used for Insiders, the Committee's delegate(s)) has from time to time approved, and will comply with and be subject to the terms and conditions of this Plan.

21.4 "***Board***" means the Board of Directors of the Company.

21.5 "***Cause***" means (a) Employee's conviction (including a guilty plea or plea of *nolo contendere*) of any felony or any other crime involving fraud, dishonesty or moral turpitude; (b) Employee's commission or attempted commission of or participation in a fraud or act of dishonesty or misrepresentation against the Company that results (or could reasonably be expected to result) in material harm or injury to the business or reputation of the Company; (c) Employee's material violation of any contract or agreement between Employee and the Company, or of any Company policy, or of any statutory duty Employee owes to the Company; or (d) Employee's conduct that constitutes gross insubordination, incompetence or habitual neglect of duties and that results in (or could reasonably be expected to have resulted in) material harm to the business or reputation of the Company. The determination as to whether an Employee is being terminated for Cause shall be made in good faith by the Company and shall be final and binding on the Employee. The foregoing definition does not in any way limit the Company's ability to terminate an Employee's employment or consulting relationship at any time as provided in Section 14 above, and the term "Company" will be interpreted to include any Subsidiary or Parent, as appropriate. Notwithstanding the foregoing, the foregoing definition of "Cause" may, in part or in whole, be modified or replaced in each individual employment agreement or Award Agreement with any Employee, provided that such document supersedes the definition provided in this Section 21.5.

21.6 "***Code***" means the United States Internal Revenue Code of 1986, as amended, and the regulations promulgated thereunder.

21.7 "***Committee***" means the Compensation Committee of the Board.

21.8 "***Common Stock***" means the common stock of the Company.

21.9 "***Company***" means Sierra Oncology, Inc., or any successor corporation.

21.10 "***Corporate Transaction***" means the occurrence of any of the following events: (a) any "Person" (as such term is used in Sections 13(d) and 14(d) of the Exchange Act) becomes the "beneficial owner" (as defined in Rule 13d-3 of the Exchange Act), directly or indirectly, of securities of the Company representing more than fifty percent (50%) of the total voting power represented by the Company's then- outstanding voting securities; provided, however, that for purposes of this subclause (a) the acquisition of additional securities by any one Person who is considered to own more than fifty percent (50%) of the total voting power of the securities of the Company will not be considered a Corporate Transaction; (b) the consummation of the sale or disposition by the Company of all or substantially all of the Company's assets;
(c) the consummation of a merger or consolidation of the Company with any other corporation, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior thereto continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity or its parent) at least fifty percent (50%) of the total voting power represented by the voting securities of the Company or such surviving entity or its parent outstanding immediately after such merger or consolidation; (d) any other transaction which qualifies as a "corporate transaction" under Section 424(a) of the Code wherein the stockholders of the Company give up all of their equity interest in the Company (except for the acquisition, sale or transfer of all or substantially all of the outstanding shares of the Company) or (e) a change in the effective control of the Company that occurs on the date that a majority of members of the Board are replaced during any twelve (12) month period by members of the Board whose appointment or election is not endorsed by as majority of the members of the Board prior to the date of such appointment or election. For purpose of this subclause (e), if any Person is considered to be in effective control of the Company, the acquisition of additional control of the Company by the same Person will not be considered a Corporate Transaction. For purposes of this definition, Persons will be considered to be acting as a group if they are owners of a corporation that enters into a merger, consolidation, purchase or acquisition of stock, or similar business transaction with the Company. Notwithstanding the foregoing, to the extent that any amount constituting deferred compensation (as

defined in Section 409A of the Code) would become payable under this Plan by reason of a Corporate Transaction, such amount shall become payable only if the event constituting a Corporate Transaction would also qualify as a change in ownership or effective control of the Company or a change in the ownership of a substantial portion of the assets of the Company, each as defined within the meaning of Code Section 409A, as it has been and may be amended from time to time, and any proposed or final Treasury Regulations and IRS guidance that has been promulgated or may be promulgated thereunder fromtime to time.

21.11 "***Director***" means a member of the Board.

21.12 "***Disability***" means in the case of incentive stock options, total and permanent disability as defined in Section 22(e)(3) of the Code and in the case of other Awards, that the Employee is unable to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or can be expected to last for a continuous period of notless than 12 months.

