UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2020

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 001-38096

G1 THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**26-3648180**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709
(Address of principal executive offices including zip code)
Registrant's telephone number, including area code: (919) 213-9835

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock $.0001 par value	**GTHX**	**The Nasdaq Stock Market**

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

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

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

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

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

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant as of June 30, 2020, the last business day of the Registrant's most recently completed second fiscal quarter, was $820.8 million based on the closing price of the shares of common stock on The Nasdaq Stock Market on that date.

The number of shares of the Registrant's Common Stock outstanding as of February 22, 2021 was 41,959,379.

Documents Incorporated by Reference

Portions of the Registrant’s Definitive Proxy Statement relating to the Annual Meeting of Stockholders, scheduled to be held on June 17, 2021, are incorporated by reference into Part III of this report. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the Registrant’s fiscal year ended December 31, 2020.

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Special note regarding forward-looking statements

This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "will," "would," or the negative of these words or other comparable terminology.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in the "Risk Factors" section 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. Such forward looking statements speak only as of the date of this Annual Report. Except as may be required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

You should read this Annual Report and the documents that we have filed as exhibits to 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.

This Annual Report includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

PART I

Item 1. Business.

Overview

We are a commercial-stage biopharmaceutical company focused on the development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. Our first FDA-approved product, COSELA™ (trilaciclib) is the first and only therapy indicated to proactively help protect bone marrow from the damage of chemotherapy (myeloprotection) and is the first innovation in managing myelosuppression in decades. Our therapeutic candidates were developed from a technology platform that targets key cellular pathways including transient arrest of the cell cycle at the G1 phase, prior to the beginning of DNA replication. Our therapies are designed to improve outcomes for patients across multiple oncology indications.

We were incorporated under the laws of the State of Delaware in May 2008 under the name "G-Zero Therapeutics, Inc." In September 2012, we changed our name to "G1 Therapeutics, Inc." Our principal executive offices are located at 700 Park Offices Drive, Suite 200, Research Triangle Park, NC 27709, and our telephone number is (919) 213-9835.

We manage our operations as a single segment for the purposes of assessing performance and making operating decisions. All of our assets are held in the United States.

"G1 Therapeutics," "COSELA" and our logo are our trademarks. All other service marks, trademarks and trade names appearing in this Annual Report 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. We shall use "COSELA" when we are referring to our FDA approved drug and "trilaciclib" when we are referring to our development of COSELA for additional indications. "Myeloprotection" is synonymous with the term "myelopreservation." We used "myelopreservation" in our communications and disclosures prior to the FDA's approval of trilaciclib (COSELA) and we will use the term "myeloprotection" following FDA's approval in order to align more closely with the FDA's terminology.

Product Pipeline

We are advancing two clinical stage programs. Our lead compound trilaciclib is a first-in-class therapy designed to improve outcomes for patients who are treated with chemotherapy. Trilaciclib helps protect HSPCs in bone marrow by transiently inhibiting CDK4/6 leading to a temporary arrest of susceptible host cells during chemotherapy in ES-SCLC patients. This reduces the duration and severity of neutropenia and other myelosuppressive consequences of chemotherapy. In addition, trilaciclib activates and enhances the immune system response driving increased anti-tumor efficacy, which we continue to explore in clinical trials.

On February 12, 2021, COSELA™ (trilaciclib) for injection was approved by the U.S. Food and Drug Administration (FDA) to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive stage small cell lung cancer (ES-SCLC). We are also exploring potential use of trilaciclib in a variety of other tumors, including colorectal cancer (CRC), triple negative breast cancer (TNBC), neoadjuvant breast cancer, non-small cell lung cancer (NSCLC), and bladder cancer.

Rintodestrant is an oral selective estrogen receptor degrader (SERD) which we are developing as a monotherapy and in combination with a CDK4/6 inhibitor, Ibrance® (palbociclib), for the treatment of ER+, HER2- breast cancer. We will evaluate partnering options for rintodestrant following a data read-out from our ongoing combination study with palbociclib.

In 2020, we out-licensed global rights to lerociclib, an internally discovered and differentiated oral CDK4/6 inhibitor designed to enable more effective combination treatment strategies across multiple oncology indications. We also have intellectual property focused on cyclin-dependent kinase targets.

G1 Therapeutics Product Pipeline

Candidate	Indication	Status	Development & Commercialization Rights (all indications)
trilaciclib	Extensive-stage small cell lung cancer (ES-SCLC)	COSELA (trilaciclib) Approved by FDA	G1 Therapeutics owns all global development and commercial rights across all indications, with the exception of Greater China (Simcere)
	Colorectal cancer (CRC)	Registrational trial (initiated in 2020)	
	1L/2L Triple negative breast cancer (TNBC)	Registrational trial (initiating in 1H 2021)	
	Neoadjuvant breast cancer (I-SPY 2 TRIAL™)	Phase 2 trial (initiated in 2020)	
	2L/3L Non-small cell lung cancer (NSCLC)	Phase 2 trial (initiating in 1H 2021)	
	1L Bladder cancer	Phase 2 trial (initiating in 1H 2021)	
rintodestrant	ER+, HER2- breast cancer	Phase 2a (initiated in 2019)	G1 - Global
lerociclib	Multiple	Clinical Stage	EQRx: Global and Japan (ex. Asia Pacific) Genor Biopharma: Asia Pacific (ex. Japan)

Trilaciclib helps protect HSPCs in bone marrow by transiently inhibiting CDK4/6 leading to a temporary arrest of susceptible host cells during chemotherapy in ES-SCLC patients. This reduces the duration and severity of neutropenia and other myelosuppressive consequences of chemotherapy. In addition, trilaciclib has demonstrated immune system response enhancement which we are exploring in clinical trials to show increased anti-tumor efficacy.

Trilaciclib, a transient IV CDK4/6 inhibitor, is a novel therapeutic approach which is given before chemotherapy that temporarily blocks progression through the cell cycle. This provides two benefits. First, it proactively helps protect HSPCs in bone marrow leading to preservation of neutrophils, erythrocytes, and platelets (called myeloprotection) which reduces the occurrences and severity of neutropenia and other myelosuppressive consequences of chemotherapy. This myeloprotection benefit has been conclusively proven in double-blind placebo-controlled clinical trials in extensive-stage small cell lung cancer. Second, trilaciclib activates and enhances the immune system response driving increased anti-tumor efficacy, which we are exploring in clinical trials. Our randomized clinical trials have demonstrated that trilaciclib can provide myeloprotection benefits and has the potential to improve survival as a result of its anti-tumor efficacy benefit.

Chemotherapy is an effective and important weapon against cancer. However, chemotherapy does not differentiate between healthy cells and cancer cells and kills both, including important stem cells in the bone marrow (hematopoietic stem and progenitor cells, or HSPCs) that produce white blood cells, red blood cells and platelets, and immune cells. This chemotherapy-induced bone marrow damage is known as myelosuppression. When white blood cells, red blood cells and platelets become depleted, chemotherapy patients are at increased risk of infection, experience anemia and fatigue, and are at increased risk of bleeding. Myelosuppression often requires the administration of rescue interventions such as growth factors and blood or platelet transfusions and may also result in chemotherapy dose delays and reductions. Immune cell damage may decrease the ability of the immune system to fight the cancer, as well as infection.

