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, 2018

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	**20-0138994**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**
c/o 2150 – 885 West Georgia Street Vancouver, British Columbia, Canada	**V6C 3E8**
(Address of principal executive offices)	**(Zip Code)**

(604) 558-6536
(Registrant's telephone number, including area code)

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

Title of Each Class	**Name of Exchange on Which Registered**
Common Stock, $0.001 par value per share	**The Nasdaq Stock Market LLC**

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

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

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

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

Indicate by check mark whether the Registrant has submitted electronically, 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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 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 $2.96 of the registrant's common stock as reported on The Nasdaq Global Market on June 29, 2018, the last business day of the registrant's most recently completed second quarter, was $193.5 million.

The number of shares of Registrant's Common Stock outstanding as of February 22, 2019 was 74,467,746.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement ("Proxy Statement") relating to the 2019 Annual Meeting of Stockholders will be filed with the Commission within 120 days after the end of the Registrant's 2018 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, including statements regarding our future clinical development activities, expected timing and results of clinical trials, future results of operations and financial position, our business strategy and plans and our objectives for future operations, 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.

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 clinical stage drug development company advancing targeted therapeutics for the treatment of patients with unmet medical needs in hematology and oncology. We have a highly experienced management team with a proven track record of success in hematology and oncology drug development. We are an ambitious company, oriented towards achieving the successful registration and commercialization of our product candidates.

During the third quarter of 2018, we acquired from Gilead Sciences, Inc. (Gilead) our lead drug candidate momelotinib, a potent, selective and orally-bioavailable dual JAK1/JAK2 (Janus kinase 1 and 2) and ACVR1 (Activin A receptor type 1) inhibitor. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis and has demonstrated a potentially differentiated therapeutic profile encompassing anemia-related clinical benefits, as well as achieving substantive splenic volume reduction and constitutional symptom control (see additional discussion below under *Momelotinib – A Potent and Selective JAK1, JAK2 and ACVR1 Inhibitor*).

In December 2018, we reported new clinical data for momelotinib collated from the two completed SIMPLIFY Phase 3 clinical trials and a translational biology study in transfusion dependent patients with myelofibrosis. Data from the latter study were also concurrently presented in a poster at the 60th American Society of Hematology Annual Meeting & Exposition in San Diego, California. We reported aggregated transfusion independence responses from more than 150 intermediate and high-risk transfusion dependent myelofibrosis patients demonstrating robust and consistent response rates within and across the clinical studies. More than 44% of these patients became transfusion free for at least 12 weeks and nearly 50% were transfusion independent for at least 8 weeks.

We are advancing discussions with regulators to determine the registration path for momelotinib and expect to report next steps in the first half of 2019. Our anticipated registration strategy envisions conducting one additional Phase 3 trial in second line myelofibrosis patients, in order to recapitulate the meaningful clinical benefits observed in the two previously completed Phase 3 trials.

We are also advancing SRA737, our potent, highly selective, orally bioavailable small molecule inhibitor of Checkpoint kinase 1 (Chk1). Chk1 is a key regulator of cell cycle progression and the DNA Damage Response (DDR) replication stress response. In cancer cells, intrinsic replication stress (RS) is induced by factors such as oncogenes (e.g., *CCNE1* or *MYC*), genetic mutations in DNA repair machinery (e.g., *BRCA1* or *FANCA*), genetic mutations leading to a dysregulated cell cycle (e.g., *TP53* or *RAD50*) or other genomic alterations. Replication stress can also be induced by certain exogeneous factors, such as the use of low-dose gemcitabine (LDG). In general, replication stress results in persistent DNA damage and genomic instability leading to an increased dependency on Chk1 for survival. Targeted inhibition of Chk1 by SRA737 may therefore be synthetically lethal to cancer cells with elevated intrinsic replication stress, either alone or in combination with LDG, in a range of tumor indications. The combination of SRA737 with other modalities, such as other agents that target the DDR network and immuno-oncology agents, may also provide synergistic anti-tumor activity via a variety of potential biological mechanisms. Importantly, the oral bioavailability of SRA737 may afford greater dosing flexibility for both monotherapy and combination therapy settings than is possible with intravenously administered agents.

We are pursuing an innovative development plan for SRA737, which is currently being evaluated in two Phase 1/2 clinical trials in patients with advanced cancer. Our SRA737-01 trial is intended to evaluate SRA737's potential to induce synthetic lethality as monotherapy, while the SRA737-02 trial is intended to evaluate the combination of SRA737 potentiated by subtherapeutic LDG.

During the second quarter of 2018, we further refined our SRA737-01 monotherapy study to focus on high grade serous ovarian cancer (HGSOC), supported by emerging data in the field that provides clinical validation for

Chk1 inhibition in this indication. Accordingly, we prioritized the enrollment of genetically defined HGSOC patients into this trial, while continuing to enroll patients into the trial's other indications.

We commenced the Cohort Expansion Phase 2 portion of the SRA737-02 Phase 1/2 LDG Combination trial during the second quarter of 2018, which has been enrolling patients across four indications. We also modified this study to add and prioritize for the enrollment of a cohort of genetically defined HGSOC patients, replacing an originally proposed cohort of urothelial cancer patients.

We expect to report preliminary data from both trials in the first half of 2019.

In addition, we are designing clinical trials and conducting preclinical research evaluating SRA737 in combination with other DDR-targeted agents, including poly ADP-ribose polymerase (PARP) inhibitors, as well as with immuno-oncology therapeutics, that could guide the next wave of clinical development for our asset, potentially further broadening its therapeutic utility. In the first quarter of 2018, we announced an agreement with Janssen Research & Development, LLC (Janssen), under which they have agreed to supply us with the PARP inhibitor niraparib, facilitating the potential initiation of a PARP inhibitor combination trial with SRA737 for the treatment of prostate cancer. We are currently evaluating the optimal timing to commence this trial within the context of our recently expanded portfolio.

Our pipeline also includes SRA141, a potent, selective, orally bioavailable small molecule inhibitor of cell division cycle 7 kinase (Cdc7). Cdc7 is a key regulator of DNA replication and is involved in the DDR network, making it a compelling emerging target for the potential treatment of a broad range of tumor types. During the third quarter of 2018, we successfully completed the Investigational New Drug Application (IND) process with the U.S. Food and Drug Administration (FDA) for SRA141 and we have prepared for a potential Phase 1/2 trial with this drug candidate in patients with advanced colorectal cancer. We are currently evaluating the optimal timing to commence this trial within the context of our recently expanded portfolio.

We retain the global commercialization rights to momelotinib, SRA737 and SRA141.

Our Strategy

Key elements of our long-term business strategy are to:

- ***Achieve Regulatory Approval for Momelotinib***. We are advancing discussions with regulators to determine the registration path for momelotinib and anticipate reporting next steps in the first half of 2019. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis and has demonstrated a potentially differentiated therapeutic profile encompassing anemia-related clinical benefits, as well as achieving substantive splenic volume and constitutional symptom control. Our anticipated registration strategy envisions conducting one additional Phase 3 trial in second line myelofibrosis patients to recapitulate the meaningful clinical benefits observed in the two previously completed Phase 3 trials.
- ***Continue the Clinical Development of SRA737***. We plan to advance SRA737 for the possible treatment of a broad range of cancers, initially focusing on indications where we believe SRA737 has the best potential for demonstrating anti-tumor activity and where there is a significant unmet medical need. The two Phase 1/2 clinical trials for SRA737 currently underway in the United Kingdom are designed to evaluate the safety, tolerability and preliminary efficacy of SRA737 both as monotherapy and in combination with low-dose gemcitabine. Within these trials, we are evaluating the efficacy of SRA737 in prospectively-selected subjects with genetically defined tumors predicted to be more likely to derive benefit from Chk1 inhibition. These studies are designed to help assess potential patient selection strategies for further clinical development.
- ***Pursue a Multi-Faceted Development Strategy for Our Product Candidates***. We intend to expand the commercial market opportunities for momelotinib, SRA737 and SRA141 by exploring their potential

to treat a wide variety of cancer indications, and possibly non-cancer indications, as monotherapy and in combination with other therapeutic agents.

- ***Maximize the Global Commercial Value of Our Product Candidates***. As we further develop our product candidates, we plan to build a commercial infrastructure with the capability to directly market our products, once approved, to hematologists and oncologists in North America and possibly other major geographies that are core to our commercial strategy. We plan to enter into collaborations for the marketing and commercialization of our products in additional geographies at an appropriate time.
- ***Opportunistically Broaden Our Proprietary Pipeline by Acquiring Product Candidates.*** We plan to opportunistically acquire additional oncology product candidates through in-licensing or other strategic opportunities in order to expand our pipeline and leverage the full potential of our development capabilities.

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 18,000 patients are living with myelofibrosis in the United States. 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 the most important 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).

There are no effective treatments for myelofibrosis-associated anemia, with the National Comprehensive Cancer Network, describing all therapeutic options to address this issue 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 wholly 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 total symptom score; 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 total symptom score. 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 Janus kinase 1 (JAK1), Janus kinase 2 (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, 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 both ACVR1 and JAK1/2 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 over 550 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 7 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

We are currently advancing discussions with regulators to determine the registration path for momelotinib and expect to report next steps in the first half of 2019. Our anticipated registration strategy envisions conducting one

additional Phase 3 trial in second line myelofibrosis patients, to recapitulate the meaningful clinical benefits observed in the two previously completed Phase 3 trials.

Our DDR Programs – SRA737 and SRA141

Background on DDR and its Role in Cancer

Cancer is a leading cause of death in the developed world and the second leading cause of death in the United States, with more than 600,000 deaths and approximately 1.8 million new cases estimated to occur in the United States in 2019, according to the American Cancer Society (ACS). The International Agency for Research on Cancer projects that in 2030, 21.7 million people will be diagnosed with cancer and 13 million will die of cancer in that year worldwide.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. A cancer patient often receives treatment with a combination of these methods. Surgery and radiation therapy are particularly effective for patients in whom the disease is localized. Physicians generally use systemic drug therapies in situations where the cancer has spread beyond the primary site or cannot otherwise be treated through surgery or radiation. The goal of drug therapy is to kill cancer cells or to damage cellular components required for the rapid growth and survival of cancer cells. In many cases, drug therapy entails the administration of several different drugs in combination. Over the past several decades, drug therapy has evolved from non-specific drugs that kill both healthy and cancerous cells, to drugs that target specific molecular pathways to preferentially kill cancer cells. While heightened vigilance, new diagnostic tests, combination regimens and targeted therapies have resulted in improvements in overall survival for some cancer patients, we believe that there is still a necessity for continued innovation in the treatment of cancer.

Our genomic DNA is continuously subject to damage due to external sources, such as chemicals, radiation and viruses, or internal sources, such as reactive oxygen species generated during cellular metabolism or the process of DNA replication itself. Our cells have developed a highly coordinated array of mechanisms to monitor and detect DNA damage, pause the cell cycle, and resolve DNA damage in order to maintain genomic integrity, that are collectively known as the DNA Damage Response (DDR) network.

While the DDR network is instrumental in maintaining genomic integrity in normal cells, mutations within the network occur frequently in certain cancers resulting in genomic instability, an established hallmark of cancer and enabler of mutagenesis. The genomic instability and mutational capacity of tumors provides them with a selective advantage over normal cells by enabling continual proliferation and survival, as well as by engendering adaptive mechanisms for developing resistance to chemotherapy and other standards-of-care. Tumor cells accommodate genomic instability despite the genetic mutation of certain DDR and cell cycle genes through an enhanced dependency on the remaining components of the DDR network.

In contrast, non-transformed normal cells have redundant cell cycle checkpoints and multiple complementary DNA repair pathways, which should render them less sensitive to DDR targeting agents. This strategy has been likened to striking at an “Achilles’ heel” of cancer, and therapeutic strategies increasingly are focusing on targeting the DDR network to exploit this intrinsic weakness of tumors.

Research into the DDR network has already contributed to the discovery of new treatments for cancer patients. Poly ADP-Ribose Polymerase inhibitors (PARPi) are the first approved DDR-targeting drugs. These agents demonstrate robust efficacy in patients with underlying defects in homologous recombination repair (HRR), an important DNA repair pathway within the DDR network.

Notwithstanding this success, the DDR network represents fertile ground for the development of new cancer therapies. While PARP inhibitors represent a major advance in the treatment of cancers with HRR deficiencies, other DDR targets with distinct biological functions are likely to provide broad benefit to patients whose tumors

harbor distinct DDR network alterations. Among these emerging targets are Chk1 and Cdc7, where recent clinical and preclinical research suggest significant therapeutic potential through modulation of these proteins in hyperproliferating tumors with DDR alterations and genomic instability. Our DDR program is oriented to expanding beyond the scope of PARP inhibitors by striking at targets that control DNA replication, cell cycle progression and unique aspects of the DDR network.

Chk1 – A Central Regulator of the 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.

Checkpoint kinase 1 (Chk1) is a serine-threonine kinase and master regulator of cell cycle progression and the DDR replication stress response. 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.

Functional alterations in genes such as *CCNE1, MYC, RAS, ATM, BRCA1, BRCA2,* and *TP53*, which are prevalent in certain cancer cells, have been demonstrated to significantly increase RS. In such cancer cells, high levels of intrinsic RS result in near threshold levels of genomic instability. Consistent with this observation, inhibition of Chk1 has been shown to be synthetically lethal to cancer cells harboring these genomic alterations.

The standard chemotherapeutic drug gemcitabine profoundly depletes DNA replication building blocks, thereby functioning as a strong extrinsic inducer of replication stress, even at subtherapeutic concentrations. This provides a unique opportunity to potentially treat tumors harboring varying degrees of intrinsic replication stress with this novel combination.

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

Overview

SRA737 is a potent, highly selective, orally bioavailable small molecule inhibitor of Chk1 being 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. In May 2017, we received clearance to enhance these studies by incorporating the prospective enrollment of patients with genetically-defined tumors.

SRA737-01 Phase 1/2 Monotherapy Trial

This clinical study is evaluating SRA737 monotherapy in subjects with genetically-defined tumors that harbor genomic alterations linked to increased replication stress, and therefore hypothesized to be more sensitive to Chk1 inhibition. The multicenter, open-label Phase 1/2 trial consists of two phases, a Dose Escalation Phase 1 and a Cohort Expansion Phase 2.

During the first quarter of 2018, we provided an update on the SRA737 development program. For the SRA737-01 Phase 1/2 Monotherapy trial, we reported that the Dose Escalation Phase 1 portion of the study was in the final stages of optimizing the SRA737 dose regimen and that the Cohort Expansion Phase 2 portion of the study was ongoing, enrolling genetically-defined patients across five specific indications.

During the second quarter of 2018, we further refined our monotherapy study to focus on high grade serous ovarian cancer (HGSOC), supported by emerging data in the field that provides clinical validation for Chk1 inhibition in this indication. Accordingly, we prioritized the enrollment of genetically defined HGSOC patients into this trial, while continuing to enroll patients into the trial's other indications. We anticipate preliminary data from our monotherapy trial will be reported in the first half of 2019.

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 clinical study consists of three segments:

- A Standard-Dose Triplet Combo Dose Escalation Phase 1. This phase evaluated a triplet combination of SRA737 with standard-dose gemcitabine and cisplatin in subjects with solid tumors.
- A Low-Dose Gemcitabine Combo Dose Escalation Phase 1, where cohorts of 3 to 6 subjects are being given escalating doses of SRA737 on an intermittent schedule in addition to low dose gemcitabine until the combination maximum tolerated dose (MTD) is reached.
- A Low-Dose Gemcitabine Combo Cohort Expansion Phase 2, exploring the preliminary efficacy of SRA737 plus low-dose gemcitabine in prospectively enrolled genetically-defined subjects with tumors that harbor genomic alterations hypothesized to confer sensitivity to Chk1 inhibition via synthetic lethality.

During the first quarter of 2018, we provided an update on this trial, reporting that:

- the Standard-Dose Triplet Combo Dose Escalation Phase 1 was complete,
- the Low-Dose Gemcitabine Combo Dose Escalation Phase 1 had made significant progress,
- the Low-Dose Gemcitabine Combo Cohort Expansion Phase 2 was anticipated to commence in the second quarter of 2018 with targeted enrollment of genetically-selected patients across four indications.

During the second quarter of 2018, we modified this study to add and prioritize enrollment for a cohort of genetically defined HGSOC patients, replacing an originally proposed cohort of urothelial cancer patients.

Preliminary data from this trial is anticipated to be reported in the first half of 2019.

SRA737 PARPi Combination Program Initiation and Supply Agreement

In February 2018, we announced an agreement with Janssen where they will supply the PARP inhibitor niraparib, facilitating the initiation of a PARPi combination trial with SRA737 for the treatment of prostate cancer.

Preclinical studies performed by ourselves and others have demonstrated synergy between PARP inhibitors and inhibitors of the Chk1 pathway, including SRA737, in contexts where PARP inhibitors have minimal activity, such as HRR proficient and PARP inhibitor resistant cancer cell lines. PARP inhibitors impede the repair of single-strand DNA breaks, resulting in stalled DNA replication forks and the generation of double strand breaks that make the cell highly reliant on HRR, which is regulated by Chk1. The combined inhibition of both pathways is the basis for our drug combination strategy of SRA737 with niraparib.

The open-label, multicenter Phase 1b/2 dose-ranging study we have prepared to conduct will assess the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of SRA737 in combination with niraparib in patients with metastatic castration-resistant prostate cancer. Janssen will provide us with niraparib, while we will conduct and control the study. We are currently evaluating the optimal timing to commence this trial within the context of our recently expanded portfolio.

SRA737 Potential Combination with Immuno-Oncology Therapeutics

Emerging preclinical and clinical data demonstrate that dual targeting of the DDR network (via certain genetic mutational backgrounds or small molecule inhibitors) in conjunction with immuno-oncology agents can result in synergistic efficacy. We have been conducting preclinical research evaluating SRA737 in combination with immuno-oncology agents in order to assess anticipated synergies between these two drug classes. During the fourth quarter of 2018, we reported preclinical data demonstrating that SRA737 synergizes with immune checkpoint blockade in small cell lung cancer (SCLC) models in a poster presented at the American Association for Cancer Research Conference on Tumor Immunology and Immunotherapy in Miami Beach, Florida.

Additional SRA737 Trials and Development Activities

In order to obtain regulatory approval and potentially commercialize SRA737, we will need to complete the clinical trials described above and then conduct registration-oriented Phase 2 and possibly Phase 3 clinical trials in well-defined, tissue-specific, or possibly genetically-specific, patient populations in order to thoroughly and robustly evaluate the safety and efficacy of SRA737.

We anticipate including U.S. clinical trial sites in the subsequent development of SRA737 and, as appropriate, we intend to submit an IND to the FDA.