21.13 "***Dividend Equivalent Right"*** means the right of an Employee, granted at the discretion ofthe Committee or as otherwise provided by the Plan or an Award Agreement, to receive a credit for the account of such Employee in an amount equal to the cash, stock or other property dividends in amounts equal equivalent to cash, stock or other property dividends for each Share represented by an Award held bysuch Employee.

21.14 "***Effective Date***" means September 20, 2018.

21.15 "***Employee***" means any person, including Officers, providing services as an employee to the Company or any Parent, Subsidiary or Affiliate. Neither service as a director nor payment of a director's fee by the Company will be sufficient to constitute "employment" by the Company.

21.16 "***Exchange Act***" means the United States Securities Exchange Act of 1934, as amended.

21.17 "***Exercise Price***" means, with respect to an Option, the price at which a holder may purchase the Shares issuable upon exercise of an Option.

21.18 "***Fair Market Value***" means, as of any date, the value of a share of the Company's Common Stock determined as follows:

(a) if such Common Stock is publicly traded and is then listed on a national securities exchange, its closing price on the date of determination on the principal national securities exchange on which the Common Stock is listed or admitted to trading as reported in *The Wall Street* Journal or such other source as the Board or the Committee deems reliable;

(b) if such Common Stock is publicly traded but is neither listed nor admitted to trading on a national securities exchange, the average of the closing bid and asked prices on the date of determination as reported in *The Wall Street Journal* or such other source as the Board or the Committee deems reliable; or

(c) if none of the foregoing is applicable, by the Board or the Committee in good faith.

21.19 "***Insider***" means an officer or director of the Company or any other person whose transactions in the Company's Common Stock are subject to Section 16 of the Exchange Act.

21.20 "***IRS***" means the United States Internal Revenue Service.

21.21 "***Option***" means an award of an option to purchase Shares pursuant to Section 5.

21.22 "***Outside Director***" means a Director who is not an Employee of the Company or any Parent or Subsidiary and who is an "independent" director under the rules of The Nasdaq Stock Market, asmay be amended from time to time.

21.23 "***Parent***" means any corporation (other than the Company) in an unbroken chain of corporations ending with the Company if each of such corporations other than the Company owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one ofthe other corporations in such chain.

21.24 ***"Performance Factors"*** means the factors selected by the Committee to determinewhether performance goals established by the Committee applicable to Awards have been satisfied.

21.25 "***Performance Period***" means the period of service determined by the Committee duringwhich years of service or performance is to be measured for the Award.

21.26 "***Permitted Transferee***" means any child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law (including adoptive relationships) of the Employee, any person sharing the Employee's household (other than a tenant or employee), a trust in which these persons(or the Employee) have more than 50% of the beneficial interest, a foundation in which these persons (or the Employee) control the management of assets, and any other entity in which these persons (or the Employee) own more than 50% of the voting interests.

21.27 "***Plan***" means this Sierra Oncology, Inc. 2018 Equity Inducement Plan.

21.28 "***Restricted Stock Unit***" means an Award granted pursuant to Section 6 of the Plan.

21.29 "***SEC***" means the United States Securities and Exchange Commission.

21.30 "***Securities Act***" means the United States Securities Act of 1933, as amended.

21.31 "***Service***" shall mean service as an Employee to the Company or a Parent, Subsidiary or Affiliate, subject to such further limitations as may be set forth in the Plan or the applicable Award Agreement. An Employee will not be deemed to have ceased to provide Service in the case of (a) sick leave,
(b) military leave, or (c) any other leave of absence approved by the Company; provided, that such leave isfor a period of not more than 90 days (x) unless reemployment upon the expiration of such leave is guaranteed by contract or statute, or (y) unless provided otherwise pursuant to formal policy adopted fromtime to time by the Company and issued and promulgated to employees in writing. In the case of any Employee on an approved leave of absence or a reduction in hours worked (for illustrative purposes only, a change in schedule from that of full-time to part-time), the Committee may make such provisions regarding suspension of or modification of vesting of the Award while on leave from the employ of the Company or a Parent, Subsidiary or Affiliate or during such change in working hours as it may deem appropriate, except that in no event may an Award be exercised after the expiration of the term set forth inthe applicable Award Agreement. In the event of military leave, if required by applicable laws, vesting shall continue for the longest period that vesting continues under any other statutory or Company approved leaveof absence and, upon a Employee's returning from military leave (under conditions that would entitle himor her to protection upon such return under the Uniform Services Employment and Reemployment Rights