On February 12, 2021, COSELA was approved by the FDA to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC. We expect COSELA to be commercially available through G1's specialty distributor network in early March. COSELA is administered intravenously as a 30-minute infusion completed within 4 hours prior to the start of chemotherapy on each day that chemotherapy is administered, and is the first and only FDA-approved therapy that helps proactively deliver multilineage myeloprotection to patients with extensive-stage small cell lung cancer being treated with chemotherapy. The approval of COSELA is based on data from three randomized, placebo-controlled trials that showed patients receiving COSELA prior to chemotherapy had clinically meaningful and

statistically significant reduction in the duration and severity of neutropenia, reduction of red blood cell transfusions, as well as improvements in other myeloprotection measures, compared to patients receiving chemotherapy without COSELA.

In June 2020, we entered into a three-year co-promotion agreement for COSELA in the United States and Puerto Rico with Boehringer Ingelheim. The agreement is limited to support for SCLC. Under the terms of the agreement, we will book revenue in the United States and Puerto Rico and retain development and commercialization rights to COSELA. We will lead marketing, market access and medical engagement initiatives; Boehringer Ingelheim will lead sales force engagements.

In August 2020, we entered into an exclusive license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd ("Simcere") for development and commercialization rights for trilaciclib in all indications in Greater China (mainland China, Hong Kong, Macau and Taiwan). Under the terms of the agreement, we received an upfront payment of $14.0 million and will be eligible to receive up to $156.0 million in development and commercial milestone payments. Simcere will also pay us tiered low double-digit royalties on annual net sales of trilaciclib in Greater China. As part of the agreement, Simcere will participate in global clinical trials of trilaciclib and the companies will be responsible for all development and commercialization costs in their respective territories.

We are also executing on our tumor-agnostic strategy to evaluate the potential benefits of trilaciclib to patients with other tumors that are treated with chemotherapy. We have two on-going trials: a pivotal 1L colorectal cancer (CRC) study and a Phase 2 neoadjuvant breast cancer (I-SPY 2). We intend to initiate another pivotal study in mTNBC (including 1L and 2L patients) and have two additional Phase 2 studies: a 2L/3L non-small cell lung cancer (NSCLC) trial in post-checkpoint patients and a 1L bladder cancer trial with chemotherapy and a checkpoint inhibitor. These studies across treatment settings and tumor types will evaluate trilaciclib's dual benefits in both multi-lineage myeloprotection and anti-tumor efficacy.

Pivotal 1L Colorectal Cancer (CRC)

We enrolled the first patient in a randomized, placebo-controlled registrational trial of trilaciclib in colorectal cancer (CRC) in the first quarter of 2021. CRC is a large indication commonly treated with 5-FU-based chemotherapy. We have extensive preclinical research demonstrating myeloprotection and potential efficacy in 5-FU-based regimens with trilaciclib. Our ongoing 1L CRC trial is with FOLFOXIRI, which is the most efficacious chemo regimen in this tumor but is also highly myelosuppressive. By reducing the toxicity of FOLFOXIRI, we believe we will significantly expand its use in CRC and potentially improve overall survival.

1L/2L Metastatic Triple-Negative Breast Cancer (mTNBC)

In 2017, we initiated a randomized Phase 2 trial of trilaciclib in patients with first-/second-/third-line metastatic triple-negative breast cancer (mTNBC) receiving gemcitabine and carboplatin (GC). Enrollment was completed in the second quarter of 2018. At the 2018 San Antonio Breast Cancer Symposium (SABCS), we presented preliminary trilaciclib data demonstrating improvement in progression-free survival (PFS). In September 2019, we presented updated data demonstrating significant improvement in overall survival (OS) (preliminary). Though the trial did not meet the primary myeloprotection endpoints, patients receiving trilaciclib were able to receive approximately 50% more cumulative dose of chemotherapy, without additional hematological toxicity. These data were presented at the 2019 ESMO Congress, and were concurrently published in The Lancet Oncology. Updated safety and efficacy data from this trial were presented at the 2020 SABCS. Data included that compared to GC alone (Group 1), OS was improved in both trilaciclib arms (Groups 2 and 3) (Group 2: HR=0.31, p=0.0016; Group 3: HR=0.40, p=0.0004). Median OS was 12.6 months in Group 1, not reached for Group 2, and 17.8 months in Group 3. The median OS for Groups 2 and 3 combined was 19.8 months (HR=0.37, p<0.0001). OS findings in patients receiving trilaciclib were consistent with previously reported data from this trial. The median OS for GC alone (Group 1, 12.6 months) was consistent with the previous trial findings and historical data. Patients with both PD-L1-positive and PD-L1-negative tumors treated with trilaciclib and GC demonstrated improvement in OS compared to patients receiving GC alone, with the PD-L1-positive subset achieving statistically significant improvement. Further, data from T cell clonality analyses suggest that administering trilaciclib prior to chemotherapy enhanced immune system function. These compelling Phase 2 data supported the potential effectiveness of trilaciclib in mTNBC. We expect to initiate a randomized, placebo-controlled registrational trial in 1L patients and 2L post-checkpoint patients with mTNBC in the first half of 2021. TNBC is a difficult and aggressive tumor to treat with many new therapies only effective in certain subpopulations.

Phase 2 Neoadjuvant Breast Cancer (I-SPY 2)

In January 2020, we announced that trilaciclib will be included in a new randomized, investigational treatment arm for the ongoing Phase 2 I-SPY 2 TRIAL™ for neoadjuvant treatment of locally advanced breast cancer. The trial, initiated in the second quarter of 2020 and run by the non-profit Quantum Leap Healthcare Collaborative, is designed to rapidly screen promising experimental treatments and identify those most effective in specific patient subgroups based on molecular characteristics (biomarker signatures). Trilaciclib will be evaluated across all high-risk, early-stage breast cancer subtypes (including HR+, HER2+ and triple-negative breast cancer). All patients will receive standard neoadjuvant treatment, including chemotherapy (and anti-HER2 Mab for HER2+ disease)

prior to surgical resection of breast tissue. Biomarker data to evaluate the impact of trilaciclib on the tumor immune microenvironment, as well as pre-specified endpoints to evaluate anti-tumor efficacy and myeloprotection will be collected.

2L/3L Non-Small Cell Lung Cancer (NSCLC)

Evaluating trilaciclib in a Phase 2 2L/3L NSCLC (post-checkpoint setting) will provide us with meaningful data in an area of high unmet with a large patient population. NSCLC is a known immunogenic tumor which may provide trilaciclib an opportunity to increase anti-tumor efficacy through its distinct mechanism even after checkpoint inhibitors have failed. There is also a high complementary commercial fit with our initial SCLC indication. We expect to initiate this trial in the first half of 2021.

1L Bladder Cancer

We intend to initiate a 1L bladder cancer trial in the first half of 2021 with chemotherapy and a checkpoint inhibitor. There is a strong rationale to evaluate trilaciclib in 1L bladder cancer: (1) bladder is a known immunogenic tumor proven to be responsive to chemotherapy; (2) the most common chemotherapy regimen used in 1L bladder is gemcitabine and platinum, which is similar to the chemotherapy regimen in our TNBC study (gemcitabine and carboplatin) where we showed significant OS benefits; and (3) we have observed synergistic benefits combining trilaciclib with checkpoints.

Market opportunities for trilaciclib

Cancer is the second leading cause of death in the United States with an estimated 1.8 million new cases and 607,000 deaths in 2020, according to the American Cancer Society. Chemotherapy is the standard of care treatment for multiple cancers. We estimate that more than one million patients in the United States receive chemotherapy annually.