If the efficacy data obtained in some or all of the subsequent Phase 2 clinical trials are highly compelling, we plan to discuss accelerated registration paths and other regulatory designations with regulatory agencies. In order to obtain marketing approval to commercialize SRA737, a New Drug Application (NDA) must be submitted to, and approved by, the FDA in the United States, and a marketing authorization application must be submitted to and approved by the European Medicines Agency (EMA). Moreover, when a diagnostic device, such as a device used to identify subsets of patients with a genetic alteration who may derive meaningful benefit from a product, is essential to the safe and effective use of a therapeutic product, the FDA and other regulatory authorities generally require that the companion diagnostic be approved before or concurrent with approval of the therapeutic product and before the therapeutic product can be commercialized. Commensurate with global regulatory submissions, we will need to validate processes at large scale manufacturing facilities in advance of pre-approval inspections, marketing authorizations and product launch.

SRA141, a Highly Selective, Orally Available Cdc7 Inhibitor

Cdc7 is a serine-threonine kinase which acts as an essential regulator of both DNA replication and the DDR network. Over-expression of Cdc7 and its partner proteins is correlated with unfavorable clinical outcomes and poor survival in a broad range of solid tumors and hematological malignancies. In preclinical studies, inhibition of Cdc7 has been shown to cause cancer cell death in a p53-independent manner, and to induce tumor stasis or regression in a variety of in vivo cancer models.

SRA141 is a highly selective, orally available small molecule inhibitor of Cdc7. SRA141 was licensed to us in May 2016 from Carna Biosciences, Inc., Kobe, Japan (Carna).

Status of Our Preclinical Development Program for SRA141

We are pursuing a robust program of preclinical studies with SRA141 to evaluate tumor responses and dosing regimens across a variety of indications in order to inform our clinical development plans and possible patient

selection strategies. Preclinical data and published literature suggest a variety of solid tumors and hematological malignancies with potential for response to Cdc7 inhibitors. A genetically defined patient selection strategy focusing on drivers of Cdc7 inhibitor sensitivity may help facilitate clinical trial execution. During the third quarter of 2018, we successfully completed the IND process with the FDA for SRA141 and we have prepared for a Phase 1/2 trial with this drug candidate in patients with advanced colorectal cancer. We are currently evaluating the optimal timing to commence this trial within the context of our recently expanded portfolio.

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 inhibitor of the JAKs and Activin A receptor, 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. Milestone payments of up to an aggregate of $195.0 million may become payable to Gilead upon the achievement of certain development, regulatory and commercial milestones events, including a milestone payment of $5.0 million upon the dosing of the first patient in a registrational clinical trial. In addition, we are required to pay Gilead mid-teen to high twenty percent tiered royalties based upon net sales.

License Agreements

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 Chk1, a promising therapeutic target to treat cancer. 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. Additional milestone payments of up to an aggregate of $319.5 million may become payable to CPF upon the achievement of certain developmental, regulatory and commercial milestones. 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. License 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. We will be required to pay Carna milestone payments of up to an aggregate of $270.0 million upon achievement of certain developmental, regulatory and commercial milestone events, including a milestone payment of $4.0 million upon dosing of the first patient in the first Phase 1 clinical trial for SRA 141. In addition, for product candidates defined under the license agreement, we are required to pay Carna on a product-by-product and country-by-country basis, tiered single-digit royalties on net sales.

The license agreement will expire on the date of expiration of our obligation to pay royalties to Carna. Following the expiration of the license agreement, we will obtain a fully paid-up, non-exclusive license to develop and commercialize products relating to the licensed intellectual property worldwide for any use. Carna may terminate the license agreement if we materially breach the agreement, subject to certain cure provisions. The license agreement may also be terminated at any time by us upon 30 days' prior written notice to Carna.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for momelotinib, SRA737, SRA141 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, 2018, these rights included three issued U.S. patents comprising claims directed to compositions 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. As of December 31, 2018, these rights also include 53 issued foreign patents and one pending foreign patent application in 49 jurisdictions, including Australia, Canada, China, 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 these pending foreign patent applications, are expected to expire in 2028, absent any adjustments or extension. As of December 31, 2018, these rights also included two issued U.S. utility patents and one pending reissue application comprising claims directed to different polymorphs and salt forms of momelotinib, and methods of their use for the treatment of myelofibrotic indications. These patents will expire in 2035, absent any adjustments or extension. Note 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 2040. As of December 31, 2018, these rights also include three issued foreign patents and 14 pending foreign patent applications in 15 jurisdictions, including Australia, Brazil, Canada, China, Europe, Hong-Kong, India, Israel, New Zealand, Mexico, Japan, Korea, Singapore and Taiwan comprising claims directed to different polymorphs 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 adjustments or extension. As of December 31, 2018, these rights also included four issued foreign patents and one pending foreign patent applications in five jurisdictions, including Australia, Canada, New Zealand, Singapore and South America comprising claims directed to methods of using momelotinib for the treatment of anemia. As of December 31, 2018, these rights also included one pending U.S. utility application comprising claims directed to methods of using momelotinib for the treatment of ACVR1-mediated diseases. Any patents issuing from these utility applications are expected to expire 2037, absent any adjustments or extensions. Additionally, as of December 31, 2018, these rights also include one pending Patent Cooperation Treaty application and one pending foreign application in Taiwan comprising claims directed to methods of using momelotinib for the treatment of AVCR1-mediated diseases. Any patents issuing from this application are expected to expire after 2038, absent any adjustments or extensions. We have filed and will continue to file patent application directed to the composition of matter and methods of use related to various aspects of momelotinib as they develop.

We have exclusively licensed CPF's rights to patents owned by Cancer Research Technology (CRT), 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, 2018, these rights included one issued U.S. patent and two pending U.S. patent applications 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. Any patents issuing from this U.S. utility application are expected to expire in 2033, absent any adjustments or extensions. As of December 31, 2018, these rights also included 25 issued foreign patents and 12 pending foreign patent applications in 16 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 adjustments or extensions. Additionally, as of December 31, 2018, these rights also include three pending Patent Cooperation Treaty applications comprising claims directed to biomarkers and patient selection when using SRA737 to treat cancer indications and methods of using SRA737 in combination with PARPi and WEE1 inhibitor for inhibiting tumor reduction. 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.

We have exclusively licensed from Carna patent applications directed to the SRA141 composition of matter, alone or in combination with an M-phase inhibitor and methods of use for the combination. As of December 31, 2018, we were the exclusive licensee of two U.S. patents, expiring in 2032, absent any adjustments or extensions, and one pending U.S. patent application, both comprising composition of matter claims directed to SRA141. Any patents issuing from this U.S. utility application are expected to expire in 2032, absent any adjustments or extensions. As of December 31, 2018, this exclusively-licensed portfolio included 21 issued foreign patents and seven pending foreign patent applications in 22 foreign jurisdictions, including Australia, Canada, Europe, India, Japan, Korea and Mexico and others comprising composition of matter claims directed to SRA141. The foreign patents, and any patents issuing from these pending foreign patent applications, are expected to expire in 2032, absent any adjustments or extensions. Additionally, as of December 31, 2018, this portfolio also included one issued U.S. utility patent. The issued U.S. utility will expire in 2035 including any adjustment but absent any extensions. Additionally, as of December 31, 2018, this portfolio also includes two pending foreign patent applications in Europe, and Japan comprising composition of matter claims directed to a combination of SRA141 and an M-phase inhibitor and methods of use for the combination for treating cancer. Any patents issuing from these pending applications will expire in 2035, absent any adjustments or extensions. 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 SRA141 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 or 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, SRA737, SRA141 or any of our product candidates 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. The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third-party payors. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we 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 is currently one approved drug for the treatment of myelofibrosis that specifically targets JAK inhibition, ruxolitinib, marketed by Incyte Corporation as Jakafi® in the United States and by Novartis as Jakavi in rest of the world. In addition, there are a number of JAK inhibitor competitors in clinical development, at a similar state of development or more advanced than us. To our knowledge, Celgene Corporation is developing fedratinib, for which an NDA has been submitted with the FDA, and CTI Biopharma Corporation is developing pacritinib, which is currently in a Phase 2 dose finding study in the United States. However, to our knowledge, there are no approved drugs that target both JAK and ACVR1 inhibition on the market, nor in development. Other competitors in the myelofibrosis market include Acceleron, which is developing luspatercept in a Phase 2 clinical trial for myelofibrosis in conjunction with Celgene, and several additional companies in the early stages of development. 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, which we believe is unique to the JAK inhibitor class of agents, the market for momelotinib is competitive, and physicians and other prescribers may not recommend or prescribe momelotinib over other competing products.

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. To our knowledge, Eli Lilly and Company is developing prexasertib, an intravenous Chk1/Chk2 inhibitor in several clinical settings, the most advanced of which are in Phase 2 clinical trials. 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.

Additionally, to our knowledge, there are no approved drugs that specifically target Cdc7. To our knowledge, Takeda Pharmaceutical Company is developing an oral Cdc7 inhibitor that is currently in a Phase 2 clinical trial for metastatic pancreatic and colorectal cancers and Eli Lilly and Company has a Cdc7 inhibitor program that is currently in a Phase 1 clinical trial being conducted by Cancer Research UK. Other companies may be

conducting preclinical studies of Cdc7 inhibitors as well. If SRA141 is approved, it will compete with existing therapies 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 programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient 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 seeking to encourage the use of generic drugs.

Manufacturing

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of momelotinib, SRA737, SRA141 and other potential product candidates for preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive 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, SRA737 and SRA141 on an as-needed basis.

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 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, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

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 drug 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.

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. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients 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 (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 may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into patients, the drug is typically tested to assess endpoints such as metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the activity of the drug for a particular tissue-specific, or possibly genetically-specific patient population, dosage tolerance and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to confirm clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In most cases FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 or Phase 2 trial with other confirmatory evidence may be sufficient in certain instances, such as where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. The cost of preparing and submitting an NDA is substantial.

The submission of most NDAs is additionally subject to a substantial application user fee, and the applicant under an approved NDA is also subject to an annual program fee for each prescription drug product, which replaced the annual product and establishment fees. These fees are typically increased annually.

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 an in-depth review. 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 substantial evidence that the drug is safe and effective in the indication studied.

After FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. 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.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require 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. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

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

FDA Regulation of Companion Diagnostics

If an in vitro diagnostic is essential to the safe and effective use of a therapeutic product, then the FDA generally will require approval or clearance of the diagnostic at the same time that FDA approves the therapeutic product. The FDA has generally required in vitro companion diagnostics intended to select the patients who will respond to cancer treatment to obtain a pre-market approval, or PMA, for that diagnostic simultaneously with approval of the drug. The review of these in vitro companion diagnostics in conjunction with the review of our cancer treatments involves coordination of review by the FDA's Center for Drug Evaluation and Research and by the FDA's Center for Devices and Radiological Health.

The PMA process, including the gathering of clinical and nonclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to a substantial application fee, which is typically increased annually. In addition, PMAs for devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results when the same sample is tested multiple times by multiple users at multiple laboratories. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay or prevent approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

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.

Fast Track Designation and Accelerated Approval

FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment, and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the drug candidate. FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request. Under the fast track program and FDA's accelerated approval regulations, FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon 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.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by FDA.

In addition to other benefits such as the ability to use surrogate endpoints and engage in more frequent interactions with FDA, FDA may initiate review of sections of a fast track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the fast track designation may be withdrawn by FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for

direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling.

AE reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality-control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

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.

Exclusivity

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.

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent 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 up to a maximum of five years). The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years. For patents that might expire during the application 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.

Anti-Kickback, False Claims Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain general business and marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes, false claims statutes and other statutes pertaining to healthcare fraud and abuse. 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 to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. 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.

Federal false claims laws, including the federal civil False Claims Act, prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs where the federal government reimburses, such as Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and

Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, PPACA amended the federal Anti-Kickback Statute such that a violation of that statute can serve as a basis for liability under the federal False Claims Act. The majority of states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror or payor knows or should know is likely to influence the beneficiary to order a receive a reimbursable item or service from a particular supplier, and the additional federal criminal statutes created by the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or obtain by means of false or fraudulent pretenses, representations or promises any money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services.

Other Federal and State Regulatory Requirements

Pursuant to PPACA, the Centers for Medicare & Medicaid Services (CMS) issued a final rule that requires manufacturers of prescription drugs to collect and report information on certain payments or transfers of value to physicians and teaching hospitals, as well as investment interests held by physicians and their immediate family members. The reports must be submitted on an annual basis and the reported data are posted in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties. Effective January 1, 2022, reporting on transfers of value to physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives will also be required.

In addition, several states now require prescription drug companies to report certain expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. Some states require the reporting of certain pricing information, including information pertaining to and justifying price increases, or prohibit prescription drug price gouging. In addition, states such as California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Additional jurisdictions, such as the City of Chicago and the District of Columbia, require pharmaceutical sales representatives to be licensed and meet continuing education requirements. Several additional states are considering similar proposals. Compliance with these laws is difficult and time-consuming, and companies that do not comply with these state laws face civil penalties.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act (HITECH), and their respective implementing regulations, including the Final Omnibus Rule published on January 25, 2013, imposes specified requirements on certain types of people and entities relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to "business associates," defined as independent contractors 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. In addition, many state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect.

If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, contractual damages, reputation harm, and diminished profits or future earnings, any of which could adversely affect our ability to operate our business and our financial results.

Also, the U.S. Foreign Corrupt Practices Act and similar worldwide anti-bribery laws generally prohibit companies and their intermediaries from making improper payments to foreign officials for the purpose of obtaining or retaining business. We cannot assure you that our internal control policies and procedures will protect us from reckless or negligent acts committed by our employees, future distributors, partners, collaborators or agents. Violations of these laws, or allegations of such violations, could result in fines, penalties or prosecution and have a negative impact on our business, results of operations and reputation.

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 depend significantly on the availability of third-party coverage and reimbursement. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. Although we currently believe that third-party payors will provide coverage and reimbursement for our product candidates, if approved, these third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We may need to conduct expensive clinical studies to demonstrate the comparative cost-effectiveness of our products. The product candidates that we develop may not be considered cost-effective. It is time-consuming and expensive for us to seek coverage and reimbursement from third-party payors. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

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.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

By way of example, in March 2010, the PPACA was signed into law, which intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on

the health industry and impose additional health policy reforms. Among the provisions of the PPACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures, or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D. (The Bipartisan Budget Act of 2018 increased the manufacturers subsidy under this program from 50% to 70% beginning in 2019);
- extension of a manufacturer's Medicaid rebate liability to cover drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and Congressional challenges and amendments to certain aspects of the PPACA, and we expect there will be additional challenges and amendments to the PPACA in the future, including the potential repeal of all or part of 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 2025 unless additional Congressional action is taken. 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.

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 lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded 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 drugs.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to develop or sell any

products outside of the United States. 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.

Approval in the European Union

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. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union Member States. We would be subject to the centralized process. Under the centralized procedure, pharmaceutical companies submit a single marketing authorization application to the EMA. Once granted by the European Commission, a centralized marketing authorization is valid in all European Union Member States, as well as the European Economic Area (EEA) countries Iceland, Liechtenstein and Norway. By law, a company can only start to market a medicine 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 Medicines Directive 2001/83/EC, as amended. This directive is binding on all Member States together with ancillary legislation governing research.

Clinical Trial Authorization

Clinical trials 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 entering specified relevant information in the European trial database, EudraCT. 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 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 Clinical Trials Regulation goes into effect in 2019. 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.

Procedural Routes for Marketing Authorization

The European system for authorization of medicinal products for human use offers several routes: the centralized procedure, the decentralized procedure, and the mutual recognition procedure. 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 used when a medicinal product has already received a marketing authorization in one Member State and is compulsory to be marketed in a Member State other than that in which they were 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.

Standard for Approval of a Marketing Authorization

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 European Union-wide 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.

When the United Kingdom leaves the European Union, the United Kingdom will no longer automatically comply with the standards of clinical efficacy, safety and chemistry control, and manufacture as applied by the European Medicines Directive. Applications submitted for marketing authorization under the centralized EMA procedure will no longer be automatically validated for authorization in the United Kingdom and the benefit-risk assessments conducted by the United Kingdom may not be consistent with the EMA conclusions.

Other Regulatory Issues

An exemption to the rule requiring marketing authorization permits Member States of the European Union to make a product available for compassionate use to patients with a chronically or seriously debilitating disease or

whose disease is considered life threatening, such as cancer, 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 Directive. This lays down the principles and guidelines of 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 is responsible for coordinating the Member States' ongoing evaluation of benefit risk, supervision and pharmacovigilance of medicinal products.

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., MHRA) 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 European Union 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. The United Kingdom's exit from the European Union (Brexit) will disrupt the operation of pre- and post-authorization clinical trial infrastructure.

The United Kingdom enacted the Data Protection Act 2018 to directly enforce the General Data Protection Regulation (GDPR). The government of the United Kingdom has also stated that when the United Kingdom leaves the European Union it will still abide by the provisions of the GDPR. However, in the event of a "no deal" Brexit it is uncertain whether this commitment will still be met. In the case of a "no deal" Brexit, it is also uncertain whether clinical trial data and pharmacovigilance adverse event data originating from the United Kingdom will be compliant with European Union privacy legislation and whether the data will be incorporated

by EMA in the assessment of the ongoing benefit-risk profile and hence continued support of European Union marketing authorizations.

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.

Employees

As of December 31, 2018, we had 79 employees, of which 17 had M.D. or Ph.D. degrees and 53 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.

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 2150 – 885 West Georgia Street, Vancouver, British Columbia, Canada V6C 3E8, and our telephone number is (604) 558-6536. 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.

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 $53.3 million, $42.0 and $47.9 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of $677.4 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 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 our product candidates, momelotinib, SRA737 and SRA141, 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 and continue to operate as a public company.

Even if we succeed in commercializing momelotinib, SRA737, SRA141 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. 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 our product candidates, momelotinib, SRA737 and SRA141. If we are unable to successfully develop, obtain regulatory approval for and commercialize momelotinib, SRA737 and SRA141, or experience significant delays in doing so, our business will be materially harmed.

Our business and future success depends on our ability to successfully develop, obtain regulatory approval for and commercialize our product candidates, momelotinib, a Phase 3 product candidate, and SRA737 and SRA141, which are both at earlier stages of development. We recently invested financial resources to acquire momelotinib from Gilead. While momelotinib is a late-stage product candidate for which previous Phase 3 clinical trial data suggest the potential to provide promising safety and efficacy in patients who have an inadequate response to, progression on or are intolerant of ruxolitinib, it will likely require additional clinical testing, including at least one additional adequate and well-controlled Phase 3 clinical trial, before we can seek regulatory approval and begin commercialization, if it all. We have also invested effort and financial resources in the research and development of SRA737 and SRA141, both of which will require significant additional preclinical and clinical testing before we can seek regulatory approval and potentially generate any commercial sales. Before we can generate any revenue from sales of momelotinib, SRA737, SRA141, or any other product candidate, we must complete additional development activities, submit INDs or foreign equivalents, as well as marketing applications such as New Drug Applications (NDAs) or foreign equivalents, for regulatory review and approval in multiple jurisdictions, make substantial investments, obtain access to sufficient commercial manufacturing capacity and engage in significant marketing and commercial access efforts.