Act), he or she shall be given vesting credit with respect to Awards to the same extent as would have appliedhad the Employee continued to provide services to the Company throughout the leave on the same terms ashe or she was providing services immediately prior to such leave. Except as set forth in this Section 28.39, an employee shall have terminated employment as of the date he or she ceases provide services (regardlessof whether the termination is in breach of local employment laws or is later found to be invalid) and employment shall not be extended by any notice period or garden leave mandated by local law, *provided however*, that a change in status from an employee to a consultant or advisor shall not terminate the service provider's Service, unless determined by the Committee, in its discretion. The Committee will have sole discretion to determine whether a Employee has ceased to provide Services and the effective date on whichthe Employee ceased to provide Services.

21.32 "***Shares***" means shares of Common Stock and the common stock of any successor entity.

21.33 "***Subsidiary***" means any corporation (other than the Company) in an unbroken chain of corporations beginning with the Company if each of the corporations other than the last corporation in theunbroken chain owns stock possessing fifty percent (50%) or more of the total combined voting power of all classes of stock in one of the other corporations in such chain.

21.34 "***Treasury Regulations***" means regulations promulgated by the United States Treasury Department.

21.35 "***Unvested Shares***" means Shares that have not yet vested or are subject to a right of repurchase in favor of the Company (or any successor thereto).

SIERRA ONCOLOGY, INC.

(the "**Company**")

2018 EQUITY INDUCEMENT PLAN

(the "**Plan**")

ADDENDUM FOR CANADIAN PARTICIPANTS

A. The Company has adopted the Plan, to be effective on the Effective Date.

B. The Company desires to modify certain terms of the Plan in their application for Employees (as those terms are defined in the Plan) who are resident in Canada for purposes of the Income Tax Act (Canada) or otherwise subject to Canadian personal income tax (the "**Canadian Employees**").

NOW THEREFORE, the Company does hereby amend certain terms and conditions of the Plan as they apply to the Canadian Employees, as follows.

1. **Defined Terms**. In this Addendum, all defined terms shall have the respective meanings set forth in the Plan, unless otherwise defined herein.

2. **Effective Date**. The effective date of this Addendum is the Effective Date.

3. **Addendum.** The Company hereby amends certain terms and conditions of the Plan pursuant to which the Company may grant Options to any Canadian Eligible Person, if the participation by the Canadian Eligible Person in such distribution of securities is voluntary (as such term is interpreted pursuant to Section 2.23(2) of NI 45-106) and is otherwise permitted under NI 45-106.

4. **Options**.

(a) Notwithstanding section 5.2 of the Plan, the grant date of an Option awarded to a Canadian Employee shall be, in all cases, the date the Option is actually granted to the Canadian Employee, as evidenced by the Award Agreement.

(b) Notwithstanding section 5.1 of the Plan, satisfaction of Performance Factors, if any, will be treated as a condition subsequent to the grant to a Canadian Employee of an Option giving rise to a risk of forfeiture of the Option and not a condition precedent to the grant of the Option.

(c) For purposes of section 5.9 of the Plan, Options granted to a Canadian Employee will not be modified or altered, or new options granted in substitution therefor, if such modification, alteration or substitution has a material adverse affect on such Canadian Employee's tax treatment of such Options, except with such Canadian Employee's consent.

5. **Restricted Stock Units**.

Section 6.2 of the Plan shall be modified as it applies to Canadian Employees such that the Company agrees to issue only Shares in payment of RSUs to a Canadian Employee and the Company cannot choose, at its option, to make such payment in cash or a combination of cash and Shares, and section 6.2 shall read as follows:

"6.2. Form and Timing of Settlement to Canadian Employees. Payment of earned RSUs of a Canadian Employee shall be made as soon as practicable after the date(s) determined by the Committee and set forth in the Award Agreement. Such earned RSUs shall be settled solely by the issuance of Shares. The Committee may permit a Canadian Employee to defer settlement and the issuance of Shares in payment of an earned RSU to a date that is acceptable to the Committee, provided that, in the case of a Canadian Eligible Person that is an Employee, the terms of the Award Agreement, the RSUs and any deferral meet the conditions of section 7 of the *Income Tax Act* (Canada)."