Chemotherapy has significant clinical utility and continues to be the most effective treatment for many cancers. However, it also damages HSPCs (myelosuppression) and the immune system (immunosuppression), leading to severe adverse effects and limiting anti-tumor activity. Chemotherapy-induced myelosuppression causes abnormally low numbers of red blood cells, or anemia, abnormally low numbers of neutrophils, or neutropenia, and/or abnormally low numbers of platelets, or thrombocytopenia. The treatment of myelosuppressive side effects of chemotherapy is a large market opportunity. The only current treatment for chemotherapy-induced myelosuppression are rescue interventions like growth factors and/or transfusions. Two main types of commercially available growth factors are: granulocyte-colony stimulating factor, or GCSF, and erythropoiesis stimulating agents, or ESAs. GCSF increases production of neutrophils in patients to reduce the incidence of infection after chemotherapy. GCSF does not preserve the function of the bone marrow and immune system from chemotherapy damage. ESAs increase production of red blood cells in patients. Accordingly, ESAs also do not preserve the function of the bone marrow and immune system from chemotherapy. ESA use in oncology is limited due to a “black box” warning related to death and serious cardiovascular events. Despite these limitations, we estimate that annual worldwide sales of growth factor support therapy in oncology to be approximately $5 billion.

- *Extensive-stage small cell lung cancer (ES-SCLC).* According to the American Cancer Society, SCLC accounts for approximately 14% of all lung cancers. Approximately 30,000 people are treated annually in the United States for ES-SCLC across first line through third line. First-line treatment of ES-SCLC in the United States is typically a chemotherapy regimen of carboplatin and etoposide, which has significant myelosuppressive side effects. Combination treatment with chemotherapy and immunotherapy has emerged as the standard of care in the United States. While these patients often respond to first-line therapy, approximately 90% progress within one year and die within two years. Five-year survival rates are less than 5% for patients with extensive-stage SCLC. Topotecan, approved for SCLC in 2007, is a standard treatment used in the second/third line setting and is highly myelosuppressive. Based on market research we have completed to date, many physicians see proactive myeloprotection as a better approach for patients and would incorporate trilaciclib into their SCLC treatment regimen. We believe the SCLC opportunity exceeds $500 million in worldwide annual net sales at peak.
- *Colorectal cancer (CRC).* We are evaluating the use of trilaciclib in colorectal cancer in a Phase 3 trial that initiated in the fourth quarter of 2020 and enrolled the first patient in the first quarter of 2021. Globally, more than 500,000 patients are diagnosed with colorectal cancer each year. In the U.S., there are nearly 150,000 new cases of colorectal cancer diagnosed each year. Chemotherapy is the standard of care for colorectal cancer, and the majority of patients in the U.S., Europe and Japan receive chemotherapy as part of their treatment regimen.

- *Breast cancer*. We are evaluating the use of trilaciclib in a variety of breast cancers, including metastatic triple negative breast cancer (mTNBC) and other high-risk, early-stage breast cancer subtypes. According to the World Health Organization, an estimated 2.1 million cases of breast cancer are diagnosed annually worldwide. TNBC makes up approximately 15-20% of such diagnosed breast cancers. Because mTNBC cells lack key growth-signaling receptors, patients do not respond well to medications that block estrogen, progesterone, or HER2 receptors. Instead, treating mTNBC typically involves chemotherapy, radiation, and surgery. In general, survival rates tend to be lower with mTNBC compared to other forms of breast cancer, and mTNBC is also more likely than some other types of breast cancer to return after it has been treated, especially in the first few years after treatment.
    - We expect to initiate a registrational trial in mTNBC in the first half of 2021. This trial will evaluate trilaciclib in combination with a chemotherapy regimen of gemcitabine/carboplatin in two separate cohorts: 1) as first-line treatment in 170 patients who are checkpoint-naive; and 2) as second-line treatment in 70 patients who are checkpoint-failures. Both cohorts are adequately and independently powered.
    - Trilaciclib has been included in a randomized, investigational treatment arm of the ongoing Phase 2 I-SPY 2 TRIAL for neoadjuvant treatment of locally advanced breast cancer. The study will generate data that will allow us to evaluate trilaciclib in combination with several broadly-used chemotherapy classes and a range of breast cancer subtypes. Enrollment began in the second quarter of 2020.
- We are also evaluating the use of trilaciclib in bladder cancer and NSCLC, and plan to initiate Phase 2 trials in both indications in the first half of 2021.
    - *Bladder cancer.* There are over 80,000 new cases of bladder cancer diagnosed in the U.S. each year.
    - *Non-small cell lung cancer (NSCLC)*. According to the American Cancer Society, NSCLC accounts for up to 85% of all lung cancers.

There have been a number of positive registrational studies and approvals of checkpoint inhibitors in combination with chemotherapy, and these combination regimens are emerging as a standard of care in multiple tumor types. Data from our trial of trilaciclib in combination with the checkpoint inhibitor Tecentriq showed myeloprotection benefits without impairing efficacy. The Phase 2 bladder cancer trial will explore the use of trilaciclib in combination with chemotherapy and a checkpoint inhibitor. We believe trilaciclib may improve outcomes for patients receiving either chemotherapy or a regimen of chemotherapy with an immunotherapy agent.

Advantages of trilaciclib

Trilaciclib is a transient inhibitor of CDK4/6. The mechanism of action of trilaciclib enables ES-SCLC patients to better tolerate chemotherapy, helps protect the immune system from damage, enhances the immune system through transient arrest of proliferation of T lymphocytes, and activates anti-tumor immunity. Trilaciclib has demonstrated immune system response enhancement which we are exploring in clinical trials to show increased anti-tumor efficacy. As a result, we believe that treating patients with trilaciclib prior to the administration of chemotherapy or chemotherapy/immunotherapy regimens may have the following benefits and advantages:

- *Potential to decrease the incidence of chemotherapy-induced myelosuppression*. Trilaciclib has been rationally designed and optimized to preserve HSPCs from damage by chemotherapy, thereby minimizing cytopenias across neutrophils, red cells, and platelets. Trilaciclib has the potential to decrease the clinically relevant consequences of these cytopenias and improve patient outcomes.
- *Potential to reduce chemotherapy dose-delays and dose reductions.* Chemotherapy-induced myelosuppression is the major dose limiting toxicity of chemotherapy and can lead to dose reductions and schedule delays that can limit therapeutic benefit. Trilaciclib has been designed specifically to minimize myelosuppression and has the potential to enable maintenance of the indicated and planned chemotherapeutic dose and schedule.
- *Potential to improve the patient experience as measured by validated Patient Reported Outcomes (PRO) instruments*. PRO data from our randomized trials demonstrate that patients receiving trilaciclib report less fatigue and improved physical and functional well-being.
- *Potential for use with chemotherapy/immune checkpoint inhibitors combinations.* Immune checkpoint inhibitors are often combined with chemotherapy. We have demonstrated that trilaciclib mitigates myelosuppression in first-line SCLC patients treated with the immune checkpoint inhibitor Tecentriq and chemotherapy.
- *Potential broad applicability*. We believe trilaciclib has the potential to benefit patients treated with multiple myelosuppressive chemotherapeutic regimens across a wide range of tumor types.
- *Convenience of administration*. Trilaciclib is designed to be administered via an IV infusion prior to chemotherapy treatment. This dosing regimen fits with standard clinical practice for chemotherapy administration with or without checkpoint inhibitors.