We cannot commercialize product candidates in the United States without first obtaining regulatory approval for the product candidates from the FDA. Similarly, we cannot commercialize product candidates 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. Even if momelotinib, SRA737, SRA141 or another product candidate were to be approved by the FDA or foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified 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, SRA737 or SRA141 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 development, marketing or commercialization of momelotinib, SRA737, SRA141 or any other product candidate that we may acquire or develop in the future. If competitive products developed by third parties show significant benefit in the cancer indications in which we are developing our product candidates, any planned supportive or primary registration trials may be delayed, altered, terminated or not initiated and our other product candidates may never receive regulatory approval. Our clinical development programs for our 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 any of our product candidates, we will still need to develop sales, marketing and commercialization infrastructure, or collaborate with a third party for the commercialization of our 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 any of our product candidates, we may not be able to generate sufficient revenues to continue our business.

If we are unable to successfully develop and commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We will be required to demonstrate, to the satisfaction of regulatory authorities, through clinical trials that our product candidates are safe and effective for use in their target indications before we can obtain regulatory approval for their marketing and commercial sale.

We recently acquired from Gilead our lead product candidate momelotinib, a potent, selective and orally-bioavailable JAK1, JAK2 and ACVR1 inhibitor. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis. We are currently advancing discussions with regulators to determine the approval path forward for momelotinib and anticipate reporting next steps in the first half of 2019. We cannot guarantee that the regulators will agree with us regarding the data we believe will be sufficient to support submission and approval of a marketing application for momelotinib in hematology. To the extent we cannot secure agreement from the FDA or the EMA on such data, we may not proceed with the development of momelotinib, or there may be an increased risk of delay in obtaining approval or obtaining approval at all.

Pursuant to Clinical Trial Authorizations (CTAs) granted by the MHRA in the United Kingdom for SRA737, two Phase 1 trials were initiated in the United Kingdom which were transferred to us in January 2017, both of which have been amended to Phase 1/2 trials. We plan to continue our SRA737 development efforts by continuing these clinical trials, including through potential expansion into other countries, and potentially conducting additional preclinical and clinical studies to further our understanding of SRA737.

SRA141 has never been evaluated in a clinical trial. We recently successfully completed the IND filing process with the FDA for SRA141 and we have prepared for a Phase 1/2 trial with this product candidate in patients with advanced colorectal cancer.

The success of our product candidates and any future product candidates that we may acquire or develop will depend on many factors, including, but not limited to, the following:

- successful completion of preclinical studies;
- successful translation of preclinical results in human clinical trials;

- successful enrollment in, and completion of, clinical trials that produce data which adequately demonstrate the product candidate's benefit and risk profile;
- successful transfer of existing trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishment of clinical trial material and commercial manufacturing capabilities, or arrangements with third-party manufacturers and suppliers on commercially reasonable terms;
- effective patent and trade secret protection and regulatory exclusivity;
- establishment of a commercial sales team, if and when approved, whether alone or in collaboration with others;
- acceptance, if and when approved, by patients, the medical community and third-party payors;
- coverage and adequate reimbursement by third-party payors, including government payors;
- successful competition with other therapies;
- continued acceptable safety profile following approval;
- enforcement and protection of intellectual property rights and claims;
- achievement of desirable medicinal properties for the intended indications; and
- effective growth of an organization of scientists and businesspeople who can develop and commercialize our products, if approved, and technology.

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

If further preclinical development or clinical trials of momelotinib, SRA737, SRA141 or 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 momelotinib, SRA737, SRA141 or future product candidates.

Before obtaining marketing approval from regulatory authorities, including the FDA, for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our 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. 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, therefore, guarantee that we will be successful in obtaining the required efficacy and safety profile from momelotinib, SRA737 or SRA141. A failure of one or more preclinical studies or clinical trials can occur at any stage of testing.

We recently acquired from Gilead our lead product candidate momelotinib, a potent, selective and orally-bioavailable JAK1, JAK2 and ACVR1 inhibitor. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis, SIMPLIFY-1 and SIMPLIFY-2. 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; 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 total symptom score. 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. Based on post hoc analyses of the data for these trials, we believe the trials showed promising substantive spleen and constitutional symptom control. In addition, momelotinib has the potential for a differentiated therapeutic profile encompassing anemia-related benefits. We are currently advancing discussions with regulators to determine the approval path forward for momelotinib and anticipate reporting next steps in the first half of 2019. While we believe the safety and efficacy profile of momelotinib in patients who have an inadequate response to, progress on or are intolerant of ruxolitinib appears promising based on the prior Phase 3 trial results, the likely Phase 3 trial we plan to commence in those patients may not be successful. For example, in the SIMPLIFY-1 Phase 3 trial conducted by Gilead in ruxolitinib-naive patients, the key secondary endpoint of total symptom score, which we might choose to use as the primary endpoint in a potential future Phase 3 trial, was not met. We may also fail to observe meaningful anemia benefits in a potential future Phase 3 trial, which could reduce the potential future value of momelotinib as we believe an anemia benefit could potentially provide a competitive advantage over existing therapies.

We are currently conducting preclinical assessments and two Phase 1/2 clinical trials of SRA737, which we believe will further inform our clinical development plans and patient selection strategies. Both of the current clinical studies for SRA737 are being conducted in the United Kingdom, with one of the clinical studies also being conducted in Spain. We believe we have completed all necessary preclinical activities to support a potential future IND submission for SRA737 to the FDA. However, we have not yet discussed our plans for any IND submission with the FDA, and if pursued, we may receive feedback from the FDA that delays the submission or clearance of any IND. We have no assurance that clinical trials of SRA737 will demonstrate safety and efficacy or produce positive results sufficient to justify further development and commercialization.

SRA141 has never been evaluated in a clinical trial. We recently successfully completed the IND filing process with the FDA for SRA141 and we have prepared for a Phase 1/2 trial with this product candidate in patients with advanced colorectal cancer.

Moreover, 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 our product candidates 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 our product candidates 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 our product candidates.

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

- undesirable side effects or other unexpected characteristics of our 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;

- 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;
- 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, slower than expected enrollment, greater than expected competition for patients 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;
- 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;
- 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 our product candidates.

If we are required to conduct additional preclinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete preclinical studies and clinical trials of our 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 an IND in the United States, or additional CTAs or equivalents in other 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 our product candidates, any of which may harm our business and results of operations.

Our preclinical and clinical development for SRA737 is focused on the development of targeted therapeutics for genetically-defined cancers, which is a rapidly evolving area of science, and the approach we are taking to develop drugs may not lead to marketable products. Genetically-based patient selection strategies might also be employed in our SRA141 development programs.

The discovery and development of targeted therapeutics for genetically-defined cancers, including patients whose tumors harbor the applicable genetic alterations that we believe contribute to cancer, is an emerging field, and the scientific discoveries that form the basis for our efforts to develop genetically-selected product candidates are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. Additionally, we may consider approaches such as a basket study in which enrollment is focused on a compilation of different tumor types that share a similar genetic signature. We cannot be sure that regulatory authorities, including the FDA and the EMA, will accept our trial designs or that we will be able to obtain approval for our product candidates.

We are currently developing our SRA737 product candidate for certain genetically-defined subpopulations of the general treated cancer population, and we are enrolling selected patients into our Monotherapy and Low-Dose Gemcitabine combination studies of SRA737, based on genetic alterations in their tumors or other factors such as histology. In order to obtain marketing approval for SRA737 in the treatment of genetically-defined tumors and cancers, we will need to, among other things, demonstrate to the satisfaction of regulatory authorities that those genetic alterations have predictive clinical utility. We have applied our genetic selection criteria to patients in our Monotherapy and our Low-Dose Gemcitabine combination clinical trials, and our approach may change based on our evolving knowledge of the field and on data obtained in our preclinical research and ongoing clinical trials. The goal of our genetic screening is to enroll patients who we believe have the highest probability of responding to the product candidate in order to show compelling evidence of clinical efficacy. Successful identification of patients is dependent on several factors, including, potentially, achieving certainty as to how specific genetic alterations respond to our product candidates and developing companion diagnostics to identify such genetic alterations as appropriate. For example, although we believe, based on scientific and medical literature, and preclinical research, that we have identified certain types and combinations of genetic alterations hypothesized to confer sensitivity to Chk1 inhibition that may be predictive of response to SRA737, we have only recently begun to assess activity of SRA737 in humans and have not discussed the validity of our genetic selection criteria with regulatory authorities, including MHRA, FDA or EMA.

In addition, genetically-based patient selection strategies may also be employed in our SRA141 development programs. If so, the development of SRA141 may also be subject to the risks and uncertainties discussed above.

Our genetic selection strategy for SRA737 uses a novel algorithm and is not yet validated as predictive of clinical utility. In addition, patient populations in our trials may not be large enough to allow us to successfully determine efficacy of our product candidates, commercialize our product candidates, and achieve profitability. Regulatory authorities may require we conduct additional clinical trials specific to given tumor types.

In order to obtain marketing approval for SRA737 in patients with genetic alterations hypothesized to confer sensitivity to Chk1 inhibition we will need to, among other things, demonstrate to the satisfaction of regulatory authorities that those genetic alterations have predictive clinical utility. It may be difficult for us to demonstrate the predictive clinical utility of our genetic selection criteria, which select for patients that have various combinations of genetic alterations across multiple gene panels. Although regulatory authorities, including FDA,

have approved therapies for use in conjunction with companion diagnostic tests that aid in selecting patients for treatment based on genetic markers, to our knowledge neither the FDA nor the EMA has granted marketing approval for a therapy that requires the use of a companion diagnostic that uses broad gene panel testing to select for patients with various combinations of genetic alterations. The scientific evidence to support the feasibility of developing product candidates based on our selection criteria is both preliminary and limited. We have not discussed the validity of our genetic selection criteria with regulatory authorities, and we cannot be sure that regulatory authorities, including the FDA and EMA, will accept our genetic selection criteria.

Furthermore, we cannot be certain that the patient populations in our trials will be large enough to allow us to successfully determine efficacy of our product candidates, commercialize our product candidates, and achieve profitability. If we are unable to enroll sufficient numbers of patients whose tumors harbor the applicable genetic alterations, or if our product fails to work as we expect, or if we are unable to demonstrate the predictive clinical utility of our genetic selection criteria, our ability to assess and demonstrate the therapeutic effect of our product candidates could be compromised, resulting in longer development times, larger trials, and a greater likelihood of not obtaining regulatory approval for our product candidates. In addition, regulatory authorities may require that we study our product candidates in clinical trials specific to given tumor (i.e., tissue) types, which may increase the time and costs required. Even if our product candidates demonstrate efficacy in a particular tumor type, we cannot guarantee that any product candidate will behave similarly in multiple or all tumor types, and we may be required to obtain separate regulatory approvals for each tumor type we intend a product candidate to treat. We do not know if our approach will be successful, and if our approach is unsuccessful, our business will suffer.

Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics for SRA737 and our other product candidates could harm our drug development strategy and operational results.

In any pivotal clinical trials of SRA737 we anticipate the potential requirement to screen and identify patients with specific genetic alterations who may derive meaningful benefit, as we have begun to do in our Monotherapy and Low-Dose Gemcitabine combination studies of SRA737. To achieve this, our product development programs for SRA737 and marketing approvals will be dependent on the development and commercialization of a companion diagnostic by us or by third party collaborators. It is feasible that a companion diagnostic might also be required in our SRA141 and other potential development programs.

Companion diagnostics are developed in conjunction with clinical programs for the associated product and are subject to regulation as medical devices by the FDA and comparable regulatory authorities, and, to date, the FDA has required premarket approval of all companion diagnostics for cancer therapies. Generally, when a companion diagnostic is essential to the safe and effective use of a therapeutic product, the FDA requires that the companion diagnostic be approved before or concurrent with approval of the therapeutic product and before a product can be commercialized. The approval of a companion diagnostic as part of the therapeutic product's labeling limits the use of the therapeutic product to only those patients who express the specific genetic alteration that the companion diagnostic was developed to detect.

If FDA or a comparable regulatory authority requires approval of a companion diagnostic for any of our product candidates, whether before or after the product candidate obtains marketing approval, we, and/or third-party collaborators, may encounter difficulties in developing and obtaining approval for these companion diagnostics. Any delay or failure by us or third-party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval or continued marketing of our related product candidates.

We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process for the companion diagnostic or in transferring that process to commercial partners or negotiating insurance reimbursement plans, all of which may prevent us from completing our clinical trials or commercializing our products on a timely or profitable basis, if at all.

We have acquired or licensed our product candidates from third parties that had already conducted or were in the process of conducting preclinical studies or clinical trials with our product candidates. We may discover that development efforts of third parties, including but not limited to historical studies and trials conducted by third parties, did not comply with all applicable rules and regulations, and we may experience difficulties or delays in assuming responsibility for or completing such ongoing or previously completed clinical development activities. Our acquisition of momelotinib has resulted in us being required to take over responsibility for conducting ongoing momelotinib trials. Further development and commercialization of momelotinib will require significant financial and operational resources from us.

Prior to our acquisition of momelotinib and licensing of SRA737, third parties had been responsible for all development activities for such product candidates, 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 or SRA737. For example, we will need to modify the PIP Gilead agreed to for momelotinib with the European Union's regulatory authorities and conduct the pediatric studies, unless a waiver or deferral is granted, before we can submit a marketing authorization application. Similarly, we will need to submit a pediatric study plan to FDA and conduct the pediatric study, unless a waiver or deferral is granted, prior to submission of an NDA. In addition, a foreign regulatory authority that inspected a SIMPLFY-1 investigational site and CRO concluded that the clinical trial at that site was not conducted in accordance with good GCPs. We do not know what effect, if any, this finding will have on review of any future marketing applications by the FDA or foreign regulatory authorities.

In connection with our acquisition of momelotinib, following a transition period we are assuming the responsibility for all currently 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 Phase 3 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. If we are unable to successfully assume the responsibilities of these trials, if we experience delays in doing so, or if we encounter additional difficulties or delays due to deficiencies in the assumed trials prior to our acquisition of momelotinib, the development of momelotinib may be delayed or suspended. 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.

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.

We have received approval from the MHRA for amendments to the SRA737-01 Monotherapy and the SRA737-02 Low-Dose Gemcitabine combination clinical trial protocols. These amendments are designed to enhance the ongoing clinical trials including by expanding the enrollment of patients we predict may be most likely to benefit from SRA737, based on specific genetic alterations in their tumors. These amendments may provide us with the opportunity to more accurately and widely evaluate SRA737's activity across a number of distinct cancer indications and genetic alterations. If the MHRA, FDA, EMA, 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 momelotinib, SRA737, SRA141, or other product candidates, and our development programs may be adversely affected.

For example, we are currently pursuing a development program for SRA737 that relies upon a seamless trial design, which presents additional risks compared to traditional three-phase development programs. In a seamless design, an early phase trial assesses clinical activity of a product candidate in a broad range of subjects, and the trial is later expanded to include additional cohorts (for example, including cohorts with entry criteria based in part on the characteristics of the subjects in whom clinical activity was observed during the initial period of the trial, such as genetic markers). The protocol may also be amended with regard to the expansion cohorts to focus, for example, on different treatment endpoints, different doses, or other trial parameters. Through this iterative process, the traditionally distinct Phase 1, Phase 2, and Phase 3 trials are combined into one or more adaptive, or combined-phase, trials.

Whereas the traditional three-phase development program provides for communication with regulatory agencies between each phase, and for the development and review of statistical plans for trials in each phase, a seamless design may require more frequent and fluid communication with regulators to vet the iterative protocol amendments, and new statistical plans may be necessary for each expansion cohort. If we are unable to receive timely or complete feedback to our frequent amendments to protocols and statistical plans from regulatory authorities, our development programs may be delayed and/or we may be required to conduct additional clinical trials.

If we fail to obtain additional capital, we may be unable to acquire additional product candidates and complete the development and commercialization of our product candidates.

We expect to spend substantial capital to acquire additional product candidates and advance momelotinib, SRA737 and SRA141 in preclinical and clinical development, seek regulatory approvals for our product candidates, establish a commercial sales force to market and manufacture products, if any, that are approved for commercial sale. We also incur significant additional 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 progress and 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 future product candidates;
- the costs, timing and outcome of regulatory review of momelotinib, SRA737, SRA141 and any future product candidates;
- the costs of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our 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;
- 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 our product candidates, should any of our product candidates receive marketing approval; and

- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

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, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of our product candidates, 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. We have no committed source of additional capital and if we 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 development or commercialization of our product candidates or other research and development initiatives. In particular, unless we are able to obtain additional financing, we may not have sufficient funds to undertake our contemplated trials evaluating SRA737 in combination with a PARP inhibitor, as well as with immuno-oncology therapeutics, or to continue development of SRA141. We could be required to seek collaborators for our product candidates, including SRA737 and SRA141, 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.

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

We may experience difficulties in patient enrollment in our 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;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

Our clinical trials 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, because our product candidates are experimental, 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.

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 the development of our product candidates or any future product candidates we may develop.

We may expend our limited resources to pursue a particular product candidate 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 research and development efforts on certain selected product candidates. As a result, we may advertently or inadvertently forgo or delay pursuit of opportunities with other product candidates 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.

The manufacture of momelotinib, SRA737 and SRA141 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 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.

Currently, SRA737 and SRA141 are manufactured using unoptimized processes by third-party manufacturers, and momelotinib is manufactured using an optimized drug substance process by third-party manufacturers. Although we have secured sufficient quantities of drug substance and drug product to supply our current momelotinib program, starting with the planned potential Phase 3 trial of momelotinib, we will need to obtain additional supplies from third-party manufacturers that we have engaged, or expect to engage. In addition, we may need to develop a pediatric formulation for momelotinib in the future. 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 to become limited or interrupted or fail to be of satisfactory quantity or quality.

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 momelotinib, SRA737 and SRA141, 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 our product candidates receive marketing approval. We have engaged, or expect to engage, third-party manufacturers to obtain materials and consumables necessary for the manufacture of momelotinib, SRA737 and SRA141.

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;
- 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; and
- 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 any product candidates, 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 or clinical studies or 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 our product candidates 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 product candidates 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.

Any performance failure on the part of our existing or future manufacturers or suppliers, or any interruption or poor yield or quality of manufactured or supplied materials, could delay development or marketing approval. 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 our product candidates or the materials for trials relating to 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 our product candidates or related medicines and materials may adversely affect our development timeline, our future profit margins or our ability to commercialize any 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 our product candidates. Undesirable side effects caused by any of 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 our 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; or

- we may be required to change the way the product is administered or conduct additional preclinical studies or clinical trials.