6. Payment for Share Purchases.

Section 7(b) of the Plan shall be modified as at applies to Canadian Employees with respect to the consideration that may be paid by Canadian Employees for Shares purchased pursuant to the Plan. In no circumstances shall a Canadian Employee be permitted to make, and the Committee shall not approve, a payment by the Canadian Employee by the surrender of any Shares that were acquired at any time by the Canadian Employee on the exercise of any Option.

7. Withholding Taxes.

(a) Section 8.1 of the Plan shall be modified as it applies to Canadian Employees and shall read as follows:

"8.1 Withholding for Canadian Employees. The Company or any Affiliate shall deduct and withhold any taxes and other required source deductions which the Company or Affiliate, as the case may be, is required by law or regulation of any governmental authority whatsoever to deduct, withhold or remit in connection with the grant, exercise or settlement of any Award. Without limiting the generality of the foregoing, whenever a settlement or payment is made by the issuance of Shares to a Canadian Employee in satisfaction of Awards granted under this Plan, the Company or Affiliate, as the case may be, may, at its discretion (i) deduct and withhold those amounts it is required to remit from any cash remuneration or other amount payable to the Canadian Employee, whether or not such amount payable is related to the Plan, or the exercise or settlement of any Awards; (ii) permit the Canadian Employee to make a cash payment to the Company or Affiliate, as the case may be, equal to the amount required to be remitted; or (iii) sell, on behalf of the Canadian Employee, that number of Shares to be issued on the exercise or settlement such that the amount of the proceeds of such sale will be sufficient to satisfy any taxes or other source deductions required to be remitted for the account of the Canadian Employee. If the Company or Affiliate, as the case may be, considers that the foregoing steps undertaken in connection with this section 13.1 result in inadequate withholding or a late remittance of taxes or other source deductions, then the delivery of Shares to be issued on the exercise or settlement of Awards may be made conditional upon the Canadian Employee (or other person) reimbursing or compensating the Company or Affiliate or making arrangements satisfactory to the Company or Affiliate for the payment in a timely manner of all taxes and other source deductions required to be remitted."

(b) Section 8.2 of the Plan shall not apply to Canadian Employees. For greater certainty, the Committee shall not approve funding by a Canadian Employee of withholding taxes or other source deductions by the withholding of Shares the Canadian Employee is otherwise

entitled to receive or the surrender by the Canadian Employee of any Shares that were acquired at any time by the Canadian Employee on the exercise of any Option.

NOTICE OF STOCK OPTION GRANT

SIERRA ONCOLOGY, INC. 2018 EQUITY INDUCEMENT PLAN

Unless otherwise defined herein, the terms defined in the Sierra Oncology, Inc. (the "***Company***") 2018 Equity Inducement Plan (the "***Plan***") shall have the same meanings in this Notice of Stock Option Grant (the "***Notice of Grant***") and the attached Stock Option Agreement (the "***Option Agreement***"). You have been granted an Option to purchase shares of Common Stock of the Company under the Plan subject to the terms and conditions of the Plan, this Notice of Grant and the attached Option Agreement.

Name: _____

Address: _____

Date of Grant: _____

Vesting Commencement Date: _____

Exercise Price per Share: _____

Total Number of Shares: _____

Type of Option: Non-Qualified Stock Option

Expiration Date: _____, 20__; This Option expires earlier if your Service terminates earlier, as described in the Stock Option Agreement.

Vesting Schedule:

Additional Terms: If this box is checked, the additional terms and conditions set forth on Attachment 1 hereto (as executed by the Company) are applicable and are incorporated herein by reference. No document need be attached as Attachment 1 if the box is not checked.