- *Potential to reduce the cost of rescue interventions*. Chemotherapy-induced myelosuppression leads to severe adverse side effects, such as fatigue due to anemia, infections due to neutropenia, and bleeding due to thrombocytopenia. These adverse side effects often require costly rescue interventions such as hospitalizations, transfusions, antibiotic usage and/or treatment with growth factor support. Because trilaciclib has been designed specifically to minimize myelosuppression, we believe that it has the potential to reduce these costs. The positive multilineage myeloprotection data we have reported to date and our market research with payers supports the value proposition of trilaciclib.
- *Potential to preserve/enhance anti-tumor immunity and prolong OS in certain settings.* Chemotherapy can damage the immune system and impair anti-tumor immunity. Trilaciclib has demonstrated the potential to preserve and enhance immune system function during chemotherapy. Trilaciclib has the ability to improve anti-tumor efficacy through a combination of three potential factors: (1) myeloprotection benefits increasing patients' ability to receive more chemotherapy, (2) protection of the immune system allowing it to work after chemotherapy, and (3) enhancing anti-tumor immune response by (a) reducing immunosuppressive Treg populations, (b) activating T-cell mediated response, and (c) enhancing tumor antigen presentation. The improvement in OS observed in the randomized trial of TNBC patients may be due to trilaciclib's ability to enhance anti-tumor immunity during chemotherapy.

Trilaciclib: preclinical and clinical development

Preclinical development

We have published extensive biochemical, cellular and *in vivo* data on trilaciclib. Our preclinical data show that trilaciclib can induce transient and reversible cell-cycle arrest of HSPCs; helps protect HSPCs from damage by chemotherapy; preserve bone marrow and immune system function; improve CBC recovery; helps protect from bone marrow exhaustion; prevent myeloid skewing and consequent lymphopenia; activate T-cells in the tumor microenvironment; and enhance chemotherapy and checkpoint inhibitor anti-tumor activity.

Completed Phase 1 clinical trial

In 2015, we completed a Phase 1 clinical trial of trilaciclib in 45 healthy volunteers in the Netherlands. In this trial, subjects in seven cohorts were administered a single ascending dose of trilaciclib between 6 mg/m² and 192 mg/m². The purpose of this trial was to evaluate the safety including dose limiting toxicities, or DLTs, serious adverse events, or SAEs, adverse events, or AEs, and pharmacokinetics, or PK, and identify a biologically effective dose of trilaciclib. Published data from this trial demonstrated that trilaciclib was well tolerated, with no DLTs or SAEs reported. These data demonstrated that the administration of trilaciclib resulted in the robust cell-cycle arrest of HSPCs for at least 32 hours and supported a starting dose of 200 mg/m ^{2} for the initial studies in patients.

Completed randomized clinical trials
Trilaciclib (IV CDK4/6 inhibitor):

Indications	**Regimen**	**Status**	**Phase**	**Publications**
1st-line Small Cell Lung Cancer (study 1 in package insert)	+Tecentriq/ carboplatin/ etoposide	COSELA™ (trilaciclib) approved to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC.	2	International Journal of Cancer (Daniel *et al.)*, December 2020
1st -line Small Cell Lung Cancer (study 2 in package insert)	+ etoposide/ carboplatin		1b/2	Annals of Oncology (Weiss *et al.)* August 2019
2nd /3rd –line Small Cell Lung Cancer (study 3 in package insert)	+ topotecan		1b/2	Advances in Therapy (Hart *et al.)*, November 2020
metastatic Triple Negative Breast Cancer	+gemcitabine/carboplatin	Phase 3 in 1H 2021	2	Lancet Oncology (Tan *et al.*), September 2019

Phase 2 clinical program in SCLC (study 1 in package insert)

Based on these encouraging preliminary data, we advanced both SCLC trials into the randomized, placebo-controlled, double-blind Phase 2 segment. Enrollment in the first-line SCLC Phase 2 trial was completed in the second quarter of 2017 and positive multilineage myeloprotection results were reported in March 2018, with additional data reported at the European Society for Medical Oncology (ESMO) 2018 Congress and published in Annals of Oncology (Weiss *et al*.) in 2019. Enrollment in the second-/third-line SCLC Phase 2 trial was completed in the second quarter of 2018, with positive multilineage myeloprotection data reported in the fourth quarter of 2018 and full data presented at an oral session at the American Society of Clinical Oncology (ASCO) 2019 Annual Meeting. These data were also published in the International Journal of Cancer (Daniel *et al.;* 2020).

In December 2016, we entered into a non-exclusive agreement with Genentech to evaluate the combination of Genentech's immune checkpoint, anti-PD-L1 antibody Tecentriq with trilaciclib. Our first trial under the agreement is in first-line treatment for patients with extensive stage SCLC receiving carboplatin and etoposide. We initiated enrollment in this randomized, double-blinded, placebo-controlled Phase 2 trial in the second quarter of 2017. The goals of the clinical trial are to evaluate the safety, OS, myeloprotection, PK, and anti-tumor activity of trilaciclib in combination with Tecentriq and chemotherapy. We completed enrollment in the first quarter of 2018. We reported positive multilineage myeloprotection data and preliminary progression free survival (PFS) in November 2018, and presented updated safety and anti-tumor efficacy data at the 2019 ESMO Congress.

Phase 1b/2 clinical trial in first-line treatment of SCLC (study 2 in package insert)

In 2015, we initiated a Phase 1b/2 clinical trial in first-line extensive-stage SCLC patients across multiple sites in the United States and Europe. The Phase 1b segment of the trial was designed to confirm the trilaciclib dose to be used in the randomized, placebo-controlled Phase 2 segment. The goals of the trial are to evaluate the safety, myeloprotection, pharmacokinetics, and anti-tumor activity of trilaciclib in combination with the existing first-line chemotherapy standard of care regimen of etoposide and carboplatin and to confirm the dose to be used in future trials. All patients in the Phase 1b segment were administered three-week cycles of trilaciclib plus etoposide/carboplatin, with an estimated four to six cycles administered in total per patient based on historical practice. Trilaciclib was administered as an IV infusion prior to every dose of etoposide/carboplatin.

In the Phase 1b section of this trial, as reported at the American Society of Clinical Oncology meetings in June 2017, we treated 19 patients with multiple cycles of trilaciclib and chemotherapy and did not have a single episode of febrile neutropenia – one of the most common adverse consequences of these chemotherapy regimens. We also observed a dose dependent reduction in grade 3/4 hematologic adverse events. The results from the Phase 1b study support the hypothesis that trilaciclib could ameliorate the significant acute and long-term consequences of chemotherapy-induced myelosuppression by preserving hematopoietic and immune system function. Based on these results, we initiated the randomized, placebo-controlled Phase 2 segment of the trial in fourth-quarter of 2016 with a trilaciclib dose of 240 mg/m^2 and completed enrollment of a total of 77 patients in the second quarter of 2017. We reported positive multilineage myeloprotection data from the Phase 2 segment of the trial in March 2018, with additional data from the trial presented at the 2018 ESMO Congress and final data published in Annals of Oncology (Weiss *et al*.; 2019).