If preliminary data demonstrate that any of our product candidates 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 such product candidate.

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 the product candidate, which in turn could delay or prevent us from generating significant revenues from the sale of the product.

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 our product candidates.

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. For example, the CRO of our current ongoing clinical trials of SRA737 was recently acquired by a large global CRO and there may be interruptions in service during their integration. 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 our product candidates. As a result, our financial results and the commercial prospects for our product candidates 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 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;
- 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; or
- the quality or stability of the product candidates may fall below acceptable standards.

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 of our current or future product candidates, the commercial prospects for that product will be harmed and our ability to generate product revenue from that product may be delayed or eliminated. 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 our product candidates 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 our product candidates, the market may not be receptive to our products.

Even if we obtain regulatory approval for momelotinib or one of our other product candidates, they 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 competitive products;
- safety and efficacy of our products;
- 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
- sequencing of available products.

If our product candidates are approved for commercial sale and fail 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 our product candidates. 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 product candidates, including momelotinib, to treat life-threatening illnesses 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, 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 our product candidates 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 our product candidates, in this patient population is high and could have a negative impact on the safety profile of our product candidate, which could cause significant delays or an inability to successfully commercialize our product candidate and could materially harm our business. In addition, in order to perform the controlled clinical trials required for regulatory approval and successful commercialization of our product candidates, we may also need to restructure or pause any ongoing compassionate use and/or expanded access programs, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

The terms of our Loan and Security Agreement require us to meet certain operating and financial covenants and place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business.

Our Loan and Security Agreement is secured by a lien covering substantially all of our assets, excluding our intellectual property and certain other assets. Subject to the terms of the Loan and Security Agreement, we have the option to prepay all, but not less than all, of the amounts borrowed under the Loan and Security Agreement, subject to certain penalty payments, prior to the August 1, 2022 maturity date, at which time all amounts borrowed will be due and payable.

The Loan and Security Agreement contains customary covenants that include, among others, covenants that limit our (including our subsidiaries') ability to dispose of assets, enter into mergers or acquisitions, incur indebtedness, incur liens, pay dividends or make distributions on our capital stock, make investments or loans, and enter into certain affiliate transactions, in each case subject to customary exceptions for a credit facility of this size and type.

The Loan and Security Agreement contains customary events of default that include, among others, non-payment defaults, covenant defaults, a default in the event a material adverse change occurs, defaults in the event our assets are attached, or we are enjoined from doing business, bankruptcy and insolvency defaults, cross-defaults to certain other material indebtedness, material judgment defaults, and inaccuracy of representations and warranties. The occurrence of an event of default could result in an increase to the applicable interest rate of 5.0%,

acceleration of and present occurrence of the maturity date, and the consequent obligation for us to repay in full in cash all amounts outstanding under the Loan and Security Agreement, and a right by the lender to exercise all remedies available to it under the Loan and Security Agreement and related agreements, including the right to dispose of the collateral as permitted under applicable law. The Loan and Security Agreement contains customary affirmative and negative covenants, indemnification provisions and events of default. The affirmative covenants include, among others, covenants requiring us to maintain our legal existence and governmental approvals, deliver certain financial reports and maintain certain intellectual property rights. The negative covenants include, among others, restrictions on transferring or licensing our assets, changing our business, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, and creating other liens on our assets, in each case subject to customary exceptions. If we default under the Loan and Security Agreement, the lenders will be able to declare all obligations immediately due and payable and take control of our collateral, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. Further, if we were to be liquidated, the lender's rights to repayment would be senior to the rights of the holders of our common shares to receive any proceeds from the liquidation. If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility

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 relationship 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. 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 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 is currently one approved drug that specifically targets JAK inhibition, ruxolitinib, marketed by Incyte Corporation as Jakafi® in the United States and by Novartis as Jakavi in rest of the world. In

addition, there are a number of JAK inhibitor competitors in clinical development, at a similar state of development or more advanced than us. To our knowledge, Celgene Corporation is developing fedratinib, for which an NDA has been submitted with the FDA, and CTI Biopharma Corporation is developing pacritinib, which is currently in a Phase 2 dose finding study in the United States. However, to our knowledge, there are no approved drugs that target both JAK and ACVR1 inhibition on the market, nor in development. Other competitors in the myelofibrosis market include Acceleron, which is developing luspatercept in a Phase 2 clinical trial for myelofibrosis in conjunction with Celgene, and several additional companies in early stages of development. 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, which we believe is unique to the JAK inhibition class of agents, the market for momelotinib is competitive, and physicians and other prescribers may not recommend or prescribe momelotinib over other competing products.

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 state 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. To our knowledge, Eli Lilly and Company is developing prexasertib, an intravenous Chk1/Chk2 inhibitor in several clinical settings, the most advanced of which are in Phase 2 clinical trials. There are also preclinical programs focused on developing Chk1 inhibitors. If SRA737 is approved, it will compete with existing therapies for the indication or indications for which it is approved.

Additionally, to our knowledge, there are no approved drugs that specifically target Cdc7. To our knowledge, Takeda Pharmaceutical Company is developing an oral Cdc7 inhibitor that is currently in a Phase 2 clinical trial for metastatic pancreatic and colorectal cancers and Eli Lily and Company has a Cdc7 inhibitor program that is currently in a Phase 1 clinical trial being conducted by CRUK. Other companies may be conducting preclinical studies of Cdc7 inhibitors as well. If SRA141 is approved, it will compete with existing therapies 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 programs.

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 seeking to encourage the use of generic drugs. If we fail to complete 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 are dependent on our management, scientific and medical personnel, including Nick Glover, Ph.D., our President and Chief Executive Officer, Barbara

Klencke, M.D., our Chief Development Officer and Mark Kowalski M.D., Ph.D., our Chief Medical Officer. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, 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 our product candidates. 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 our product candidates 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. As we advance momelotinib through Phase 3 development, we will need to develop or expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. We must also successfully integrate the employees and operations related to the development 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, administrative and sales and marketing personnel, improve our managerial, development, operational and finance systems, and expand our facilities, all of which may impose a strain on our administrative and operational infrastructure. Our future financial performance will depend, in part, on our ability to manage this growth effectively. We may not be able to accomplish these tasks; which failure could prevent us from successfully developing our product candidates.

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

We may seek additional capital through a combination of public and private equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital

through the sale of equity or convertible debt securities, the ownership interests of our stockholders will be 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 product candidates or grant licenses on terms unfavorable to us.

We may form or seek strategic alliances, licensing arrangements or other collaborations in the future. 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 may form or seek strategic alliances or licensing arrangements, or create joint ventures or collaborations with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may acquire or develop. Any of these 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 our product candidates if we become dependent upon the other party and such other party does not prioritize the development of our 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 our product candidates, including SRA737 and SRA141, because our product candidates may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy. 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.

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

We may acquire additional businesses or product candidates from third parties that we believe will complement or augment our existing pipeline of product candidates, including, for example our recent acquisition of momelotinib from Gilead. 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 acquisitions, including our recent 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 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.

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

We currently have no sales, marketing or distribution capabilities and have no experience in marketing products. If any of our product candidates is approved for sale, we may develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other companies to recruit, hire, train and retain qualified marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue collaborative arrangements regarding the sales and marketing of our products, however, 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 our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

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

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 electronic and 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 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 or could have access to our computer networks, mobile networks, 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 those systems, are very large and complex. Failure by any of these third-party providers to adequately deliver the contracted services, or maintain confidentiality, could have an adverse effect on our business, which in turn may materially adversely affect our operating results and financial condition. All information technology systems,

despite implementation of security measures, may be vulnerable to disability, failures or unauthorized access. 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.

Despite the implementation of what we believe are appropriate security measures on internal information technology systems, our internal information technology systems and those of our CROs and other contractors and consultants may become vulnerable to damage from security breaches and/or unauthorized access. The prevalent use of mobile devices also increases the risk of data security incidents. In the ordinary course of our business, we collect, store, process and transmit large amounts of sensitive information, including intellectual property, proprietary business information, personal information and other confidential information. It is critical that we do so in a secure manner in order to ensure the confidentiality, integrity and availability of such sensitive information. We have in the past experienced, and may in the future experience, a security breach. Any material system failure or security breach 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 our product candidates 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 were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be significantly delayed.

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

Cyberattacks are frequent and may be sophisticated and intense to the point that they are difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, the deployment of harmful malware, denial-of-service, and/or other means to threaten data confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information and trade secrets, 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 that results in one or more third parties obtaining access to confidential information about our company. Although we devote resources to protect our information technology systems and continue to assess and, as necessitated, enhance our cybersecurity protection, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches 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. 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.

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 epidemics 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. We rely on third-party

manufacturers to produce and process our product candidates. Our ability to obtain supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. Our corporate headquarters are located in Vancouver, British Columbia, 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.

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 any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

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

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

- decreased demand for our product candidates;
- 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 any product candidate; 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 our product candidates, 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.

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, 2018, we had U.S. federal net tax operating loss carryforwards of $74.3 million, of which $31.4 million expire in 2037 and $42.9 million are eligible for indefinite carryforwards, and state operating loss carryforwards of $56.3 million expiring in years ranging from 2022 to 2038. We also had U.S. net tax credit carryforwards of $1.1 million which begin to expire in 2032 and net tax credit carryforwards in a foreign jurisdiction of $0.2 million which begin to expire in 2037.

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. An ownership change under Section 382 was deemed to have occurred in 2017. As such, certain tax attributes existing as of the date of the ownership change are not available for future use. The loss of these attributes did not have any impact on the financial statements since our net U.S. deferred tax assets are offset by a full valuation allowance.

We have experienced ownership changes in the past and may experience 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 are a U.S.-based multinational company subject to tax in certain U.S. and foreign tax jurisdictions. United States 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.

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. 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 these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

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 our product candidates or future 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 to our licensor;
- changes in the competitive landscape or market opportunity for our product candidates;
- 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 by any of our product candidates of regulatory approval and market acceptance, and the demand for such product candidates;
- regulatory developments affecting our product candidates or those of our competitors; and
- changes in general market and economic conditions.

If our quarterly operating results or expected results from development of our product candidates 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.

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

We are currently 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. For example, on November 9, 2016, a purported securities class action lawsuit was filed in the United States District Court for the Southern District of New York against us and certain of our executive officers (the New York Lawsuit). The New York Lawsuit was brought by purported stockholders of our company seeking to represent a class consisting of stockholders who purchased stock between July 15, 2015 and June 6, 2016. The New York Lawsuit asserts claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and seeks unspecified damages and other relief. On March 13, 2018, the United States District Court for the Southern District of New York granted the defendants' motion to dismiss and entered a final judgment dismissing the New York Lawsuit with prejudice. The plaintiffs filed an appeal and on December 3, 2018, the United States Court of Appeals for the Second Circuit affirmed the district court's final judgment of dismissal.

Also, on November 18, 2016, a purported securities class action lawsuit was filed in the Superior Court of the State of California for the County of San Mateo against us, certain of our executive officers and directors, and the underwriters for our initial public offering (IPO) of our common stock. On February 9, 2017, a substantially identical putative class action suit was filed in the Superior Court of the State of California for the County of San Mateo asserting the same claims on behalf of the same putative class (the two California lawsuits together, the California Lawsuits). The California Lawsuits were brought by purported stockholders of the company seeking to represent a class consisting of stockholders who purchased stock pursuant to and/or traceable to our Registration Statement on Form S-1. The lawsuits assert claims under Sections 11 and 15 of the Securities Exchange Act of 1934 and seek unspecified damages and other relief. On August 1, 2018, all parties reached a mutually acceptable proposed resolution to the California Lawsuits by way of a mediated settlement, which is subject to final approval by the court. The California Lawsuits remain pending. We are generally obliged, to the extent permitted by law, to indemnify our executive officers who are named as defendants in these types of lawsuits. Regardless of the outcome, this or 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.

Risks Related to Government Regulation

We may be unable to obtain U.S. or foreign regulatory approval of our product candidates, and, as a result, we may be unable to commercialize our product candidates.

Our product candidates are, 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 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 our 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;
- 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;
- the FDA or foreign regulatory authorities may not approve our companion diagnostic, if a companion diagnostic is required;
- 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; 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.

Even if we comply with all of the regulatory requirements of the FDA and foreign regulatory authorities, we may not obtain regulatory approval for any of our product candidates in development. If we fail to obtain regulatory approval for any of our product candidates in development, we will have fewer commercialized products than we anticipate and correspondingly lower 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.

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, a new clinical trial regulation goes into effect in 2019 that harmonizes the assessment and supervision of clinical trials throughout Europe via a revised European Union clinical trial 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. 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 EU 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, as discussed below

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.

Furthermore, negotiations around Brexit have caused uncertainty in the current regulatory framework in Europe. Brexit has resulted in a decision to move the EMA from the United Kingdom to the Netherlands, with operations currently scheduled to begin in the Netherlands by March 2019. In the United Kingdom, this transition may cause disruption in the administrative and medical scientific links between the EMA and MHRA. Although the government of the United Kingdom has stated its intent to comply with legislation regarding the authorization of medical products as it leaves the European Union, the EMA and the United Kingdom are drawing up contingency plans should a "no deal" exit occur. A "no deal" exit would 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. There would 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 would create supply difficulties for ongoing clinical trials and may damage the integrity of the pharmacovigilance database for the safety of new products.

When the United Kingdom leaves the European Union, it will no longer automatically comply with the standards of clinical efficacy, safety and chemistry control, and manufacture as applied by the European Medicines Directive. Applications submitted for marketing authorization under the centralized EMA procedure will no longer be automatically validated for authorization in the United Kingdom, and the benefit-risk assessments conducted by the United Kingdom may not be consistent with the EMA conclusions.

The cumulative effects of the disruption to the regulatory framework may add considerably to the development lead time to marketing authorization and commercialization of products in the European Union and/or the United Kingdom. In view of the current lack of detail and resolution with regard to the Brexit implementation, we are unable to confidently predict the effects of such disruption to the regulatory framework in Europe.

Even if we receive regulatory approval of our 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 our product candidates 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 our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted

distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or a foreign regulatory authority approves our product candidates, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and current good clinical practices (cGCPs) for any clinical trials that we conduct post-approval.

Moreover, if we obtain regulatory approval for our product candidates, 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 our product candidates 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.

Later discovery of previously unknown problems with our product candidates, 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 our product candidates, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- 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 our product candidates; 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.

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 our product candidates and may harm our reputation.

We are or may in the future be subject to federal, state, and foreign healthcare and data privacy laws and regulations pertaining to, among other things, fraud and abuse and patients' rights. These laws and regulations include:

- 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 health information, and requires notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- 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 physicians, other healthcare providers and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members, which is published in a searchable form on an annual basis; effective January 1, 2022, we will also be required to report on transfers of value to physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives;
- 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; and
- in the European Union, the GDPR was adopted in May 2016 and took effect on May 25, 2018. The GDPR is intended to harmonize data protection requirements across the European Union Member States by establishing new and expanded operational requirements for entities that process, or control personal data generated in the European Union, 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. The United Kingdom enacted the Data Protection Act 2018 to directly enforce the GDPR. The government of the United Kingdom has also stated that when the United Kingdom leaves the European Union it will still abide with the provisions of the GDPR. However, in the event of a "no deal" Brexit, it is uncertain whether this commitment will still be met. In the case of a "no deal" Brexit, it is also uncertain whether clinical trial data and pharmacovigilance adverse event data originating from the United Kingdom will be compliant with European Union privacy legislation and whether the data will be incorporated by EMA in the assessment of the ongoing benefit-risk profile and hence continued support of European Union marketing authorizations.

If our operations are found to be in violation of any such health care laws and regulations, we may be subject to 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, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely 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 could cause us to incur significant legal expenses 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.

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, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. 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 our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

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 in the early stages of 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 coverage 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. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive regulatory approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-government payers.

Historically, Medicare Part D enrollees have had a partial gap in their coverage (known as the "coverage gap" or "donut hole") wherein their coinsurance increases from 25% to a higher percentage (35% for brand drugs in 2018) after they reach an initial coverage limit, and remains at that level until they reach a catastrophic coverage threshold where the coinsurance is considerably reduced. However, beginning in 2019, Medicare Part D enrollees will continue to pay a 25% coinsurance during this interval – the same percentage that they were responsible for before they reached the initial coverage limit – thereby closing the coverage gap. The cost of closing the coverage gap is being borne by innovator companies and the government through subsidies. Beginning in 2011, each manufacturer of a drug approved under an NDA was required to enter into a Medicare Part D coverage gap discount agreement and provide a 50% discount on those drugs dispensed to Medicare Part D enrollees in the coverage gap, in order for its drugs to be reimbursed by Medicare Part D. The Bipartisan Budget Act of 2018 increased the manufacturer's subsidy under this program from 50% to 70% of the negotiated price, beginning in 2019.

Certain products we develop, such as SRA737 and SRA141, if approved, may need to be administered under the supervision of a physician on an outpatient basis. Under applicable U.S. law, certain drugs that are not usually self-administered (including certain injectable drugs) may be eligible for coverage under the Medicare Part B program if:

- they are incident to a physician's services;
- they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice; and
- they have been approved by the FDA and meet other requirements of the statute.

There may be significant delays in obtaining coverage for newly-approved products, and coverage may be more limited than the purposes for which the drug is approved by the FDA or foreign regulatory authorities. Moreover, eligibility for coverage does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent.

Reimbursement may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare Part D coverage policy and payment limitations in setting their own reimbursement rates. However, no uniform policy requirement for coverage and reimbursement for products exists among third-party payors in the United States. 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 our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new drugs that we develop and for

which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of oncology companies. A number of legislative and regulatory changes in the healthcare system in the United States and other major healthcare markets have been proposed in recent years, and such efforts have expanded substantially in recent years. These developments have included prescription drug benefit legislation that was enacted and took effect in January 2006, healthcare reform legislation enacted by certain states, and major healthcare reform legislation that was passed by Congress and enacted into law in the United States in 2010. The U.S. Congress and the Trump administration have similarly expressed concerns over the pricing of pharmaceutical products and there can be no assurance as to how this scrutiny will impact future pricing of pharmaceutical products generally. For example, President Trump outlined a blueprint of activities and proposals intended to lower prescription drug prices, which the Department of Health and Human Services is beginning to roll out. Future developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price.

For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act (PPACA), contains provisions that affect companies in the pharmaceutical industry and other healthcare related industries by imposing additional costs and changes to business practices. Provisions affecting pharmaceutical companies include the following.