You understand that your employment relationship with the Company is for an unspecified duration, can be terminated at any time (i.e., is "at-will"), and that nothing in this Notice, the Option Agreement or the Plan changes the at-will nature of that relationship. By accepting this Option, you and the Company agree that this Option is granted under and governed by the terms and conditions of the Plan, the Notice of Grant and the Option Agreement. By accepting this Option, you consent to electronic delivery as set forth in the Option Agreement.

PARTICIPANT:

Signature _____

Print Name: _____

SIERRA ONCOLOGY, INC.

By:

Name: _____

Its: _____

STOCK OPTION AGREEMENT

SIERRA ONCOLOGY, INC.

2018 EQUITY INDUCEMENT PLAN

You have been granted an Option by Sierra Oncology, Inc. (the "***Company***") under the 2018 Equity Inducement Plan (the "***Plan***") to purchase Shares (the "***Option***"), subject to the terms, restrictions and conditions of the Plan, the Notice of Stock Option Grant (the "***Notice of Grant***") and this Stock Option Agreement (the "***Agreement***").

Grant of Option. You have been granted an Option for the number of Shares set forth in the Notice of Grant at the exercise price per Share set forth in the Notice of Grant (the "***Exercise Price***"). In the event of a conflict between the terms and conditions of the Plan and the terms and conditions of this Agreement, the terms and conditions of the Plan shall prevail. The Option is designated as a Nonqualified Stock Option ("***NSO***").

Termination Period.

General Rule. If your Service terminates for any reason except death or Disability, and other than for Cause, then this Option will expire at the close of business at Company headquarters on the date three (3) months after your termination of Service (subject to the expiration detailed in Section 6). If your Service is terminated for Cause, this Option will expire upon the date of such termination. The Company determines when your Service terminates for all purposes under this Agreement. You acknowledge and agree that the Vesting Schedule may change prospectively in the event that your service status changes between full and part-time status in accordance with Company policies relating to work schedules and vesting of awards. You acknowledge that the vesting of the Shares pursuant to this Notice is earned only by continuing Service and that any unvested portion of your Option will expire on the termination of your employment for any reason.

Death; Disability. If you die before your Service terminates (or you die within three (3) months of your termination of Service other than for Cause), then this Option will expire at the close of business at Company headquarters on the date twelve (12) months after the date of your death (subject to the expiration detailed in Section 6). If your Service terminates because of your Disability, then this Option will expire at the close of business at Company headquarters on the date twelve (12) months after your termination date (subject to the expiration detailed in Section 6).

Black-Out Period. Notwithstanding the foregoing, if any post-termination exercise period set forth above terminates on a date that falls within a Blackout Period (as defined below) or within ten (10) business days following the expiration of a Blackout Period, such expiration date shall be automatically extended without any further act or formality to that date which is ten (10) business days after the end of such Blackout Period, with such tenth (10th) business day to be considered the expiration date of such Option for all purposes under the Plan, subject to earlier expiration detailed in Section 6. For purposes of this Agreement, "***Blackout Period***" means the period during which designated directors, officers and employees of the Company cannot trade Shares pursuant to the Company's policy respecting restrictions on director', officers' and employee trading which is in effect at the time.

No Notice. You are responsible for keeping track of these exercise periods following your termination of Service for any reason. The Company will not provide further notice of such periods. In no event shall this Option be exercised later than the Expiration Date set forth in the Notice of Grant.

Exercise of Option.

Right to Exercise. This Option is exercisable during its term in accordance with the Vesting Schedule set forth in the Notice of Grant and the applicable provisions of the Plan and this Agreement. In the event of your death, Disability, or other cessation of Service, the exercisability of the Option is governed by the applicable provisions of the Plan, the Notice of Grant and this Agreement. This Option may not be exercised for a fraction of a Share.

Method of Exercise. This Option is exercisable by delivery of an exercise notice in a form specified by the Company (the "***Exercise Notice***"), which shall state the election to exercise the Option, the number of Shares in respect of which the Option is being exercised (the "***Exercised Shares***"), and such other representations and agreements as may be required by the Company pursuant to the provisions of the Plan. The Exercise Notice shall be delivered in person, by mail, via electronic mail or facsimile or by other authorized method to the Secretary of the Company or other person designated by the Company. The Exercise Notice shall be accompanied by payment of the aggregate Exercise Price as to all Exercised Shares. This Option shall be deemed to be exercised upon receipt by the Company of a fully executed Exercise Notice accompanied by the aggregate Exercise Price and any applicable tax withholding due upon exercise of the Option.