Phase 1b/2 clinical trial in second/third-line treatment of SCLC (study 3 in package insert)

In 2015, we initiated a Phase 1b/2 clinical trial in second/third-line SCLC patients across multiple sites in the United States and Europe. The Phase 1b segment of the trial was designed to confirm the trilaciclib dose to be used in the randomized, placebo-controlled Phase 2 segment of the trial. The goals of the trial are to evaluate the safety, myeloprotection, PK, and anti-tumor activity of trilaciclib in combination with the existing second/third-line chemotherapy standard of care regimen of topotecan and to confirm the dose to be used in future trials. All patients in the Phase 1b segment were administered three-week cycles of trilaciclib plus topotecan until the progression of disease. Trilaciclib was administered as an IV infusion prior to every dose of topotecan. Trilaciclib doses of 200 to 280 mg/m^2 and topotecan doses of 0.75 to 1.5 mg/m^2 were tested across 7 cohorts in the completed Phase 1b open-label segment of the trial. The doses chosen for the randomized, placebo-controlled Phase 2 segment of this trial were trilaciclib 240 mg/m^2 + topotecan 0.75 mg/m^2 and trilaciclib 240 mg/m^2 + topotecan 1.5 mg/m^2.

In the Phase 1b segment we treated 32 patients with trilaciclib and topotecan without any episodes of febrile neutropenia or treatment related SAEs. Preliminary results from Phase 1b were reported at the IASCLC World Conference on Lung Cancer in December 2016. Based on these results, the Phase 2 segment was initiated in the first quarter of 2017 and consists of a double blind-design with 91 patients randomized on a 2:1 basis to receive trilaciclib plus topotecan, or placebo plus topotecan. We completed enrollment in this trial in the second quarter of 2018 and reported multilineage myeloprotection data in the fourth quarter of 2018. Safety and anti-tumor efficacy data were presented at the 2019 ASCO Annual Meeting. These data were published in the 2019 Advanced in Therapy (Hart *et al*.; 2020).

Our double-blind placebo controlled trials of trilaciclib in SCLC trials demonstrated that, when added to standard of care chemotherapy or chemotherapy/checkpoint inhibitor regimens, trilaciclib mitigates clinically significant chemotherapy-induced myelosuppression. The FDA granted Breakthrough Therapy Designation for trilaciclib based on myeloprotection data from our three

randomized, double-blind, placebo-controlled SCLC clinical trials, as well as safety data collected across all completed and ongoing clinical trials. The Breakthrough Therapy program is designed to expedite development and review of drugs intended for serious or life-threatening conditions. In August 2020, the FDA accepted our New Drug Application (NDA) for trilaciclib in SCLC, granting Priority Review with a Prescription Drug User Fee Act (PDUFA) action date of February 15, 2021. COSELA™ (trilaciclib) was approved by the U.S. Food and Drug Administration on February 12, 2021 to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC. Discussions with European regulatory authorities have indicated existing data is sufficient to support a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for trilaciclib for myeloprotection in SCLC, which we plan to pursue in collaboration with a partner.

Phase 2 clinical trial in metastatic Triple Negative Breast Cancer (mTNBC)

In January 2017, we initiated an open label, randomized, Phase 2 trial that enrolled 102 patients with first, second or third-line mTNBC across multiple sites in the United States and Europe. The goals of the clinical trial are to evaluate the safety, myeloprotection, PK, and anti-tumor activity of trilaciclib in combination with the existing chemotherapy standard of care regimen of gemcitabine and carboplatin (GC). We completed enrollment in the second-quarter of 2018. At the December 2018 SABCS, we presented preliminary data demonstrating improvement in progression-free survival (PFS). We presented additional safety and anti-tumor efficacy data at the 2019 ESMO Congress. The results of the trial demonstrated significant improvement in overall survival (OS) (preliminary). Though the trial did not meet the primary myeloprotection endpoint, patients receiving trilaciclib were able to receive ~50% more cycles of chemo, without additional hematological toxicity. These data were presented at the 2019 ESMO Congress and concurrently published in The Lancet Oncology (Tan *et al.*; 2019). Updated safety and efficacy data from this trial were presented at the 2020 SABCS. Data included that compared to GC alone (Group 1), OS was improved in both trilaciclib arms (Groups 2 and 3) (Group 2: HR=0.31, p=0.0016; Group 3: HR=0.40, p=0.0004). Median OS was 12.6 months in Group 1, not reached for Group 2, and 17.8 months in Group 3. The median OS for Groups 2 and 3 combined was 19.8 months (HR=0.37, p<0.0001). OS findings in patients receiving trilaciclib were consistent with previously reported data from this trial. The median OS for GC alone (Group 1, 12.6 months) was consistent with the previous trial findings and historical data. Patients with both PD-L1-positive and PD-L1-negative tumors treated with trilaciclib and GC demonstrated improvement in OS compared to patients receiving GC alone, with the PD-L1-positive subset achieving statistically significant improvement. Further, data from T cell clonality analyses suggest that administering trilaciclib prior to chemotherapy enhanced immune system function.

Two ongoing clinical trials
Trilaciclib (IV CDK4/6 inhibitor)

Phase 3 clinical trial in first line Colorectal Cancer

We initiated this trial in the fourth quarter of 2020, and in January of 2021 we enrolled the first patient into our pivotal trial in first line colorectal cancer. CRC is a large indication commonly treated with 5-FU-based chemotherapy. We have extensive preclinical research demonstrating myeloprotection and potential efficacy in 5-FU-based regimens with trilaciclib. The Phase 3 trial is being conducted across multiple sites in the United States and Europe. The study will evaluate the safety myeloprotection and antitumor efficacy of trilaciclib in combination with FOLFOXFIRI, the most efficacious chemotherapy regimen in CRC. The primary endpoint is myeloprotection; secondary endpoints include progression-free survival (PFS) / overall survival (OS), and patient reported outcomes (PRO). We expect to enroll approximately 300 participants.

Phase 2 clinical trial in neoadjuvant Breast Cancer (I-SPY 2 Trial)

In January 2020, we announced that trilaciclib would be evaluated in a new randomized investigational treatment arm of the ongoing consortium I-SPY 2 trial for neoadjuvant treatment of locally advanced breast cancer. The neoadjuvant I-SPY 2 trial will generate myeloprotection and anti-tumor efficacy data across the different subtypes of breast cancer. This trial is a standing Phase 2 randomized, controlled multicenter trial with adaptive randomization design to rapidly screen and identify promising new treatments in specific subgroups of adults with newly diagnosed high risk locally-active breast cancer (Stage II/III). Trilaciclib is being evaluated across all high-risk, early-stage breast cancer subtypes (including HR+, HER2+ and triple-negative breast cancer). All patients will receive standard neoadjuvant treatment, including chemotherapy (and anti-HER2 Mab for HER2+ disease) prior to surgical resection of breast tissue.

Clinical trials expected to initiate in 2021
Trilaciclib (IV CDK4/6 inhibitor)

Indications	Regimen	Phase	Status
1st line Triple Negative Breast Cancer	+ gemcitabine and carboplatin (checkpoint-naïve)	Phase 3	Expected 1H 2021initiation
2nd line Triple Negative Breast Cancer	+ gemcitabine and carboplatin (post-checkpoint)	Phase 3	Expected 1H 2021initiation
2nd / 3rd line Non-Small Cell Lung Cancer	+ docetaxel (post-checkpoint)	Phase 2	Expected 1H 2021initiation
1st line Bladder Cancer	+ gemcitabine and platinum (combo with a checkpoint inhibitor)	Phase 2	Expected 1H 2021initiation

Trilaciclib: regulatory status

COSELA for injection was approved by the FDA in February 2021 to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC). The approval was based on three SCLC trials demonstrating that trilaciclib, when added to standard of care chemotherapy or chemotherapy/checkpoint inhibitor regimens, mitigates clinically significant chemotherapy-induced myelosuppression. Discussions with European regulatory authorities have indicated existing data is sufficient to support an MAA to the EMA for trilaciclib for myeloprotection in ES-SCLC.