- mandatory rebates for drugs sold into the Medicaid program were increased, and the rebate requirement was extended to drugs used in risk-based Medicaid managed care plans;
- the 340B Drug Pricing Program under the Public Health Services Act was extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities;
- expansion of eligibility criteria for Medicaid programs;
- expansion of entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the “donut hole”; the Bipartisan Budget Act of 2018 increased the manufacturer’s subsidy under this program from 50% to 70% of the negotiated price, beginning in 2019; and
- pharmaceutical companies are required to pay an annual non-tax-deductible fee to the federal government based on each company’s market share of prior year total sales of branded products to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs and Department of Defense. Since we expect our branded pharmaceutical sales, if any of our products are approved, to constitute a small portion of the total federal health program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.

There have been judicial and Congressional challenges and amendments to certain aspects of the PPACA. President Trump has suggested that he plans to seek repeal of all or portions of the PPACA and indicated that Congress should replace the PPACA with new legislation, and in 2017, President Trump issued the Executive Order Promoting Healthcare Choice and Competition, directing certain federal agencies to modify their implementation of the PPACA. We expect there will be additional challenges, amendments and modifications to the PPACA in the future, including potential repeal of PPACA in full or in part. The full effect of the U.S.

healthcare reform legislation on our business activities is unknown. The financial impact of the U.S. healthcare reform legislation will depend on a number of factors, including but not limited to, the policies reflected in implementing regulations and guidance and changes in sales volumes for products affected by the new system of rebates, discounts and fees. The legislation may also have a positive impact on our future net sales, if any, by increasing the aggregate number of persons with healthcare coverage in the United States. Further, new litigation is currently pending before the U.S. Supreme Court to invalidate certain provisions of the PPACA.

Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. Further federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Our ability to obtain services, reimbursement or funding may be impacted by possible reductions in federal spending in the United States as well as globally.

U.S. federal government agencies currently face potentially significant spending reductions. Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least $1.2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts would include aggregate reductions to Medicare payments to providers of up to two percent per fiscal year, which went into effect beginning on April 1, 2013 and will stay in effect through 2025 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, which was enacted on January 1, 2013, among other things, reduced Medicare payments to several providers, including hospitals and imaging centers. The full impact on our business of these automatic cuts is uncertain.

If government spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop. Any reductions in government spending in countries outside the United States may also impact us negatively, such as by limiting the functioning of international regulatory agencies in countries outside the United States or by eliminating programs on which we may rely.

Obtaining and maintaining regulatory approval for our 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 our 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 studies 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 our 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.

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 Cuts and Jobs Act (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 created in tax years beginning after December 31, 2017 (iii) a partial limitation on the deductibility of business interest expense, (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) and (v) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate.

In addition, beginning in 2022, the tax legislation 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.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the federal tax law.

Risks Related to Our Intellectual Property

We depend on intellectual property licensed from CPF and Carna, and the termination of these licenses could result in the loss of significant rights, which would harm our business.

Pursuant to a license agreement with CPF, we hold an exclusive license from CPF to use certain patented technology, including certain patent rights, know-how and materials related to SRA737. Either party may terminate the agreement if the other party materially breaches the agreement, subject to certain cure provisions, and CPF may terminate the agreement in certain limited circumstances. We may also terminate the agreement at any time upon 90 days' prior written notice to CPF. Additionally, pursuant to a license agreement with Carna, we hold an exclusive license from Carna to use certain patented technology, including certain patent rights and know-how related to SRA141. Carna may terminate the agreement in the event of our material breach, subject to certain cure provisions, and we may terminate the agreement at any time upon 30 days' prior written notice to Carna.

Disputes may arise between us and our licensors regarding intellectual property subject to these license agreements, including with respect to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the amount and timing of milestone and royalty payments;
- the rights of our licensors under the license agreements;
- our right to sublicense patent and other 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 our product candidates, 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.

Any disputes with our licensors over intellectual property that we have licensed from them may prevent or impair our ability to maintain our current licensing arrangements. We depend on these licensed technologies and products to develop our product candidates. Termination of our license agreements could result in the loss of significant rights and could materially harm our ability to further develop and commercialize our product candidates.

If we are not able to obtain and enforce patent protection for our technologies or product candidates, 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, for our product candidates, methods used to

manufacture our product candidates and methods for treating patients using our product candidates, 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. Our licensors have filed, and we will continue to file, patent applications directed to the compositions of matter and methods of use related to various aspects of our product candidates.

We and our current or future licensors and licensees may not be able to apply for or prosecute patents on certain aspects of our product candidates or 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 our product candidates or technologies 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 product candidates 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 our product candidates 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 our product candidates, we may be open to competition from generic versions of our product candidates. 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 our early-stage product candidates.

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 our product candidates and 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.

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

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.

We, our licensors 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, our licensors 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, our licensors 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 or the patents of our licensors, 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 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 any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates and technologies or we could lose certain rights to grant sublicenses.

In connection with our recent acquisition of momelotinib from Gilead, we are required to make aggregate milestone payments of up to $195.0 million to Gilead upon the achievement of certain development, regulatory and commercial milestones, including a milestone payment of $5.0 million upon the initiation of a registrational clinical trial, as well as mid-teen to high twenty percent tiered 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.

Additionally, our current license agreements impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. For example, we are required to use commercially reasonable efforts to develop and commercialize licensed products, and are required to pay CPF and Carna milestone payments in an aggregate amount of up to $319.5 and $270.0 million, respectively, based upon the achievement of certain developmental, regulatory and commercial milestones of SRA737 and SRA141, including a milestone payment of $4.0 million to Carna upon dosing of the first patient in the first Phase 1 clinical trial for SRA141. We are also required to pay CPF tiered high single-digit to low double-digit royalties on the net sales of SRA737 and to pay Carna tiered single-digit royalties on the net sales of SRA141. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. We may also be required to negotiate to return our licensed intellectual property related to SRA737 to CPF if we cease or scale back development and commercialization of SRA737 for oncology-related indications. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, we may be required to pay significant milestone and royalty payments, depending on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

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.

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. Factors affecting the market price of our common stock include, but are not limited to:

- the timing and results of development activities related to our product candidates;

- 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 and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- disputes with CPF or Carna regarding our licensed technology and products, or with Gilead regarding our acquisition of momelotinib and assumption of the related clinical trials;
- 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 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 or technologies on favorable terms or at all;
- our failure to commercialize our product candidates;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of our product candidates;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- 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;
- 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;
- general political and economic conditions; 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 are currently vigorously defending 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.

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

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

We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act (JOBS Act) enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 (Section 404) of the Sarbanes-Oxley Act of 2002, as amended (Sarbanes-Oxley Act), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock that is held by non-affiliates to exceed $700 million as of the prior June 30th, whichever is earliest; and (ii) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations.

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 an emerging growth company, 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.

Additionally, 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.

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 Vancouver, British Columbia, Canada, where we occupy approximately 8,300 square feet of office space under lease that expires in February 2023, with the option to extend for an additional 5 years. We believe that this facility is sufficient to meet our current needs.

Item 3. Legal Proceedings.

On November 9, 2016, a purported securities class action lawsuit was filed in the United States District Court for the Southern District of New York against us and certain of our executive officers (the New York Lawsuit). The New York Lawsuit was brought by purported stockholders of our company seeking to represent a class consisting of stockholders who purchased stock between July 15, 2015 and June 6, 2016. The New York Lawsuit asserts claims under Sections 10(b) and 20(a) of the Exchange Act and seeks unspecified damages and other relief. On March 13, 2018, the United States District Court for the Southern District of New York granted the defendants' motion to dismiss and entered a final judgment dismissing the New York Lawsuit with prejudice. Plaintiffs thereafter filed an appeal. On December 3, 2018, the United States Court of Appeals for the Second Circuit affirmed the district court's final judgment of dismissal. We believe that the claims in the New York Lawsuit are without merit and intend to defend the lawsuit vigorously. At this point in time, we do not expect the outcome of these claims will have a material impact on our consolidated financial statements.

On November 18, 2016, a purported securities class action lawsuit was filed in the Superior Court of the State of California for the County of San Mateo against us, certain of our executive officers and directors, and the underwriters for our initial public offering of our common stock. On February 9, 2017, a substantially identical putative class action suit was filed in the Superior Court of the State of California for the County of San Mateo asserting the same claims on behalf of the same putative class (the two lawsuits together, the California Lawsuits). The California Lawsuits were brought by purported stockholders of our company seeking to represent a class consisting of stockholders who purchased stock pursuant to and/or traceable to our Registration Statement on Form S-1. The lawsuits assert claims under Sections 11 and 15 of the Exchange Act and seek unspecified

damages and other relief. On August 1, 2018, all parties reached a mutually acceptable proposed resolution to the California Lawsuits by way of a mediated settlement, which is subject to final approval by the court. While we believe that the claims are without merit, we believe settlement will reduce the ultimate cost and distraction of further litigation. We do not believe that our portion of the settlement amount will have a material impact on our consolidated financial statements.

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.

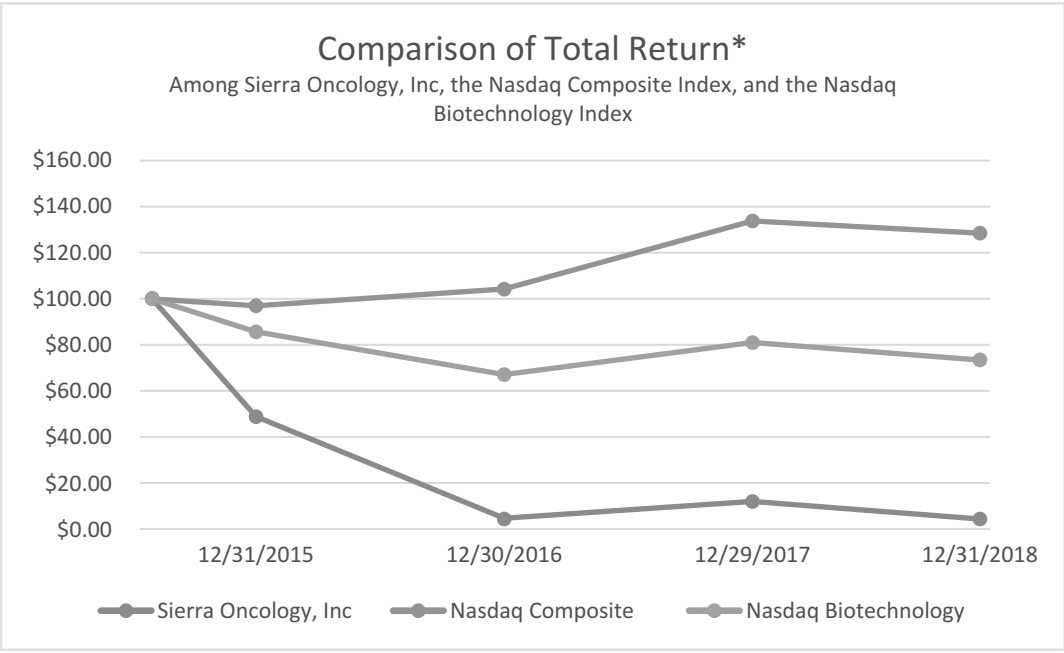
PART II

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 February 22, 2019, there were 75 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.

Stock Price Performance Graph

The graph below shows a comparison from July 16, 2015, the date on which our common stock first began trading on the Nasdaq Global Market, of the cumulative total return on an assumed investment of $100.00 in cash in our common stock as compared to the same investment in the Nasdaq Composite Index and the Nasdaq Biotechnology Index, all through to December 31, 2018. Such returns are based on historical results and are not intended to suggest future performance.



* $100 invested on July 16, 2015 in stock or index. Fiscal year ending December 31.

Cumulative Total Return Comparison

	July 16, 2015	December 31, 2015	December 30, 2016	December 29, 2017	December 31, 2018
Sierra Oncology, Inc.	$100.00	$48.83	$ 4.84	$ 12.11	$ 4.29
Nasdaq Composite	$100.00	$96.98	$104.26	$133.70	$128.51
Nasdaq Biotechnology	$100.00	$85.49	$ 66.95	$ 81.05	$ 73.49

This performance graph is not deemed to be "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act, or incorporated by reference into any of our filings under the Securities Act or the Exchange Act, except as shall be expressly set forth by specific reference to such filing.

Use of Proceeds from Registered Securities

On July 15, 2015, our Registration Statement on Form S-1 (File No. 333-204921) relating to the IPO of our common stock was declared effective by the SEC. Pursuant to such Registration Statement, we sold an aggregate of 9,315,000 shares of our common stock at a price of $17.00 per share for aggregate cash proceeds of approximately $143.6 million, net of underwriting discounts and commissions and offering costs.

We intend to use the remaining net proceeds from our IPO to advance the development of product candidates momelotinib, SRA737 and SRA141, acquire or in-license additional product candidates and technologies, and for other general corporate purposes.

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 2019 Annual Meeting of Stockholders. See Part III, Item 12 "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters."

Item 6. Selected Consolidated Financial Data.

The following tables set forth certain selected consolidated financial data. You should read the selected consolidated financial data below in conjunction with Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of the results that may be expected in the future.

	Year Ended December 31,				
	2018	2017	2016	2015	2014
	(in thousands except share and per share data)				
Consolidated Statements of Operations Data:					
Operating expenses[(1)]:					
Research and development	$ 41,078	$ 30,157	$ 33,895	$ 26,356	$ 19,078
General and administrative	14,339	12,462	14,180	9,472	3,500
Total operating expenses	55,417	42,619	48,075	35,828	22,578
Loss from operations	(55,417)	(42,619)	(48,075)	(35,828)	(22,578)
Other income (expense), net:					
Change in fair value of preferred stock warrants	—	—	—	(17,443)	(1,380)
Other income	1,780	760	351	66	87
Total other income (expense), net	1,780	760	351	(17,377)	(1,293)
Loss before provision for (benefit from) income taxes, net	(53,637)	(41,859)	(47,724)	(53,205)	(23,871)
Provision for (benefit from) income taxes, net	(302)	156	143	55	2

	Year Ended December 31,				
	2018	2017	2016	2015	2014
	(in thousands except share and per share data)				
Net loss	(53,335)	(42,015)	(47,867)	(53,260)	(23,873)
Adjustment to redemption value on redeemable convertible preferred stock	—	—	—	(374,015)	(49,849)
Series B and B-1 redeemable convertible preferred stock dividend	—	—	—	(5,543)	—
Series C and D redeemable convertible preferred stock dividend	—	—	—	(20,366)	—
Net loss attributable to common stockholders	$ (53,335)	$ (42,015)	$ (47,867)	$ (453,184)	$ (73,722)
Net loss per share attributable to common stockholders, basic and diluted[2]	$ (0.75)	$ (0.84)	$ (1.58)	$ (31.47)	$ (69.08)
Weighted-average shares used in computing net loss per share attributable to common stockholders, basic and diluted[2]	70,739,210	49,899,299	30,240,258	14,399,506	1,067,259

(1) Includes the following stock-based compensation:

	Year Ended December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Stock-based compensation:					
Research and development	$4,499	$3,966	$3,635	$1,846	$ 65
General and administrative	2,297	1,939	1,875	1,340	237
Total stock-based compensation	$6,796	$5,905	$5,510	$3,186	$302

(2) Basic and diluted net loss per share attributable to common stockholders is computed based on the weighted-average number of shares of common stock outstanding during each period.

	December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Consolidated Balance Sheets Data:					
Cash and cash equivalents	$ 106,046	$ 100,348	$ 109,007	$ 150,180	$ 29,154
Short-term investments	—	—	—	—	10,010
Working capital	98,653	94,253	102,625	144,456	37,630
Total assets	109,469	102,198	110,973	152,768	40,565
Term loan	4,891	—	—	—	—
Preferred stock warrant liabilities	—	—	—	—	1,810
Total liabilities	14,990	7,472	7,725	7,397	4,005
Convertible preferred stock	—	—	—	—	2,543
Redeemable convertible preferred stock	—	—	—	—	141,832
Accumulated deficit	(677,412)	(624,077)	(582,054)	(534,187)	(107,807)
Total stockholders' equity (deficit)	94,479	94,726	103,248	145,371	(107,815)

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." 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 clinical stage drug development company advancing targeted therapeutics for the treatment of patients with unmet medical needs in hematology and oncology. We have a highly experienced management team with a proven track record of success in hematology and oncology drug development. We are an ambitious company, oriented towards achieving the successful registration and commercialization of our product candidates.

During the third quarter of 2018, we acquired from Gilead Sciences, Inc. (Gilead) our lead product candidate momelotinib, a potent, selective and orally-bioavailable JAK1, JAK2 and ACVR1 inhibitor. Momelotinib has been investigated in two completed Phase 3 trials for the treatment of myelofibrosis and has demonstrated a potentially differentiated therapeutic profile encompassing anemia-related clinical benefits, as well as achieving substantive splenic volume reduction and constitutional symptom control (see additional discussion under Item 1. Business - *Momelotinib - A Potent and Selective JAK1, JAK2 and ACVR1 Inhibitor*).

In December 2018, we reported new clinical data for momelotinib collated from the two completed SIMPLIFY Phase 3 clinical trials and a translational biology study in transfusion dependent patients with myelofibrosis. Data from the latter study were also concurrently presented in a poster at the 60th American Society of Hematology Annual Meeting & Exposition in San Diego, California. We reported aggregated transfusion independence responses from more than 150 intermediate and high-risk transfusion dependent myelofibrosis patients demonstrating robust and consistent response rates within and across the clinical studies. More than 44% of these patients became transfusion free for at least 12 weeks and nearly 50% were transfusion independent for at least 8 weeks.

We are currently advancing discussions with regulators to determine the registration path for momelotinib and anticipate reporting next steps in the first half of 2019. Our anticipated registration strategy envisions conducting one additional Phase 3 trial in second line myelofibrosis patients, in order to recapitulate the meaningful clinical benefits observed in the two previously completed Phase 3 trials.

We are also advancing SRA737, our potent, highly selective, orally bioavailable small molecule inhibitor of Checkpoint kinase 1 (Chk1). Chk1 is a key regulator of cell cycle progression and the DNA Damage Response (DDR) replication stress response. In cancer cells, intrinsic replication stress is induced by factors such as oncogenes (e.g., *CCNE1* or *MYC*), genetic mutations in DNA repair machinery (e.g., *BRCA1* or *FANCA*), genetic mutations leading to a dysregulated cell cycle (e.g., *TP53* or *RAD50*) or other genomic alterations. This replication stress results in persistent DNA damage and genomic instability leading to an increased dependency on Chk1 for survival. Targeted inhibition of Chk1 by SRA737 may therefore be synthetically lethal to cancer cells with elevated intrinsic replication stress, either alone or in combination with LDG, in a range of tumor indications. The combination of SRA737 with other modalities, such as other agents that target the DDR network and certain chemotherapeutics, may also provide synergistic anti-tumor activity via a variety of potential biological mechanisms. Importantly, the oral bioavailability of SRA737 may afford greater dosing flexibility for both monotherapy and combination therapy settings than is possible with intravenously administered agents.