Exercise by Another. If another person wants to exercise this Option after it has been transferred to him or her in compliance with this Agreement and the Plan, that person must prove to the Company's satisfaction that he or she is entitled to exercise this Option. That person must also complete the proper Exercise Notice form (as described above) and pay the Exercise Price (as described below) and any applicable tax withholding due upon exercise of the Option (as described below).

Method of Payment. Payment of the aggregate Exercise Price shall be by personal check, wire transfer, cashier's check, or, with the Company's consent; any of the following, or a combination thereof:

certificates for shares of Company stock that you own, along with any forms needed to effect a transfer of those shares to the Company; the Fair Market Value of the shares, determined as of the effective date of the Option exercise, will be applied to the Option Exercise Price. Instead of surrendering shares of Company stock, you may attest to the ownership of those shares on a form provided by the Company and have the same number of shares subtracted from the Option shares issued to you. However, you may not surrender, or attest to the ownership of, shares of Company stock in payment of the Exercise Price of your Option if your action would cause the Company to recognize compensation expense (or additional compensation expense) with respect to this Option for financial reporting purposes;

cashless exercise through irrevocable directions to a securities broker approved by the Company to sell all or part of the Shares covered by this Option and to deliver to the Company from the sale proceeds an amount sufficient to pay the Option Exercise Price and any withholding taxes. The balance of the sale proceeds, if any, will be delivered to you. The directions must be given by signing a special notice of exercise form provided by the Company; or

other method authorized by the Company.

Non-Transferability of Option. In general, except as provided below, only you may exercise this Option prior to your death. You may not transfer or assign this Option, except as provided below. For instance, you may not sell this Option or use it as security for a loan. If you attempt to do any of these things, this Option will immediately become invalid. You may, however, dispose of this Option in your will or in a beneficiary designation. However, the Committee (as defined in the Plan) may, in its sole discretion, allow you to transfer this Option as a gift to one or more family members. For purposes of this

Agreement, "family member" means a child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in- law, father-in-law, son-in-law, daughter-in-law, brother-in-law or sister-in-law (including adoptive relationships), any individual sharing your household (other than a tenant or employee), a trust in which one or more of these individuals have more than 50% of the beneficial interest, a foundation in which you or one or more of these persons control the management of assets, and any entity in which you or one or more of these persons own more than 50% of the voting interest. In addition, the Committee may, in its sole discretion, allow you to transfer this Option to your spouse or former spouse pursuant to a domestic relations order in settlement of marital property rights. The Committee will allow you to transfer this Option only if both you and the transferee(s) execute the forms prescribed by the Committee, which include the consent of the transferee(s) to be bound by this Agreement. This Option may not be transferred in any manner other than by will or by the laws of descent or distribution or court order and may be exercised during the lifetime of you only by you, your guardian, or legal representative, as permitted in the Plan. The terms of the Plan and this Agreement shall be binding upon the executors, administrators, heirs, successors and assigns of you.

Term of Option. This Option shall in any event expire on the expiration date set forth in the Notice of Grant, which date is ten (10) years after the grant date.

Tax Consequences. You should consult a tax adviser for tax consequences relating to this Option in the jurisdiction in which you are subject to tax. YOU SHOULD CONSULT A TAX ADVISER BEFORE EXERCISING THIS OPTION OR DISPOSING OF THE SHARES. You will not be allowed to exercise this Option unless you make arrangements acceptable to the Company to pay any withholding taxes that may be due as a result of the Option exercise.