G1 received Breakthrough Therapy Designation from the FDA in 2019 based on positive myeloprotection data in small cell lung cancer patients from three randomized Phase 2 clinical trials. As is common with Breakthrough-designated products that receive priority review, G1 will conduct certain post-marketing activities, including in vitro drug-drug interaction and metabolism studies, and a clinical trial to assess impact of trilaciclib on disease progression or survival in patients with ES-SCLC with chemotherapy-induced myelosuppression treated with a platinum/etoposide-containing or topotecan-containing regimen with at least a two year follow up. G1 intends to initiate the post-approval clinical trial in 2022.

Rintodestrant: Our differentiated oral SERD

Rintodestrant is an oral SERD which we are developing as a monotherapy and in combination with a CDK4/6 inhibitor, Ibrance® (palbociclib), for the treatment of ER+, HER2- breast cancer. Based on compelling preclinical efficacy and safety data, we filed an Investigational New Drug application (IND) with the FDA in the fourth quarter of 2017. In 2018, we initiated a Phase 1 (dose escalation/dose expansion) clinical trial in ER+, HER2- breast cancer. Preliminary data from the Phase 1b portion of this trial were presented at the 2019 ESMO Congress, showing that rintodestrant was well tolerated and demonstrated evidence of anti-tumor activity in heavily pre-treated patients. The mature monotherapy data were presented at the 2020 SABCS, confirming the safety and efficacy results of the preliminary analysis. Based on those results we advanced an 800 mg dose of rintodestrant into a 40-patient Phase 2 combination trial with palbociclib, a CDK4/6 inhibitor. We completed enrollment of patients in this trial in October 2020 and expect to disclose initial safety and efficacy data in the second quarter of 2021. Palbociclib is being provided under a non-exclusive clinical supply agreement that we signed with Pfizer in February 2020. We will evaluate partnering options for rintodestrant following the data read-out from our combination study.

Market opportunity for rintodestrant

Breast cancer accounts for 30% of all female cancers in the United States. The major cause of death from breast cancer is metastases, and approximately 30% of early-stage patients develop metastatic disease. Approximately 65% of breast cancers are ER+ and depend on estrogen signaling for growth and survival of the malignant cells. Patients with ER+ breast cancers are typically treated with endocrine therapies such as aromatase inhibitors, or AIs, selective estrogen receptor modulators, or SERMs, and SERDs. AIs, which

block the generation of estrogen, and SERMs, which selectively inhibit an ER's ability to bind estrogen, both block ER-dependent signaling but leave functional ERs present in breast cancer cells. For this reason, although AIs and SERMs are effective treatments for some breast cancers, many patients acquire resistance to them by developing the ability to signal through the ER in a ligand-independent manner. In contrast, SERDs are a class of endocrine therapies that directly induce ER degradation. Therefore, it is believed that SERDs have the potential to treat ER+ tumors without allowing ligand-independent resistance to develop, and to act on AI- and SERM-resistant ER-positive tumors. Currently only one SERD, fulvestrant, is approved for the treatment of ER+ metastatic breast cancer. Randomized clinical trials have demonstrated superior anti-tumor efficacy of fulvestrant versus aromatase inhibitors.

Fulvestrant is administered as an IM injection, and requires a loading dose during the first month of treatment. This means it is typically given on days 1, 15, and 29 of treatment and then once monthly thereafter. Each treatment typically consists of two injections, one into each buttock. Injection site reactions are common, occurring in approximately 10% of patients. Injection site related events including sciatica, neuralgia, neuropathic pain, and peripheral neuropathy have been reported. Other frequently reported adverse reactions with fulvestrant include nausea (9.7%) and bone pain (9.4%).

While fulvestrant has demonstrated significant benefit to patients in the metastatic setting, the intramuscular injections have precluded its use in the adjuvant setting. Given the validated MOA of a SERD, and demonstration of superior efficacy to aromatase inhibitors, there is significant potential to improve outcomes for patients being treated in the adjuvant setting. Consequently, there are several oral SERDs in early clinical development, though no one candidate has emerged as a clear front runner as an oral alternative to fulvestrant based on early results.

Advantages of rintodestrant

We believe that rintodestrant has the following potential advantages:

- *Higher potency*. In preclinical models of ER+, HER2- breast cancer, rintodestrant is more potent than fulvestrant in binding and degrading the ER and inhibiting cell growth.
- *Improved safety and tolerability*. Early clinical data demonstrate that rintodestrant was well tolerated with a low incidence of mostly Grade 1 or Grade 2 adverse effects, and no severe adverse events. No ocular toxicity or bradycardia was observed.
- *Ease of administration*. The only approved SERD, fulvestrant, is required to be given via IM injection. We have designed rintodestrant to be administered orally.
- *Potential for usage in the adjuvant setting*. Rintodestrant has the potential to offer superior efficacy to currently available anti-estrogen therapies in the adjuvant setting.

Rintodestrant: Preclinical and clinical development

We have presented extensive biochemical, cellular and *in vivo* data on rintodestrant demonstrating that it: has drug-like properties, is highly potent, is active on ER mutant receptors, is highly selective, leads to complete ER degradation, demonstrated a favorable safety profile, and has oral efficacy.

We initiated a Phase 1b (dose escalation/dose expansion) clinical trial in 2018 with the goal of evaluating the safety, tolerability, and PK of the drug in breast cancer patients. Preliminary Phase 1 data were presented at the 2019 ESMO Congress. In the trial, rintodestrant was well tolerated and demonstrated evidence of anti-tumor activity in heavily pre-treated patients. The mature monotherapy data were presented at the 2020 SABCS, confirming the safety and efficacy results of the preliminary analysis.

Based on those results we advanced an 800 mg dose of rintodestrant into a 40-patient Phase 2 combination trial with palbociclib, a CDK4/6 inhibitor. We completed enrollment of patients in this trial in October 2020 and expect to disclose initial safety and efficacy data in the second quarter of 2021. We will evaluate partnering options for rintodestrant following the data read-out from our combination study. Palbociclib is being provided under a non-exclusive clinical supply agreement that we signed with Pfizer in February 2020.

Lerociclib: Our differentiated oral CDK4/6 inhibitor for patients with CDK4/6-dependent tumors

Lerociclib is a differentiated oral CDK4/6 inhibitor being developed for use in combination with other targeted therapies in multiple oncology indications. In 2020, we entered into separate, exclusive agreements with EQRx, Inc. (rights for U.S., Europe, Japan and all markets outside Asia-Pacific) and Genor Biopharma Co. Inc. (rights for Asia-Pacific, excluding Japan) for the development and commercialization of lerociclib in all indications. Combined, these agreements provided $26.0 million in upfront payments, along with sales-based royalties and the opportunity for up to $330.0 million in potential milestone payments. EQRx, Inc. and Genor Biopharma Co. Inc. are responsible for all costs related to the development and commercialization of lerociclib in their respective territories.