We are pursuing an innovative development plan for SRA737, which is currently being evaluated in two Phase 1/2 clinical trials in patients with advanced cancer. Our SRA737-01 trial is intended to evaluate SRA737's

potential to induce synthetic lethality as monotherapy, while the SRA737-02 trial is intended to evaluate the combination of SRA737 potentiated by subtherapeutic LDG.

During the second quarter of 2018, we further refined our SRA737-01 monotherapy study to focus on high grade serous ovarian cancer (HGSOC), supported by emerging data in the field that provides clinical validation for Chk1 inhibition in this indication. Accordingly, we prioritized the enrollment of genetically defined HGSOC patients into this trial, while continuing to enroll patients into the trial's other indications.

We commenced the Cohort Expansion Phase 2 portion of the SRA737-02 Phase 1/2 LDG Combination trial during the second quarter of 2018, which has been enrolling patients across four indications. We also modified this study to add and prioritize for the enrollment of a cohort of genetically defined HGSOC patients, replacing an originally proposed cohort of urothelial cancer patients.

We expect to report preliminary data from both trials in the first half of 2019.

In addition, we are designing clinical trials and conducting preclinical research evaluating SRA737 in combination with other DDR-targeted agents, including poly ADP-ribose polymerase (PARP) inhibitors, as well as with immuno-oncology therapeutics, that could guide the next planned wave of clinical development for our asset, potentially further broadening its therapeutic utility. In the first quarter of 2018, we announced an agreement with Janssen Research & Development, LLC (Janssen), under which they have agreed to supply us with the PARP inhibitor niraparib, facilitating the potential initiation of a PARP inhibitor combination trial with SRA737 for the treatment of prostate cancer. We are currently evaluating the optimal timing to commence this trial within the context of our recently expanded portfolio.

Our pipeline also includes SRA141, a potent, selective, orally bioavailable small molecule inhibitor of cell division cycle 7 kinase (Cdc7). Cdc7 is a key regulator of DNA replication and is involved in the DDR network, making it a compelling emerging target for the potential treatment of a broad range of tumor types. During the third quarter of 2018, we successfully completed the IND filing process with the FDA for SRA141 and we have prepared for a potential Phase 1/2 trial with this drug candidate in patients with advanced colorectal cancer. We are currently evaluating the optimal timing to commence this trial within the context of our recently expanded portfolio.

We retain the global commercialization rights to momelotinib, SRA737 and SRA141.

Since inception, we have devoted substantially all of our resources to research and development activities, including the clinical development of our current product candidates, momelotinib, SRA141 and SRA737, and our former lead product candidate PNT2258, and to providing general and administrative support for these operations. We have never generated revenue and have incurred significant net losses since inception. Our net losses were $53.3 million, $42.0 million and $47.9 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of $677.4 million. We expect to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- invest to further develop our product candidates, momelotinib, a small molecule inhibitor targeting JAK1, JAK2 and ACVR1; SRA737, a small molecule inhibitor targeting Chk1; and SRA141, a small molecule inhibitor targeting Cdc7;
- achieve development milestones that trigger payments due under certain agreements, including a milestone payment of $5.0 million that would be due to Gilead upon the dosing of the first patient in a registrational clinical trial for momelotinib and a milestone payment of $4.0 million that would be due to Carna Biosciences, Inc. (Carna) upon dosing of the first patient in the first Phase 1 clinical trial for SRA141;
- hire additional clinical, scientific, drug development and management personnel, as well as personnel to support any future commercialization efforts;

- 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;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval;
- acquire or in-license additional product candidates and technologies;
- develop additional product candidates;
- defend against and resolve lawsuits or other legal issues;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel to continue to operate as a public company.

We have funded our operations to date primarily from the issuance and sale of our common stock through public offerings, and our convertible and redeemable convertible preferred stock in private financings and, to a lesser extent, through debt financings and exercises of our preferred stock warrants. As of December 31, 2018, we had cash and cash equivalents of $106.0 million.

Components of Statements of Operations

Operating Expenses

Research and Development

Research and development expenses consist primarily of the following:

- fees or milestone payments incurred in connection with license and asset purchase agreements;
- 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;
- 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 clinical development of our product candidates SRA737 and SRA141. We expect our research and development expenses will increase over the next few years as we advance our development programs, including our recently acquired product candidate momelotinib, achieve development milestones that trigger payments due under certain agreements, pursue regulatory approval of our product candidates in the United States and other jurisdictions, expand our portfolio of product candidates and prepare for potential commercialization, which will require a significant investment in areas related to contract manufacturing and inventory buildup.

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 momelotinib, SRA737, SRA141 or any future product candidates. 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, SRA737, SRA141 or any future product candidates.

General and Administrative

General and administrative expenses consist of personnel-related costs, facility-related costs, allocated expenses and professional fees for services, including legal, 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, continuing to operate as a public company and other administration and professional services.

Other Income, net

Other income, net primarily consists of (i) interest and dividends earned on our cash and cash equivalents, (ii) interest expense associated with our term loan and non-cash interest costs associated with the amortization of the debt discount and accrual of the final payment fee, and (iii) 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 also 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 because we generated a loss for the year ended December 31, 2018. Our tax benefit relates to research and development tax credits in Canada and our income tax provision relates to income taxes in Canada and Australia. Our net U.S. deferred tax assets continue to be offset by a full valuation allowance.

On December 22, 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (Tax Act). The Tax Act significantly revised U.S. tax law by, among other provisions, lowering the U.S. federal statutory income tax rate from 35% to 21%, changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017 and eliminating or reducing certain income tax deductions.

The effects of changes in tax laws are required to be recognized in the period in which the legislation is enacted. However, due to the complexity and significance of the Tax Act's provisions, the Financial Accounting Standards Board (FASB) issued FASB Accounting Standards Update (ASU) No. 2018-06, *Income Taxes (Topic 740)* pursuant to the SEC staff issued Staff Accounting Bulletin No. 118 (SAB 118), which allowed companies to record the tax effects of the Tax Act on a provisional basis based on a reasonable estimate, and then, if necessary, subsequently adjust such amounts during a limited measurement period as more information becomes available. The measurement period ends when a company has obtained, prepared, and analyzed the information necessary to finalize its accounting, but cannot extend beyond one year from enactment.

In connection with our initial analysis of the Tax Act, we recorded a decrease to our net deferred tax assets of $7.2 million for the period ended December 31, 2017, to account for the rate reduction. This did not have an

impact on the consolidated financial statements since our U.S. deferred tax assets are fully offset by a valuation allowance. We finalized the analysis during the third quarter of 2018 with no material changes to the initial estimated decrease to our net deferred tax assets.

Results of Operations

Year Ended December 31, 2018 Compared to Year Ended December 31, 2017

	Year Ended December 31,		Change	
	2018	2017	$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	$ 41,078	$ 30,157	$ 10,921	36%
General and administrative	14,339	12,462	1,877	15%
Total operating expenses	55,417	42,619	12,798	30%
Loss from operations	(55,417)	(42,619)	(12,798)	30%
Other income, net	1,780	760	1,020	134%
Loss before provision for (benefit from) income taxes, net	(53,637)	(41,859)	(11,778)	28%
Provision for (benefit from) income taxes, net	(302)	156	(458)	(294%)
Net loss	$(53,335)	$(42,015)	$(11,320)	27%

Research and Development

Research and development expenses increased $10.9 million, from $30.2 million in 2017 to $41.1 million in 2018. The increase was primarily due to an increase of $7.2 million in clinical trial costs mainly related to SRA737, a $3.0 million upfront fee paid to Gilead to acquire our lead product candidate momelotinib and a $3.0 million increase in personnel-related and allocated overhead costs for the year ended December 31, 2018. These increased costs were partially offset by a $1.9 million decrease in third party manufacturing costs related to SRA737 and SRA141 and a $0.4 million decrease in research, preclinical and other support costs for the year ended December 31, 2018.

General and Administrative

General and administrative expenses increased $1.9 million, from $12.5 million in 2017 to $14.3 million in 2018. The increase was attributable to a $1.2 million increase in personnel-related and allocated overhead costs, a $0.5 million increase in professional fees and a $0.2 million increase in business development costs for the year ended December 31, 2018.

Other Income, net

Other income, net increased $1.0 million, from $0.8 million in 2017 to $1.8 million in 2018. The increase was primarily attributable to an increase in interest income as a result of higher interest rates for the year ended December 31, 2018.

Provision for (Benefit from) Income Taxes, net

Net benefit from income taxes was $0.3 million in 2018, compared to provision for income taxes of $0.2 million in 2017. The net benefit from income taxes during the year ended December 31, 2018 primarily represented benefit from foreign research and development tax credits.

Year Ended December 31, 2017 Compared to Year Ended December 31, 2016

	Year Ended December 31,		Change	
	2017	2016	$	%
	(in thousands, except percentages)			
Operating expenses:				
Research and development	$ 30,157	$ 33,895	$(3,738)	(11%)
General and administrative	12,462	14,180	(1,718)	(12%)
Total operating expenses	42,619	48,075	(5,456)	(11%)
Loss from operations	(42,619)	(48,075)	5,456	(11%)
Other income	760	351	409	117%
Loss before provision for income taxes	(41,859)	(47,724)	5,865	(12%)
Provision for income taxes	156	143	13	9%
Net loss	$(42,015)	$(47,867)	$ 5,852	(12%)

Research and Development

Research and development expenses decreased $3.7 million, from $33.9 million in 2016 to $30.2 million in 2017. The decrease was primarily due to items incurred in the year ended December 31, 2016, including, a $7.0 million upfront fee for the exclusive license of SRA737 and a $2.0 million fee that was due upon the successful transfer of the two ongoing clinical trials to us in accordance with the license agreement, a $2.3 million restructuring charge related to the halt in investment in PNT2258, and a $0.9 million upfront payment for the exclusive license of SRA141. These decreased costs were partially offset by a $4.6 million increase in third-party manufacturing costs, a $2.6 million increase in research and support costs related to SRA737 and SRA141, a $1.0 million increase in clinical trial costs and a $0.3 million increase in personnel-related and allocated overhead costs.

General and Administrative

General and administrative expenses decreased $1.7 million, from $14.2 million in 2016 to $12.5 million in 2017. The decrease was attributable to a $1.1 million decrease in business development costs, and a $0.5 million decrease in restructuring costs related to the halt in investment in PNT2258.

Liquidity and Capital Resources

Capital Resources

Since our inception, we have never generated revenue and have incurred significant net losses. We have funded our operations to date primarily from the issuance and sale of our common stock through public offerings, and our convertible and redeemable convertible preferred stock in private financings and, to a lesser extent, through debt financings and exercises of our preferred stock warrants. Our net losses were $53.3 million, $42.0 million and $47.9 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of $677.4 million. Our principal sources of liquidity as of December 31, 2018 were cash and cash equivalents of $106.0 million.

In July 2015, we completed the initial public offering (IPO) of our common stock whereby we sold an aggregate of 9,315,000 shares of our common stock, at a price of $17.00 per share. We received aggregate cash proceeds of approximately $143.6 million from the IPO, net of underwriting discounts and commissions and offering expenses.

In February 2017, we completed an underwritten public offering of an aggregate of 21,847,636 shares of common stock, at a price to the public of $1.35 per share. The aggregate net proceeds received by us from the offering were $27.4 million, net of underwriting discounts and commissions and offering expenses.

In March 2018, we completed an underwritten public offering of an aggregate of 21,850,000 shares of common stock, at a price to the public of $2.25 per share. The aggregate net proceeds received by us from the offering were $46.0 million, net of underwriting discounts and commissions and offering expenses.

In August 2018, we entered into a Loan and Security Agreement (Loan Agreement) with Silicon Valley Bank (SVB), pursuant to which we may obtain a loan of aggregate principal amount of up to $15.0 million. As of December 31, 2018, we borrowed $5.0 million under the first tranche, which bears interest at the greater of 6.0% or a floating per annum rate 1.0% above the prime rate (for an interest rate of 6.50% at December 31, 2018) and matures on August 1, 2022.

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

- invest to further develop our product candidates, momelotinib, a small molecule inhibitor targeting JAK1, JAK2 and ACVR1; SRA737, a small molecule inhibitor of Chk1; and SRA141, a small molecule inhibitor targeting Cdc7;
- achieve development milestones that trigger payments due under certain agreements, including a milestone payment of $5.0 million that would be due to Gilead upon the dosing of the first patient in a registrational clinical trial for momelotinib and a milestone payment of $4.0 million that would be due to Carna upon dosing of the first patient in the first Phase 1 clinical trial for SRA141;
- hire additional clinical, scientific, drug development and management personnel, as well as personnel to support any future commercialization efforts;
- 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;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval;
- acquire or in-license additional product candidates and technologies;
- develop additional product candidates;
- defend against and resolve lawsuits or other legal issues;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel to continue to operate as a public company.

To fund our current operating plans, we will need to raise additional capital. Our existing cash and cash equivalents will not be sufficient for us to complete development of our product candidates and, if applicable, to prepare for commercializing any product candidate that may receive approval. Accordingly, we will continue to require substantial additional capital to continue our clinical development and potential commercialization activities; however, we believe that our existing cash and cash equivalents will be sufficient to fund our current operating plans through at least the next twelve months. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities. However, 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 our future funding requirements will depend on many factors, including the pace and results of our preclinical and clinical development efforts.

We plan to continue to fund our current operating plans' needs through equity financings or other arrangements. 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. There can be no assurance that such additional financing, if available, can be obtained on terms acceptable to us. If we are unable to obtain such additional financing, we would need to reevaluate our future operating plans.

Cash Flows

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

	Year Ended December 31,		
	2018	2017	2016
		(in thousands)	
Cash used in operating activities	$(45,115)	$(36,163)	$(41,163)
Cash used in investing activities	(118)	(92)	(171)
Cash provided by financing activities	51,131	27,588	196
Effect of foreign exchange rate changes on cash, cash equivalents and restricted cash	(88)	(4)	(60)
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 5,810	$ (8,671)	$(41,198)

Cash Flows from Operating Activities

In 2018, cash used in operating activities of $45.1 million was attributable to a net loss of $53.3 million, partially offset by $6.8 million in non-cash charges and a net change of $1.4 million in our net operating assets and liabilities. The non-cash charges consisted primarily of $6.8 million in stock-based compensation.

In 2017, cash used in operating activities of $36.2 million was attributable to a net loss of $42.0 million and a net change of $0.3 million in our net operating assets and liabilities, partially offset by $6.2 million in non-cash charges. The non-cash charges consisted primarily of $5.9 million in stock-based compensation.

In 2016, cash used in operating activities of $41.2 million was attributable to a net loss of $47.9 million, partially offset by $6.5 million in non-cash charges and a net change of $0.2 million in our net operating assets and liabilities. The non-cash charges consisted primarily of $5.5 million in stock-based compensation and a $0.8 million in non-cash restructuring charges.

Cash Flows from Investing Activities

Cash used in investing activities for each of December 31, 2018, 2017 and 2016 was primarily attributable to the purchase of property and equipment.

Cash Flows from Financing Activities

In 2018, cash provided by financing activities was $51.1 million, attributable to net proceeds of $46.0 million received from the sale and issuance of our common stock upon our follow-on offering, $5.0 million of proceeds received from borrowing under the Loan Agreement and $0.2 million of proceeds received from the exercise of options to purchase common stock.

In 2017, cash provided by financing activities was $27.6 million, attributable to net proceeds of $27.4 million received from the sale and issuance of our common stock upon our follow-on offering in February 2017, and $0.2 million of proceeds received from the exercise of options to purchase common stock.

In 2016, cash provided by financing activities was $0.2 million, consisting of proceeds received from the exercise of options to purchase common stock.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2018, which represent material expected or contractually committed future obligations.

	Payments Due By Period				
	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More Than 5 Years
			(in thousands)		
Purchase commitments[1]	$ 9,824	$7,260	$2,564	$ —	$—
Operating lease obligations[2]	831	243	419	169	—
Term loan[3]	6,148	329	4,115	1,704	—
Total contractual obligations	$16,803	$7,832	$7,098	$1,873	$—

(1) Reflects payments we are required to make pursuant to clinical trial and manufacturing agreements.

(2) Reflects payments we are required to make under operating lease agreements. Costs such as taxes and other operating costs are not included in the amounts disclosed. (See Note 7 to the financial statements under Item 8 of this Form 10-K.)

(3) Reflects contractually required principal, interest payments and final payment fee we are required to make under the Loan Agreement entered into with SVB. The projected interest payment and final payment fee obligations are based upon the loan amount outstanding and interest rate as of the balance sheet date and assume retirement at the scheduled maturity date of the loan. (See Note 7 to the financial statements under Item 8 of this Form 10-K.)

Under the terms of the agreements with Gilead, CRT Pioneer Fund LP (CPF) and Carna, we will be required to pay future milestones if certain developmental, regulatory and commercial milestones are achieved. Future milestones for which we cannot reliably estimate the timing have been excluded from the table above.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with 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 accrue 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 base our expense accruals related to clinical trials on patient enrollment and our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions that conduct and manage clinical trials on our behalf. The financial terms of these agreements vary for each contract and may result in uneven payment flows. Payments under some of these contracts depend on several factors, such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If 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. For service contracts entered into that include a nonrefundable prepayment for service, the upfront payment is deferred and recognized in the statement of operations as the services are rendered.

Contingent milestone payment obligations due to third parties under license agreements are accrued when the milestones are considered probable of occurring.

To date, we have not experienced significant changes in our estimates of accrued 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 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 grant date fair value of the stock-based awards is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. The fair value of any options issued to non-employees is recorded as expense over the vesting period, which is generally the service period.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the estimated fair value of stock-based awards. These assumptions include:

Expected Term—The expected term represents the period that stock-based awards are expected to be outstanding. As our 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, we estimate the expected term by using the midpoint between the vesting commencement date and the contractual expiration period of the stock-based award. The expected term for options issued to non-employees is the contractual term.

Expected Volatility—Since we have limited information on the volatility of common stock due to its short trading history, the expected volatility is derived from the historical stock volatilities of comparable peer public companies within our industry that are considered to be comparable to our business over a period equivalent to the expected term of the stock-based awards.

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 we have not paid nor anticipate paying any dividends on our common stock in the foreseeable future.

Forfeiture Rate—Prior to January 1, 2017, we recorded stock-based compensation costs related to stock options net of estimated forfeitures. The forfeiture rate was estimated based on an analysis of actual forfeitures experience, analysis of employee turnover behavior and other factors. Effective January 1, 2017, we made an accounting policy election to account for forfeitures when they occur.

Fair Value of Common Stock—The fair value of our common stock is used to estimate the fair value of the stock-based awards at grant date.

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.

Off-Balance Sheet Arrangements

As of December 31, 2018, 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.

Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (FASB) issued FASB Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)*. The amendments in this update require that organizations recognize lease assets and lease liabilities on the balance sheet and disclose key information about leasing arrangements. This ASU is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, with early adoption permitted. We will adopt the new standard effective January 1, 2019 on a modified retrospective basis and will elect the practical expedients package as permitted under the transition guidance. We estimate that we will recognize right-of-use assets and total lease liabilities of approximately $1 million on our consolidated balance sheet as of January 1, 2019. Other than disclosed, we do not expect the new standard to have a material impact on our consolidated financial statements.

In June 2018, the FASB issued FASB ASU No. 2018-07, Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. This ASU is intended to simplify aspects of share-based compensation issued to non-employees by making the guidance consistent with accounting for employee share-based compensation. This ASU is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, with early adoption permitted. We will adopt the new standard effective January 1, 2019 and have determined that the adoption of this new accounting guidance will not have a material impact on our consolidated financial statements.

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 and foreign currency risk.

Interest Rate Sensitivity

We had cash and cash equivalents of $106.0 million as of December 31, 2018, which consisted primarily of bank deposits and money market funds. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our consolidated financial condition or results of operations. We do not believe that our cash or cash equivalents have significant risk of default or illiquidity.

In addition, we had an outstanding balance of $5.0 million under our Loan Agreement as of December 31, 2018. Borrowings under the Loan Agreement bear interest at the greater of 6% or a floating per annum rate of 1.0% above the prime rate (for an interest rate of 6.50% at December 31, 2018). The effect of a hypothetical 10% change in interest rates would not have a material impact on our operating loss.

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, British Pounds and Australian Dollars. 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.

Item 8. Consolidated Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Shareholders of
Sierra Oncology, Inc.:
Vancouver, British Columbia, Canada

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, 2018 and 2017, 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, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, 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.

/s/ Deloitte & Touche LLP

Grand Rapids, Michigan
February 28, 2019

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, 2018	December 31, 2017
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 106,046	$ 100,348
Prepaid expenses and other current assets	2,706	1,377
Total current assets	108,752	101,725
Property and equipment, net	168	154
Other assets	549	319
TOTAL ASSETS	$ 109,469	$ 102,198
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accrued liabilities	$ 8,812	$ 6,133
Accounts payable	1,287	1,339
Total current liabilities	10,099	7,472
Term loan	4,891	—
TOTAL LIABILITIES	14,990	7,472
Commitments and Contingencies (Note 7)		
STOCKHOLDERS' EQUITY:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized as of December 31, 2018 and December 31, 2017; nil shares issued and outstanding as of December 31, 2018 and December 31, 2017	—	—
Common stock, $0.001 par value; 500,000,000 shares authorized as of December 31, 2018 and 2017; 74,365,965 and 52,395,223 shares issued and outstanding as of December 31, 2018 and 2017	74	52
Additional paid-in capital	771,817	718,751
Accumulated deficit	(677,412)	(624,077)
TOTAL STOCKHOLDERS' EQUITY	94,479	94,726
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 109,469	$ 102,198

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,		
	2018	**2017**	**2016**
Operating expenses:			
Research and development	$ 41,078	$ 30,157	$ 33,895
General and administrative	14,339	12,462	14,180
Total operating expenses	55,417	42,619	48,075
Loss from operations	(55,417)	(42,619)	(48,075)
Other income, net	1,780	760	351
Loss before provision for (benefit from) income taxes, net	(53,637)	(41,859)	(47,724)
Provision for (benefit from) income taxes, net	(302)	156	143
Net loss and comprehensive loss	(53,335)	(42,015)	(47,867)
Net loss per common share, basic and diluted	$ (0.75)	$ (0.84)	$ (1.58)
Weighted-average shares used in computing net loss per common share, basic and diluted	70,739,210	49,899,299	30,240,258

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)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance—December 31, 2015	30,058,105	$ 30	$679,528	$(534,187)	$145,371
Issuance of common stock for exercise of stock options	312,841	—	211	—	211
Stock-based compensation	—	—	5,510	—	5,510
Vesting of early exercised stock options	—	—	23	—	23
Net loss	—	—	—	(47,867)	(47,867)
Balance—December 31, 2016	30,370,946	30	685,272	(582,054)	$103,248
Issuance of common stock for exercise of stock options	176,641	—	166	—	166
Cumulative effect of adoption of new accounting standard	—	—	8	(8)	—
Stock-based compensation	—	—	5,905	—	5,905
Issuance of common stock, net of offering costs of $2.1 million	21,847,636	22	27,400	—	27,422
Net loss	—	—	—	(42,015)	(42,015)
Balance—December 31, 2017	52,395,223	52	718,751	(624,077)	94,726
Issuance of common stock for exercise of stock options	120,742	—	180	—	180
Stock-based compensation	—	—	6,796	—	6,796
Issuance of common stock, net of offering costs of $3.2 million	21,850,000	22	45,974	—	45,996
Issuance of common stock warrant	—	—	116	—	116
Net loss	—	—	—	(53,335)	(53,335)
Balance—December 31, 2018	74,365,965	$ 74	$771,817	$(677,412)	$ 94,479

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,		
	2018	**2017**	**2016**
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (53,335)	$ (42,015)	$ (47,867)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	6,796	5,905	5,510
Depreciation	111	258	197
Non-cash restructuring charges	—	—	811
Other	(68)	31	15
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(1,341)	(115)	(362)
Accrued liabilities	2,770	990	(1,713)
Accounts payable	(48)	(1,217)	2,246
Net cash used in operating activities	(45,115)	(36,163)	(41,163)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	(118)	(92)	(214)
Proceeds from sale of property and equipment	—	—	43
Net cash used in investing activities	(118)	(92)	(171)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock upon follow-on offering, net of offering costs	45,996	27,422	—
Proceeds from issuance of term loan, net of issuance costs	4,955	—	—
Proceeds from exercise of common stock options	180	166	211
Payment of deferred offering costs	—	—	(15)
Net cash provided by financing activities	51,131	27,588	196
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(88)	(4)	(60)
NET INCREASE (DECREASE) IN CASH, CASH EQUIVALENTS AND RESTRICTED CASH	5,810	(8,671)	(41,198)
CASH, CASH EQUIVALENTS AND RESTRICTED CASH—Beginning of period	100,536	109,207	150,405
CASH, CASH EQUIVALENTS AND RESTRICTED CASH—End of period	$106,346	$100,536	$109,207
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Cash paid for income taxes, net	$ 15	$ 260	$ 107
Cash paid for interest	$ 87	$ —	$ —
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING INFORMATION:			
Property and equipment purchases included in accounts payable and accrued liabilities	$ 11	$ 4	$ 85
Issuance of common stock warrant	$ 116	$ —	$ —

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

1. The Company and Basis of Presentation

Organization and Description of Business

Sierra Oncology, Inc. (together with its subsidiaries, collectively referred to as the "Company"), a Delaware corporation, is a clinical stage drug development company advancing targeted therapeutics for the treatment of patients with unmet medical needs in hematology and oncology. Pursuant to an asset purchase agreement entered into in August 2018 (Note 7), the Company acquired its lead drug candidate, momelotinib, a potent, selective and orally-bioavailable JAK1, JAK2 and ACVR1 inhibitor that has been investigated in two completed Phase 3 clinical trials for the treatment of myelofibrosis and has demonstrated a potentially differentiated therapeutic profile encompassing anemia-related benefits, as well as achieving substantive splenic volume reduction and constitutional symptom control. The Company is also advancing SRA737 and SRA141. SRA737 is a potent, highly selective, orally bioavailable small molecule inhibitor of Checkpoint kinase 1 (Chk1), a key regulator of cell cycle progression and the DNA Damage Response (DDR) replication stress response. SRA141 is a potent, selective and orally bioavailable small molecule inhibitor of cell division cycle 7 kinase (Cdc7), a key regulator of DNA replication and involved in the DDR network.

The Company's primary activities since inception have been conducting research and development activities, conducting preclinical and clinical testing, recruiting personnel, 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 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 need to obtain adequate additional financing to fund the development of its product candidates.

As of December 31, 2018, the Company had $106.0 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 though it may pursue raising additional capital through equity financings or other arrangements.

Follow On Offerings

On February 14, 2017, the Company completed an underwritten public offering of 19,500,000 shares of common stock. As part of the underwritten public offering, on February 21, 2017 the Company issued an additional 2,347,636 shares of common stock representing the underwriters' exercise of a majority of their over-allotment option. All shares were offered by the Company at a price to the public of $1.35 per share. The aggregate net proceeds received by the Company from the offering were $27.4 million, net of underwriting discounts and commissions and offering expenses of $2.1 million.

On March 6, 2018, the Company completed an underwritten public offering of an aggregate of 21,850,000 shares of common stock, including the underwriters' exercise of their overallotment option, at a price to the public of $2.25 per share. The aggregate net proceeds received by the Company from the offering were $46.0 million, net of underwriting discounts and commissions and offering expenses of $3.2 million.

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 value of stock options and the warrant issued, 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 income, net in the consolidated statements of operations. The net foreign exchange transaction gains (losses) included in other income, net in the accompanying consolidated statements of operations for the year ended December 31, 2018 were insignificant, and were $0.1 million for the years ended December 31, 2017 and 2016.

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 invested in a money market fund, represents collateral for a corporate credit card facility and is included in other assets in the accompanying consolidated balance sheets. Restricted cash at December 31, 2017 also included security deposits required for a facility lease that expired in February 2018.

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 liabilities approximate their fair value at December 31, 2018 and 2017, due to their short duration. The term loan bears interest at prevailing market rates for instruments with similar characteristics, accordingly, the carrying value of this instrument approximates its fair value.

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. 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. 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.

Other Assets

Other assets consist primarily of restricted cash pledged as collateral for a corporate credit card facility, long-term prepaid rent and deferred income tax assets in foreign jurisdictions.

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. In the event that a clinical trial is terminated early, the Company records an accrual for the estimated remaining costs to complete the trial in the period of termination.

Upfront payments made in connection with license and asset purchase 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.

Research and development costs include fees incurred in connection with license and asset purchase agreements, 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, 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 employee stock-based compensation awards is the date of grant and the expense is recognized on a straight-line basis over the vesting period.

Stock-based compensation arrangements with non-employees are recognized at the grant date and remeasured to fair value at each reporting period. The expense is recognized over the vesting period, which is generally the service period.

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. Accordingly, the Company has a single reporting segment.

Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (FASB) issued FASB Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)*. The amendments in this update require that organizations recognize lease assets and lease liabilities on the balance sheet and disclose key information about leasing arrangements. This ASU is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, with early adoption permitted. The Company will adopt the new standard effective January 1, 2019 on a modified retrospective basis and will elect the practical expedients package as permitted under the transition guidance. The Company estimates that it will recognize right-of-use assets and total lease liabilities of approximately $1 million on its consolidated balance sheet as of January 1, 2019. Other than disclosed, the Company does not expect the new standard to have a material impact on its consolidated financial statements.

In June 2018, the FASB issued FASB ASU No. 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. This ASU is intended to simplify aspects of share-based compensation issued to non-employees by making the guidance consistent with accounting for employee share-based compensation. This ASU is effective for financial statements issued for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, with early adoption permitted. The Company will adopt the new standard effective January 1, 2019 and has determined that the adoption of this new accounting guidance will not have a material impact on its consolidated financial statements.

3. Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period without consideration for common stock equivalents. Diluted net loss per share is computed by dividing net loss by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, stock options and the warrant 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,		
	2018	2017	2016
Options to purchase common stock	10,504,412	7,470,601	6,543,654
Warrant for common stock	73,529	—	—
Total potential dilutive shares	10,577,941	7,470,601	6,543,654

4. Fair Value Measurements

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

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial Assets				
Money market funds	$105,224	$—	$—	$105,224
Restricted money market funds	300	—	—	300
Total financial assets	$105,524	$—	$—	$105,524

	December 31, 2017			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial Assets				
Money market funds	$99,792	$—	$—	$99,792
Restricted money market funds	188	—	—	188
Total financial assets	$99,980	$—	$—	$99,980

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

There were no transfers between Levels 1, 2 or 3 during the years ended December 31, 2018 and 2017.

5. Balance Sheet Components

Cash and Cash Equivalents

Cash and cash equivalents consist of the following:

	December 31,	
	2018	2017
	(in thousands)	
Cash	$ 822	$ 556
Cash equivalents:		
Money market accounts	105,224	99,792
Total cash and cash equivalents	$106,046	$100,348

In November 2016, the FASB issued new guidance ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash*, which requires the beginning-of-period and end-of-period totals on the statement of cash flows to include restricted cash and restricted cash equivalents, as well as disclosure of how the statement of cash flows reconciles to the balance sheet if restricted cash is shown separately from cash and cash equivalents on the balance sheet. The company adopted the guidance effective January 1, 2018 retrospectively to all periods presented. As a result, the consolidated statement of cash flows no longer presents transfers to or from restricted cash.

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, 2018	December 31, 2017
	(in thousands)	
Cash and cash equivalents	$106,046	$100,348
Restricted cash included in other assets	300	188
Total cash, cash equivalents and restricted cash shown in the consolidated statement of cash flows	$106,346	$100,536

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist of the following:

	December 31,	
	2018	2017
	(in thousands)	
Prepaid research and development project costs	$ 762	$ 549
Other receivables	751	103
Prepaid insurance	555	478
Income taxes receivable	163	—
Other	475	247
Total prepaid expenses and other current assets	$2,706	$1,377

Property and Equipment, net

Property and equipment, net consists of the following:

	December 31,	
	2018	2017
	(in thousands)	
Software	$ 325	$ 254
Leasehold improvements	112	79
Computer equipment	89	93
Furniture and fixtures	3	3
Property and equipment, gross	529	429
Less: accumulated depreciation	(361)	(275)
Total property and equipment, net	$ 168	$ 154

Depreciation related to the Company's property and equipment for the years ended December 31, 2018, 2017 and 2016 was $0.1 million, $0.3 million and $0.2 million, respectively.

Accrued Liabilities

Accrued liabilities consist of the following:

	December 31,	
	2018	2017
	(in thousands)	
Accrued research and development costs	$4,485	$2,763
Accrued employee related costs	3,223	2,699
Accrued professional fees	357	317
Accrued restructuring costs (Note 11)	33	137
Other	714	217
Total accrued liabilities	$8,812	$6,133

6. Term Loan

On August 21, 2018, the Company entered into a Loan and Security Agreement (Loan Agreement) with Silicon Valley Bank (SVB), pursuant to which the Company may obtain a loan of aggregate principal amount of up to $15.0 million (Term Loans), which becomes available in three tranches, each of an aggregate principal amount of up to $5.0 million. Contemporaneously with executing the Loan Agreement, the Company drew down the first $5.0 million tranche. The second and third $5.0 million tranches may be drawn only upon the achievement of certain development milestones. Borrowings under the Loan Agreement bear interest at the greater of (i) 6.0% or (ii) a floating per annum rate 1.0% above the prime rate (for an interest rate of 6.50% at December 31, 2018), with interest only due and payable monthly, until March 1, 2020 (unless extended under the conditions set forth in the Loan Agreement), at which time interest and principal will be due and payable in equal monthly payments; and are subject to a final payment fee equal to 6.75% of the aggregate principal amount.

The Company may prepay all, but not less than all, of the loaned amounts subject to a prepayment fee in the amount of 3.0% of the outstanding principal balance if such prepayment occurs prior to August 21, 2019; 2.0% of the outstanding principal balance if such prepayment occurs on or after August 21, 2019, but prior to August 21, 2020; or 1.0% of the outstanding principal balance if such prepayment occurs on August 21, 2020 or at any time thereafter prior to the maturity date of the Term Loans on August 1, 2022.

The Loan Agreement is secured by substantially all of the Company's personal property, except for its intellectual property and requires the Company to maintain the lesser of $10 million or 80% of its cash and cash equivalents with SVB. The Loan Agreement contains customary covenants that limit the Company's ability to dispose of assets, enter into mergers or acquisitions, incur indebtedness, incur liens, pay dividends or make distributions on the Company's capital stock, make investments or loans, and enter into certain affiliate transactions, among others. The Loan Agreement contains customary events of default that include, among others, non-payment defaults, covenant defaults, the occurrence of a material adverse change, and inaccuracy of representations and warranties. The occurrence of an event of default could result in an increase of 5% to the applicable interest rate, and the consequent obligation for the Company to repay all amounts outstanding under the Loan Agreement.

In connection with the Loan Agreement, the Company issued a warrant to SVB to purchase 73,529 of the Company's common stock at a price per share of $1.87. The warrant was immediately exercisable, will expire on August 21, 2028, contains a cashless exercise provision and is classified as equity. If the Company is to draw the second or third tranche available under the Loan Agreement, the Company will grant an additional amount of common stock issuable upon exercise of the warrant based upon the principal amount

advanced. In no event will the number of common stock issuable pursuant to the exercise of the warrant exceed 220,588 in aggregate.

The fair value of the warrant and the debt issuance costs were recorded as debt discounts and together with the final payment fee are being amortized using the effective interest rate method over the term of the loan. As of December 31, 2018, the effective interest rate on the initial tranche of the loan was 9.89% and the unamortized debt discount was $0.1 million. Amortization of the debt discount and the accrual of final payment was $0.1 million for the year ended December 31, 2018.

Scheduled payments due under the Loan Agreement, excluding the final payment fee of $0.3 million and interest payments, are as follows:

	December 31, 2018
	(in thousands)
2020	$1,667
2021	2,000
2022	1,333
Total	$5,000

For the year ended December 31, 2018, the Company recognized $0.2 million of interest expense related to the Loan Agreement.

7. Commitments and Contingencies

Asset Purchase Agreement

In August 2018, the Company entered into an asset purchase agreement with Gilead Sciences, Inc. (Gilead) whereby the Company acquired worldwide rights to the pharmaceutical product momelotinib, an investigational inhibitor of Janus kinase, together with all related intellectual property rights and certain other related assets. The Company paid Gilead an upfront payment of $3.0 million in August 2018. The related expense was included in research and development for the year ended December 31, 2018 in the accompanying consolidated statement of operations. The Company will be required to pay Gilead milestone payments of up to an aggregate of $195.0 million upon the achievement of certain development, regulatory and commercial milestones events, including a milestone payment of $5.0 million upon the dosing of the first patient in a registrational clinical trial. These milestones will be accrued once they are considered probable of occurring. In addition, the Company is required to pay Gilead mid-teen to high twenty percent tiered royalties based upon net sales.