Withholding Taxes and Stock Withholding. Regardless of any action the Company or your actual employer (the "***Employer***") takes with respect to any or all income tax, social insurance, payroll tax, payment on account or other tax-related withholding ("***Tax-Related Items***"), you acknowledge that the ultimate liability for all Tax-Related Items legally due by you is and remains your responsibility and that the Company and/or the Employer (1) make no representations or undertakings regarding the treatment of any Tax-Related Items in connection with any aspect of the Option grant, including the grant, vesting or exercise of the Option, the subsequent sale of Shares acquired pursuant to such exercise and the receipt of any dividends; and (2) do not commit to structure the terms of the grant or any aspect of the Option to reduce or eliminate your liability for Tax-Related Items. You acknowledge that if you are subject to Tax-Related Items in more than one jurisdiction, the Company and/or the Employer may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

Prior to exercise of the Option, you shall pay or make adequate arrangements satisfactory to the Company and/or the Employer to satisfy all withholding and payment on account obligations of the Company and/or the Employer. In this regard, you authorize the Company and/or the Employer to withhold all applicable Tax-Related Items legally payable by you from your wages or other cash compensation paid to you by the Company and/or the Employer. With the Company's consent, these arrangements may also include, if permissible under local law, (a) withholding Shares that otherwise would be issued to you when you exercise this Option, by considering applicable statutory or other withholding rates, including up to maximum rates, (b) having the Company withhold taxes from the proceeds of the sale of the Shares, either through a voluntary sale or through a mandatory sale arranged by the Company (on your behalf and you hereby authorize such sales by this authorization), (c) your payment of a cash amount, or (d) any other arrangement approved by the Company; all under such rules as may be established by the Committee and in compliance with the any insider trading or 10b-51 trading policies of the Company, if applicable; provided however, that if you are a Section 16 officer of the Company under the Exchange Act, then the Committee (as constituted in accordance with Rule 16b-3 under the Exchange Act) shall establish the method of withholding from alternatives (a)-(d) above, and the Committee shall establish the method prior

to the Tax-Related Items withholding event. The Fair Market Value of these Shares, determined as of the effective date of the Option exercise, will be applied as a credit against the withholding taxes. You shall pay to the Company or the Employer any amount of Tax-Related Items that the Company or the Employer may be required to withhold as a result of your participation in the Plan or your purchase of Shares that cannot be satisfied by the means previously described. Finally, you acknowledge that the Company has no obligation to deliver Shares to you until you have satisfied the obligations in connection with the Tax-Related Items as described in this Section.

Acknowledgement. The Company and you agree that the Option is granted under and governed by the Notice of Grant, this Agreement and the provisions of the Plan (incorporated herein by reference). You: (i) acknowledge receipt of a copy of the Plan prospectus, (ii) represent that you have carefully read and are familiar with their provisions, and (iii) hereby accept the Option subject to all of the terms and conditions set forth herein and those set forth in the Plan and the Notice of Grant. You hereby agree to accept as binding, conclusive and final all decisions or interpretations of the Committee upon any questions relating to the Plan, the Notice of Grant and the Agreement.

Consent to Electronic Delivery of All Plan Documents and Disclosures. By your acceptance of this Option, you consent to the electronic delivery of the Notice of Grant, this Agreement, account statements, Plan prospectuses required by the Securities and Exchange Commission, U.S. financial reports of the Company, and all other documents that the Company is required to deliver to its security holders (including, without limitation, annual reports and proxy statements) or other communications or information related to the Option. Electronic delivery may include the delivery of a link to a Company intranet or the internet site of a third party involved in administering the Plan, the delivery of the document via e-mail or such other delivery determined at the Company's discretion. You acknowledge that you may receive from the Company a paper copy of any documents delivered electronically at no cost if you contact the Company by telephone, through a postal service or electronic mail at _____. You further acknowledge that you will be provided with a paper copy of any documents delivered electronically if electronic delivery fails; similarly, you understand that you must provide on request to the Company or any designated third party a paper copy of any documents delivered electronically if electronic delivery fails. Also, you understand that your consent may be revoked or changed, including any change in the electronic mail address to which documents are delivered (if you have provided an electronic mail address), at any time by notifying the Company of such revised or revoked consent by telephone, postal service or electronic mail at _____. Finally, you understand that you are not required to consent to electronic delivery.

Compliance with Laws and Regulations. The exercise of this Option will be subject to and conditioned upon compliance by the Company and you with all applicable state, federal and foreign laws and regulations and with all applicable requirements of any stock exchange or automated quotation system on which the Company's Common Stock may be listed or quoted at the time of such issuance or transfer. The Shares issued pursuant to this Agreement shall be endorsed with appropriate legends, if any, determined by the Company.