Our Business Strategy

Our goal is to be a leader in the discovery and development of novel treatments that improve outcomes for people with cancer. Our strategy includes the following key components:

- ***Commercialize COSELA™ (trilaciclib) for ES-SCLC in the U.S. and establish as the standard of care.*** COSELA (trilaciclib) for Injection was approved by the FDA in February 2021 decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC). Our commercial launch is underway. We are exploring partnership opportunities to commercialize trilaciclib ex-US.
- ***Maximize long-term value of trilaciclib by executing a robust development plan across multiple indications.*** We believe that trilaciclib has the potential to be used to treat patients receiving myelosuppressive chemotherapy across multiple oncology indications.
- ***Evaluate partnership options for rintodestrant following Phase 2 trial in combination with CDK4/6 inhibitor.*** Our short-term goal is to generate additional clinical data to demonstrate the safety and efficacy of rintodestrant in combination with palbociclib and evaluate partnership opportunities upon data read-out.
- ***Continue to manage capital efficiently.*** We believe our current cash on hand and access to our debt facility provides cash runway into 2023. We will continue to efficiently execute our development plan and look to leverage co-development opportunities with our partners.

Commercialization

In February 2021, the U.S. Food and Drug Administration (FDA) approved COSELA (trilaciclib) to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC). The commercial launch of COSELA is being supported by our sales collaboration with Boehringer Ingelheim. G1 Therapeutics is managing all marketing, market access and clinical nurse educator functions, as well as product distribution. The G1 to One program will serve as a patient hub and provide patient and healthcare provider services. COSELA is due to be commercially available in the coming weeks.

We have been using branded COSELA marketing materials to actively promote COSELA since approval and supporting COSELA use to doctors, oncology nurses, and payors. Our entire field force is currently communicating the advantages of COSELA, with materials in hand and with COSELA to be in channel in early March 2021, ready to improve the chemotherapy experience of ES-SCLC patients receiving chemo.

We plan to globally commercialize our product candidates through the establishment of collaboration agreements with global and/or regional pharmaceutical companies to leverage our and their development and commercialization infrastructures and capabilities, enabling us to cost-effectively maximize the global commercial opportunities of our product candidates.

Manufacturing

We do not own or operate, and currently have no plans to establish any manufacturing facilities. We rely, and expect to continue to rely, on third parties (contract manufacturing organizations, or CMOs) for the manufacture of our product candidates. To date, we have obtained drug substances and drug products for trilaciclib, rintodestrant and lerociclib for our preclinical studies and clinical trials from multiple third-party manufacturers. Redundant suppliers are in place for some of our drug substances and drug products. As development proceeds for our product candidates, we will evaluate qualifying additional redundant manufacturers for drug substances and drug products.

Although we are reliant on third parties to manufacture our product candidates, we have personnel with extensive manufacturing experience to oversee the relationships with our CMOs. CMOs are subject to extensive governmental regulations and we depend on them to manufacture our product candidates in accordance with current good manufacturing practices, or cGMP. We have an established quality assurance program to ensure that the CMOs involved in the manufacture of product candidates do so in accordance with cGMP and other applicable U.S. and foreign regulations. We believe that our current CMO network complies with such regulations.

Competition

The development and commercialization of new drug therapies is highly competitive. We will face competition with respect to all therapeutics we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. Any drug candidates we successfully develop and commercialize will compete with currently marketed drugs and therapies used for treatment of the same indications, and potentially with product candidates currently in development for the same indications. Many of the entities marketing or developing potentially competing products have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing. We believe the key competitive factors affecting the success of any approved product will be its efficacy, safety profile, price,

convenience of administration, and level of promotional activity. Accordingly, our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop.

COSELA™ is the first approved therapy designed and optimized to help protect HSPCs and immune system function from damage by chemotherapy. We believe administering trilaciclib with the current standard of care may minimize chemotherapy-induced myelosuppression, including the following adverse side effects: fatigue due to anemia; infections due to neutropenia; and bleeding due to thrombocytopenia. Currently, these adverse side effects often require costly rescue interventions such as hospitalizations, transfusions, antibiotic usage and/or treatment with growth factor support. Trilaciclib may reduce the need to administer the existing rescue growth factor support treatments, including Neulasta® (pegfigrastim), Neupogen® (filgrastim), Procrit® (epoeitin alpha), and Aranesp® (darbepoetin alfa) as well as biosimilars of these products. In addition, trilaciclib may compete with multiple approved drugs or drugs that may be approved in the future, such as plinabulin which is in development for chemotherapy induced-neutropenia and ALRN-6924 which is in development for chemotherapy-induced myelosuppression.

If rintodestrant is approved, it will compete with AstraZeneca's approved IM SERD, fulvestrant. Rintodestrant would also compete with other oral SERDs in development including: RAD1901, being developed by Radius Health; GDC-9545, being developed by Genentech; AZD9833, being developed by AstraZeneca; SAR439859, being developed by Sanofi; LY3484356, being developed by Eli Lilly; ARV-471, being developed by Arvenas; and ZN-c5, being developed by Zentalis. Rintodestrant may compete with multiple approved drugs or drugs that may be approved in the future for indications for which we may develop rintodestrant.

Intellectual property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our CDK4/6 inhibitors, trilaciclib and lerociclib, and our in-licensed SERD compound, rintodestrant, in clinical trials and methods of treatment using our CDK4/6 inhibitors and our in-licensed SERD compound, alone and in combination with other therapeutic agents. We also, where we believe appropriate, seek protection on processes for the production of our CDK4/6 inhibitors and in-licensed SERD compound, formulations, additional compositions, combinations of our product candidates with other active agents and dosing schedules and regimens. Our success also depends on our ability to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications covering our proprietary technology, inventions, and improvements that are important to the development and implementation of our business. In addition, we plan to seek patent term adjustments, restorations, and/or patent term extensions where applicable in the United States and other jurisdictions. We also rely on trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we expect to benefit, where appropriate, from statutory frameworks in the United States, Europe, and other countries that provide a period of clinical data exclusivity to compensate for the time required for regulatory approval of our drug products. See also the "Government Regulation and Product Approval" section below.

We are the sole owner or exclusive licensee of all of our patents and currently filed patent applications that cover our product candidates. Our intellectual property strategy includes patenting our CDK4/6 inhibitors, their uses, and methods of manufacturing as well as our in-licensed applications directed to selective estrogen receptor degraders and their uses, manufacture, and combination with our and other CDK4/6 inhibitors. We have obtained twenty-two composition-of-matter patents in the United States on a number of our CDK4/6 inhibitors, including claims that cover our product candidates trilaciclib and lerociclib, and we continue to seek composition-of-matter patents on additional CDK4/6 inhibitors both in the United States and throughout the world. In addition, we have obtained eleven patents in the United States on methods of treatment using a number of our CDK4/6 inhibitors, including claims that cover methods of using our product candidates trilaciclib and lerociclib. We continue to seek additional patents for our key CDK4/6 inhibitors and their uses in key therapeutic areas.

We have also obtained a composition-of-matter patent, and two method of treatment patents, in the United States on the SERD compounds that we have exclusively in-licensed, including rintodestrant. We also seek patent protection on methods of treatment that incorporate in-licensed SERD compounds in combination with other therapeutic agents to treat specific clinical indications and targeted patient populations. Furthermore, we seek, where appropriate, patent protection on processes of making certain SERD compounds, additional compositions, and intermediates used in the processes.

We continually assess and refine our intellectual property strategies as we develop new technologies and product candidates. We plan to file additional patent applications based on our intellectual property strategies where appropriate, including where we seek to adapt to competition or to improve business opportunities. Further, we plan to file patent applications, as we consider appropriate under the circumstances, to protect new technologies that we develop. Our patent filing strategy typically includes seeking patent protection in the United States, the European Union, and in additional countries where we believe such protection is likely to be useful, including one or more of Australia, Brazil, Canada, China, Hong Kong, India, Israel, Japan, Mexico, Macau, Russia, Singapore, and South Korea.