License Agreements

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 I clinical trials. The expense related to these payments was included in research and development for the year ended December 31, 2016. Additional milestone payments of up to an aggregate of $319.5 million may become payable to CPF upon the achievement of certain developmental, regulatory and commercial milestones and 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. The Company will be required to pay Carna milestone payments of up to an aggregate of $270.0 million upon achievement of certain developmental, regulatory and commercial milestone events, including a milestone payment of $4.0 million upon dosing of the first patient in the first Phase 1 clinical trial for SRA141. These milestones will be accrued once they are considered probable of occurring. As of December 31, 2018, the Company had not recorded any milestone payments to Carna. In addition, the Company is required to pay Carna tiered single-digit royalties on net sales of product candidates (as defined under the Carna License Agreement).

Lease Agreements

In February 2015, the Company entered into an operating lease agreement to sublease office space in Vancouver, Canada. In June 2017, the Company entered into a new operating lease agreement to continue leasing the office space in Vancouver, Canada commencing March 1, 2018. The new lease expires on February 28, 2023 and can be extended for an additional term of 5 years.

In January 2016, the Company entered into an operating lease agreement to lease office space near San Francisco, California. The operating lease agreement expires on April 30, 2019. In September 2017, the Company entered into a sublease agreement to sublet the premises to a third party until April 30, 2019. The fair value of the remaining contractual obligation, net of sublease income was included in accrued liabilities in the accompanying consolidated balance sheets as of December 31, 2018 and 2017.

In addition to base rent, these leases require payment of taxes and other operating costs. These operating costs are not included in the table below.

As of December 31, 2018, the aggregate future non-cancelable minimum lease payments associated with these operating leases are as follows:

Years Ending December 31:	Operating Leases
	(in thousands)
2019	$243
2020	208
2021	211
2022	169
Total	$831

The total rent expense for each of the years ended December 31, 2018, 2017 and 2016 was $0.5 million.

Legal

On November 9, 2016, a purported securities class action lawsuit was filed in the United States District Court for the Southern District of New York against the Company and certain of its executive officers (the New York Lawsuit). The New York Lawsuit was brought by purported stockholders of the Company seeking to represent a class consisting of stockholders who purchased stock between July 15, 2015 and

June 6, 2016. The New York Lawsuit asserts claims under Sections 10(b) and 20(a) of the Exchange Act and seeks unspecified damages and other relief. On March 13, 2018, the United States District Court for the Southern District of New York granted the defendants' motion to dismiss and entered a final judgment dismissing the New York Lawsuit with prejudice. Plaintiffs thereafter filed an appeal. On December 3, 2018, the United States Court of Appeals for the Second Circuit affirmed the district court's final judgment of dismissal. The Company believes that the claims in the New York Lawsuit are without merit and intends to defend the lawsuit vigorously. At this point in time, the Company does not expect the outcome of these claims will have a material impact on its consolidated financial statements.

On November 18, 2016, a purported securities class action lawsuit was filed in the Superior Court of the State of California for the County of San Mateo against the Company, certain of its executive officers and directors, and the underwriters for the Company's initial public offering of its common stock. On February 9, 2017, a substantially identical putative class action suit was filed in the Superior Court of the State of California for the County of San Mateo asserting the same claims on behalf of the same putative class (the two lawsuits together, the California Lawsuits). The California Lawsuits were brought by purported stockholders of the Company seeking to represent a class consisting of stockholders who purchased stock pursuant to and/or traceable to the Company's Registration Statement on Form S-1. The lawsuits assert claims under Sections 11 and 15 of the Exchange Act and seek unspecified damages and other relief. On August 1, 2018, all parties reached a mutually acceptable proposed resolution to the California Lawsuits by way of a mediated settlement, which is subject to final approval by the court. While the Company believes that the claims are without merit, it believes settlement will reduce the ultimate cost and distraction of further litigation. The Company does not expect its portion of the settlement amount to have a material impact on its consolidated financial statements.

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.

8. 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 warrant.

	December 31,	
	2018	2017
Outstanding stock options under equity incentive plans	10,504,412	7,470,601
Shares reserved for future option grants under equity plans	1,945,025	1,503,770
Shares reserved under the 2015 employee stock purchase plan	700,000	700,000
Shares reserved under warrant upon contingent events	147,059	—
Outstanding warrant	73,529	—
Total common stock reserved for issuance	13,370,025	9,674,371

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,		
	2018	2017	2016
		(in thousands)	
Research and development	$4,499	$3,966	$3,635
General and administrative	2,297	1,939	1,875
Total stock-based compensation	$6,796	$5,905	$5,510

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,		
	2018	2017	2016
Expected term (in years)	5.3 – 7.0	5.3 – 7.0	5.1 – 9.9
Expected volatility	88 – 91%	86 – 96%	77 – 87%
Risk-free interest rate	2.6 – 3.1%	1.8 – 2.3%	1.1 – 2.4%
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 vesting commencement date and the contractual expiration period of the stock-based award. The expected term for options issued to non-employees is the contractual term.

Expected Volatility—Since the Company has limited information on the volatility of common stock due to its short trading history, the expected volatility is derived from the historical stock volatilities of comparable peer public companies within its industry that are considered to be comparable to the Company's business over a period equivalent to the expected term of the stock-based awards.

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 does it anticipate paying any dividends on its common stock in the foreseeable future.

Forfeiture Rate—Prior to January 1, 2017, the Company recorded stock-based compensation costs related to stock options net of estimated forfeitures. The forfeiture rate was estimated based on an analysis of actual forfeitures experience, analysis of employee turnover behavior and other factors. Effective January 1, 2017, the Company made an accounting policy election to account for forfeitures when they occur.

Fair Value of Common Stock—The fair value of the Company's common stock is used to estimate the fair value of the stock-based awards at grant date.

On January 1, 2017, the Company adopted FASB ASU No. 2016-09 (ASU 2016-09), *Compensation—Stock Compensation (Topic 718)* using the modified retrospective approach, including making an accounting policy election to account for forfeitures when they occur, and thus recorded a $8,000 retrospective adjustment to retained earnings included in the accompanying consolidated statement of stockholders' equity for year ended December 31, 2017. In accordance with this standard, all tax effects related to share-based payments are recorded as part of the provision for income taxes including any accumulated excess tax benefits or deficiencies. Since the Company has incurred net losses since its inception and maintains a full valuation allowance on its net U.S. deferred tax assets, adoption of the new guidance had no impact on the accompanying consolidated statements of operations or cash flow presentation.

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 reserved for issuance under the 2018 Plan was set to 1,500,000. 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 capital stock on the date of grant. 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. As of December 31, 2018, 8,637,065 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 from 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 on the date of grant. 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.

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 Directors 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, 2017	1,503,770	7,470,601	$3.09	8.12	$12,363
Awards authorized under the 2015 Plan	2,095,808				
Awards authorized under the 2018 Plan	1,500,000				
Options granted	(3,566,150)	3,566,150	2.35		
Options exercised	—	(120,742)	1.49		
Options forfeited/cancelled	411,597	(411,597)	2.98		
Outstanding—December 31, 2018	1,945,025	10,504,412	$2.86	7.80	$ 545
Exercisable—December 31, 2018		5,797,657	$3.10	7.00	$ 542
Vested and expected to vest—December 31, 2018		10,504,412	$2.86	7.80	$ 545

The weighted-average grant date fair values of options granted during the years ended December 31, 2018, 2017 and 2016 was $1.75, $1.09 and $2.19 per share. The aggregate intrinsic value of options exercised was $0.2 million, $0.2 million and $1.2 million for the years ended December 31, 2018, 2017 and 2016. The total grant date fair value of options vested for the years ended December 31, 2018, 2017 and 2016 was $5.9 million, $6.5 million and $6.1 million.

As of December 31, 2018, total unrecognized stock-based compensation related to unvested stock options was $8.0 million, which the Company expects to recognize over a remaining weighted-average period of 2.1 years.

2015 Employee Stock Purchase Plan

The Company adopted the 2015 Employee Stock Purchase Plan (ESPP) and initially reserved 700,000 shares of common stock as of its effective date of July 15, 2015. The number of shares initially reserved for issuance under the ESPP will increase automatically on January 1 for nine years from the first offering date by the number of shares equal to 1% of the total outstanding shares of the Company's common stock as of the immediately preceding December 31. The aggregate number of shares issued over the term of the 2015 Employee Stock Purchase Plan will not exceed 3,400,000 shares of common stock.

Under the ESPP, participants are offered the options to purchase shares of Company's common stock at a 15% discount during a series of discrete offering periods, subject to any plan limitations. The ESPP will not become effective until such time as the Compensation Committee determines in the future, and as of December 31, 2018, the initial offering periods had not commenced. As of December 31, 2018, no shares of common stock have been issued to employees participating in the ESPP and 700,000 shares were available for issuance under the ESPP.

10. Income Taxes

On December 22, 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (Tax Act). The Tax Act significantly revised U.S. tax law by, among other

provisions, lowering the U.S. federal statutory income tax rate from 35% to 21%, changing rules related to uses and limitations of net operating loss carryforwards created in tax years beginning after December 31, 2017 and eliminating or reducing certain income tax deductions.

The effects of changes in tax laws are required to be recognized in the period in which the legislation is enacted. However, due to the complexity and significance of the Tax Act's provisions, the SEC staff issued Staff Accounting Bulletin No. 118 (SAB 118), which allowed companies to record the tax effects of the Tax Act on a provisional basis based on a reasonable estimate, and then, if necessary, subsequently adjust such amounts during a limited measurement period as more information becomes available. The measurement period ends when a company has obtained, prepared, and analyzed the information necessary to finalize its accounting, but cannot extend beyond one year from enactment.

In connection with the Company's initial analysis of the Tax Act, it recorded a decrease of its net deferred tax assets of $7.2 million for the period ended December 31, 2017, to account for the rate reduction. This did not have an impact on the Company's financial statements since its U.S. deferred tax assets are fully offset by a valuation allowance. The Company finalized the analysis during the third quarter of 2018, with no material changes to the initial estimated decrease of its net deferred tax assets, and the accounting is now complete.

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

	Year Ended December 31,		
	2018	2017	2016
	(in thousands)		
United States	$(54,395)	$(42,425)	$(48,244)
International	758	566	520
Loss before provision for (benefit from) income taxes, net	$(53,637)	$(41,859)	$(47,724)

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

	Year Ended December 31,		
	2018	2017	2016
	(in thousands)		
Current tax provision (benefit):			
Federal	$ —	$—	$—
State	—	—	—
Foreign	(180)	183	170
Total current tax provision (benefit)	(180)	183	170
Deferred tax provision (benefit):			
Foreign	(122)	(27)	(27)
Total deferred tax provision (benefit)	$(122)	$ (27)	$ (27)
Total provision for (benefit from) income taxes	$(302)	$156	$143

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,		
	2018	2017	2016
Federal statutory rate	21.0%	34.0%	34.0%
Effect of:			
Change in valuation allowance	(22.2)	69.5	(33.5)
Federal Tax Credit	2.4	(0.9)	1.6
State income tax benefit, net of federal benefit	0.3	0.1	0.1
Effect of ownership change on deferred tax assets	—	(84.8)	—
US tax reform deferred impact on tax rate change	—	(17.3)	—
Other permanent items	(1.0)	(1.0)	(2.5)
Total provision for (benefit from) income taxes	0.5%	(0.4)%	(0.3)%

The components of the deferred tax assets are as follows:

	December 31,	
	2018	2017
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 18,347	$ 9,183
Stock based compensation	3,642	2,444
License fee	2,008	1,346
59 (e) expenditures and amortization	1,435	1,435
Research and development credits	1,137	365
Other	972	698
Gross deferred tax assets	27,541	15,471
Valuation allowance	(27,317)	(15,395)
Total deferred tax assets	224	76
Deferred tax liabilities:		
Other	39	13
Total deferred tax liabilities	39	13
Total net deferred tax assets	$ 185	$ 63

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 $27.3 million and $15.4 million against the net U.S. deferred tax assets as of December 31, 2018 and 2017. The net valuation allowance increased by $11.9 million for the year ended December 31, 2018. The net valuation allowance decreased by $29.0 million for the year ended December 31, 2017, primarily due to the effects of an ownership change and the Tax Act rate change.

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 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.

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 ownership changes that have occurred, certain of the Company's tax attributes existing as of the date of the ownership change are not be available for future use. The loss of these attributes does not have any impact on the financial statements since the net U.S. deferred tax assets are offset by a full valuation allowance.

As of December 31, 2018, the Company has U.S. federal tax net operating loss carryforwards of $74.3 million, of which $31.4 million expire in 2037 and $42.9 million are eligible for indefinite carryforward, and state operating loss carryforwards of $56.3 million expiring in years ranging from 2022 to 2038. The Company also has U.S. net tax credit carryforwards of $1.1 million which begin to expire in 2032 and net tax credit carryforwards in a foreign jurisdiction of $0.2 million which begin to expire in 2037.

Uncertain Tax Positions

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

	Year Ended December 31,		
	2018	2017	2016
	(in thousands)		
Beginning balance	$ 43	$ 311	$232
Increases based on tax positions related to prior years	109	—	—
Decreases based on tax positions related to prior years	—	(79)	—
Decreases due to ownership change	—	(232)	—
Increases based on tax positions in current year	112	43	79
Settlement	—	—	—
Lapse of statute of limitations	—	—	—
Ending balance	$264	$ 43	$311

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, 2018 and 2017, 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 2015 through 2017 remain open to examination by the United States, various state jurisdictions and Canada. The tax year ended December 31, 2017 remains open to examination in Australia. Other than routine reviews by tax authorities for tax credits claimed, the Company is not under examination in any tax jurisdiction for any year.

11. Restructuring Costs

In June 2016, the Company halted investment in PNT2258 and the DNAi platform and closed the related Phase 2 clinical trials to further enrollment. As a result, the Company closed its research facility in Plymouth, Michigan, renegotiated and terminated certain contracts, and implemented staff reductions in the United States and Canada.

The following table summarizes restructuring activities for the years ended December 31, 2018, 2017 and 2016:

	Contract Termination	Employee Termination	Asset Impairment	Total
		(in thousands)		
Accrual balance at December 31, 2015	$ —	$ —	$ —	$ —
Restructuring costs charged to research and development expense	2,249	—	—	2,249
Restructuring costs charged to general and administration expense	5	332	130	467
Non-cash charges	(681)	—	(130)	(811)
Cash payments	(909)	(233)	—	(1,142)
Accrual balance at December 31, 2016	$ 664	$ 99	$ —	$ 763
Adjustments to research and development expense	(69)	—	—	(69)
Cash payments	(458)	(99)	—	(557)
Accrual balance at December 31, 2017	$ 137	$ —	$ —	$ 137
Adjustments to research and development expense	(99)	—	—	(99)
Cash payments	(5)	—	—	(5)
Accrual balance at December 31, 2018	$ 33	$ —	$ —	$ 33

The accrual balance, which was included in accrued liabilities in the accompanying balance sheet, is currently expected to be substantially paid by 2019.

12. Selected Quarterly Financial Data (Unaudited)

The following tables present certain selected unaudited consolidated quarterly financial information for each of the eight quarters ended December 31, 2018. This consolidated quarterly information has been prepared on the same basis as the consolidated financial statements and includes all adjustments necessary to state fairly the information for the periods presented. The selected consolidated quarterly financial results from operations for the years ended December 31, 2018 and 2017 are set forth therein.

	Fiscal 2018 Quarter Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(in thousands, except per share amounts)			
Operating expenses	$ 11,754	$ 12,963	$ 16,051	$ 14,649
Net loss[1]	$(11,525)	$(11,960)	$(15,567)	$(14,283)
Basic and diluted net loss per share	$ (0.19)	$ (0.16)	$ (0.21)	$ (0.19)

	Fiscal 2017 Quarter Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(in thousands, except per share amounts)			
Operating expenses	$ 11,154	$ 10,477	$10,183	$ 10,805
Net loss[1]	$(11,092)	$(10,329)	$ (9,995)	$(10,599)
Basic and diluted net loss per share	$ (0.26)	$ (0.20)	$ (0.19)	$ (0.20)

(1) Net loss from continuing operations and net loss attributable to common stockholders are the same as net loss for all periods presented.

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, 2018, 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, 2018, 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

This annual report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to exemptions provided to issuers that qualify as an "emerging growth company," as defined in Section 2(a) of the Securities Act of 1933, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. However, for as long as we remain an "emerging growth company" as defined in the JOBS Act, we intend to take advantage of the exemption permitting us not to comply with the requirement that our independent registered public accounting firm provide an attestation on the effectiveness of our 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, 2018, 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, 2018.

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, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

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 2019 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 2019 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 2019 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 2019 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 2019 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	
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 11, 2017	
3.3	Restated Bylaws.	S-1	333-204921	3.4	June 12, 2015	
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	
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 and forms of award agreements thereunder.	S-1	333-204921	10.3	July 6, 2015	
10.4*	2015 Employee Stock Purchase Plan.	S-1	333-204921	10.4	July 6, 2015	

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
10.5*	2018 Equity Inducement Plan and forms of award agreements thereunder.	10-Q	001-37490	10.2	November 8, 2018	
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*	Form of Employment Agreement between the Registrant and Nick Glover.	S-1	333-204921	10.7	July 6, 2015	
10.9+	License Agreement dated May 26, 2016 between the Registrant and Carna Biosciences, Inc.	10-Q	001-37490	10.1	August 12, 2016	
10.10+	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	
10.11	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	
10.12+	Loan and Security Agreement dated August 21, 2018, by and between the Registrant and Silicon Valley Bank.	10-Q	001-37490	10.1	November 8, 2018	
21.1	Subsidiaries of the Registrant.					X
23.1	Consent of independent registered public accounting firm.					X
24.1	Power of Attorney. Reference is made to the signature page hereto.					124
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

Exhibit Number	Description of Document	Incorporated by reference				Filed Herewith
		Form	File No.	Exhibit	Filing Date	
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	XBRL Instance Document.					X
101.SCH	XBRL Schema Linkbase Document.					X
101.CAL	XBRL Calculation Linkbase Document.					X
101.DEF	XBRL Definition Linkbase Document.					X
101.EXT	XBRL Extension label Linkbase Document.					X
101.PRE	XBRL Presentation Linkbase Document.					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.

† 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: February 28, 2019

SIERRA ONCOLOGY, INC.

By: /s/ Nick Glover
Nick Glover
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Nick Glover 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/ Nick Glover Nick Glover	President, Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2019
/s/ Sukhi Jagpal Sukhi Jagpal	Chief Financial Officer (Principal Accounting and Financial Officer)	February 28, 2019
/s/ Donald Parfet Donald Parfet	Chairman of the Board	February 28, 2019
/s/ Andrew Allen Andrew Allen	Director	February 28, 2019
/s/ Jeffrey H. Cooper Jeffrey H. Cooper	Director	February 28, 2019
/s/ Daniel Estes Daniel Estes	Director	February 28, 2019
/s/ Tran Nguyen Tran Nguyen	Director	February 28, 2019

Signature	Title	Date
/s/ Nicole Onetto Nicole Onetto	Director	February 28, 2019
/s/ Robert Pelzer Robert Pelzer	Director	February 28, 2019

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