Governing Law; Severability. If one or more provisions of this Agreement are held to be unenforceable under applicable law, the parties agree to renegotiate such provision in good faith. In the event that the parties cannot reach a mutually agreeable and enforceable replacement for such provision, then (i) such provision shall be excluded from this Agreement, (ii) the balance of this Agreement shall be interpreted as if such provision were so excluded and (iii) the balance of this Agreement shall be enforceable in accordance with its terms. This Agreement and all acts and transactions pursuant hereto and the rights and obligations of the parties hereto shall be governed, construed and interpreted in accordance with the laws of the State of Delaware, without giving effect to principles of conflicts of law. For purposes of

litigating any dispute that may arise directly or indirectly from the Plan, the Notice and this Agreement, the parties hereby submit and consent to litigation in the exclusive jurisdiction of the State of Delaware.

No Rights as Employee. Nothing in this Agreement shall affect in any manner whatsoever the right or power of the Company, or a Parent, Subsidiary or Affiliate of the Company, to terminate your Service, for any reason, with or without Cause.

Adjustment. In the event of a stock split, a stock dividend or a similar change in Company stock, the number of Shares covered by this Option and the Exercise Price per Share may be adjusted pursuant to the Plan.

Award Subject to Company Clawback or Recoupment. To the extent permitted by applicable law, the Option shall be subject to clawback or recoupment pursuant to any compensation clawback or recoupment policy adopted by the Board or required by law during the term of your employment or other Service that is applicable to you. In addition to any other remedies available under such policy, applicable law may require the cancellation of your Option (whether vested or unvested) and the recoupment of any gains realized with respect to your Option.

Entire Agreement; Enforcement of Rights. This Agreement, the Plan and the Notice constitute the entire agreement and understanding of the parties relating to the subject matter herein and supersede all prior discussions between them. Any prior agreements, commitments or negotiations concerning this Option are superseded. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, shall be effective unless in writing and signed by the parties to this Agreement. The failure by either party to enforce any rights under this Agreement shall not be construed as a waiver of any rights of such party.

BY ACCEPTING THIS OPTION, YOU AGREE TO ALL OF THE TERMS AND CONDITIONS DESCRIBED ABOVE AND IN THE PLAN.

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-205693, 333-209897, 333-216392, 333-223253, 333-228263, 333-229933, 333-236854, 333-241414, and 333-254126 on Form S-8, and Registration Statement Nos. 333-225650, 333-234554, 333-241443, and 333-260799 on Form S-3 of our report dated March 10, 2022, relating to the consolidated financial statements of Sierra Oncology, Inc. and subsidiaries (the "Company") appearing in this Annual Report on Form 10-K of the Company for the year ended December 31, 2021.

/s/ Deloitte & Touche LLP

Grand Rapids, Michigan
March 10, 2022

EXHIBIT 31.1

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Stephen Dilly, certify that:

1. I have reviewed this Annual Report on Form 10-K of Sierra Oncology, 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 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.

Date: March 10, 2022

/s/ Stephen Dilly

Dr. Stephen Dilly
Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION OF PERIODIC REPORT UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Sukhi Jagpal, certify that:

1. I have reviewed this Annual Report on Form 10-K of Sierra Oncology, 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 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.

Date: March 10, 2022

/s/ Sukhi Jagpal

Sukhi Jagpal
Chief Financial Officer
(Principal Financial Officer)

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

I, Stephen Dilly, Chief Executive Officer of Sierra Oncology, Inc. (Company), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

- the Annual Report on Form 10-K of the Company for the year ended December 31, 2021 (Report), as filed with the Securities and Exchange Commission, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: March 10, 2022

/s/ Stephen Dilly
Dr. Stephen Dilly
Chief Executive Officer
(Principal Executive Officer*)*

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

I, Sukhi Jagpal, Chief Financial Officer of Sierra Oncology, Inc. (Company), do hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of my knowledge:

- the Annual Report on Form 10-K of the Company for the year ended December 31, 2021 (Report), as filed with the Securities and Exchange Commission, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the periods presented therein.

Date: March 10, 2022

/s/ Sukhi Jagpal
Sukhi Jagpal
Chief Financial Officer
(Principal Financial Officer)