We entered into four license agreements in 2020. On May 22, 2020, we entered into a license agreement with ARC Therapeutics, LLC, ("ARC") where we out-licensed to ARC a portfolio of CDK2 inhibitors for development and commercialization. On June 15, 2020, we entered into a license agreement with Genor Biopharma Co. Inc.("Genor") for the development and commercialization of our CDK4/6 inhibitor lerociclib in the Genor Territory. On July 22, 2020, we entered into a license agreement with EQRx, Inc. ("EQRx") for the development and commercialization of lerociclib in the EQRx Territory. On August 3, 2020, we entered into a license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd, ("Simcere") for the development and commercialization of our CDK4/6 inhibitor trilaciclib in the Simcere Territory. Each of these license agreements is described below.

Our owned and in-licensed patent estate as of December 31, 2020, on a worldwide basis, includes over 350 granted or pending patent applications in more than 30 patent families with 40 granted U.S. patents. The term of individual patents depends upon the laws of the countries in which they are obtained. In the countries in which we currently file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application which serves as a priority application. However, the term of a U.S. patent may be extended to compensate for the time required to obtain regulatory approval to sell a drug (a patent term extension) or by delays encountered during patent prosecution that are caused by the United States Patent and Trademark Office (USPTO) (referred to as patent term adjustment). For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved drugs of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review and diligence during the review process. Patent term extensions cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent covering an approved drug or its method of use may be extended. A similar kind of patent extension, referred to as a Supplementary Protection Certificate, is available in Europe. Legal frameworks are also available in certain other jurisdictions to extend the term of a patent. We currently intend to seek patent term extensions on any of our issued patents in any jurisdiction where we have a qualifying patent and the extension is available; however, there is no guarantee that the applicable regulatory authorities, including the FDA and the USPTO in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. Further, even if our patent is extended, the patent, including the extended portion of the patent, may be held invalid or unenforceable by a court of final jurisdiction in the United States or a foreign country.

Our current issued patents covering the composition-of-matter for our present clinical candidates trilaciclib and lerociclib will expire in 2031, exclusive of any patent term extension. Our current issued patents covering methods of use of trilaciclib and lerociclib will expire in 2034 to 2035. Our pending applications on additional methods of use of trilaciclib and lerociclib, should they issue, will expire on dates ranging from 2034 to 2040. We plan to file additional applications on aspects of our innovations that may have patent terms that extend beyond these dates.

Our in-licensed patent covering the composition-of-matter of our clinical candidate rintodestrant will expire in 2036, exclusive of any patent term extension. Our pending applications on additional methods and compositions relating to rintodestrant, should they issue, will expire on dates ranging from 2038 to 2041.

Any of our patents, including patents that we may rely on to protect our market for approved drugs, may be held invalid or unenforceable by a court of final jurisdiction. Alternatively, we may decide that it is in our interest to settle a litigation in a manner that affects the term or enforceability of our patent. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that have been or may be granted in our patents or in third-party patents. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to obtain and maintain our proprietary position for our CDK4/6 inhibitors or our in-licensed SERD compound will depend on our success in enforcing the claims that have been granted or may grant. We do not know whether any of the pending patent applications that we have filed or may file or license from third parties will result in the issuance of any additional patents. The issued patents that we own or may receive in the future may be challenged, invalidated, or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize drugs with similar mechanisms of action and duplicate our methods of treatments or strategies without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs 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.

Trilaciclib and lerociclib patent coverage

We own five issued U.S. Patents (U.S. 8,598,186; U.S. 8,598,197; U.S. 9,957,276; U.S. 10,189,849; and U.S. 10,189,850) covering the trilaciclib compositions-of-matter and its pharmaceutical composition. We also own six issued U.S. Patents (U.S. 8,598,186; U.S. 8,598,197; U.S. 9,481,691; U.S. 9,957,276; U.S. 10,189,851; and U.S. 10,696,682) covering the lerociclib composition-of-matter and pharmaceutical composition. We own corresponding issued patents covering trilaciclib and lerociclib and their pharmaceutical compositions in Europe, Canada, Japan, Mexico, China, Macau, Australia, Russia, South Korea, India, Israel, Hong Kong, Brazil, and

Singapore. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2031, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

In addition, we own two issued U.S. Patents (U.S. 9,487,530 and U.S. 10,085,992) covering the use of trilaciclib to reduce the effect of chemotherapy on healthy cells in a subject being treated for CDK4/6 replication independent cancer. This patent family covers, for example, SCLC treatment protocols involving chemotherapeutic agents carboplatin, etoposide, and/or topotecan along with trilaciclib for protection of healthy replicating cells like hematopoietic stem and progenitor cells. The patent filing also covers chemoprotection of healthy replicating cells with trilaciclib during the treatment of CDK4/6 independent cancer including triple negative breast cancer. Patents from this family have issued in Europe, China, Hong Kong, Macau, and Japan. A patent application from this family is pending in Canada. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2034, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We have filed applications in the United States, in the European Patent Office (EPO), Canada, China, Hong Kong, Australia, Brazil, Israel, Japan, South Korea, Mexico, New Zealand, Russia, and the regional patent office of the Eurasian Patent Organization (EAPO) and the African Regional Intellectual Property Organization (ARIPO) that cover the administration of trilaciclib in combination with a checkpoint inhibitor. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2037, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family that is directed to the use of our CDK4/6 inhibitors to treat RB-positive tumors. The family includes three issued U.S. Patents (U.S. 9,527,857; U.S. 10,076,523; and U.S. 10,434,104) and one pending US patent application. The ‘857 patent covers the use of lerociclib, to treat RB-positive breast cancer, colon cancer, ovarian cancer, NSCL cancer, prostate cancer, and glioblastoma, the ‘523 patent covers the use of lerociclib to treat Rb-positive breast cancer continuously for 28 days or more, and the ‘104 patent covers the use of lerociclib to treat Rb-positive breast cancer in combination with goserelin. We have a pending U.S. patent application that has been allowed directed to the use of trilaciclib in combination with a chemotherapeutic agent to treat RB-positive tumors. Patents in this family have also issued in China, Hong Kong, Macau, and Japan, and a patent application is pending in Canada. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2034, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to the use of trilaciclib or lerociclib as an anti-neoplastic agent against certain hematological cancers. This family includes one issued U.S. Patent (10,709,711) and one pending US patent application. This patent filing is pending in Europe and Canada, and has issued in Japan and China. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2034, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We have filed patent applications in the United States, Europe, and China that covers the administration of lerociclib in combination with an EGFR inhibitor, for example osimertinib, for the treatment of EGFR-mutant cancers, most notably NSCLC. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2038, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to the use of lerociclib in combination with a Bruton’s tyrosine kinase inhibitor or other selected active agents to treat RB-positive tumors. The family includes a granted U.S. patent (U.S. 10,231,969), a pending U.S. patent application and a pending European patent application. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2035, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We have filed patent applications in the United States, European Patent Office (EPO), Canada, China, Hong Kong, Australia, Brazil, Israel, Japan, South Korea, Mexico, New Zealand, Russia, and the regional patent office of the Eurasian Patent Organization (EAPO) and the African Regional Intellectual Property Organization (ARIPO) that cover morphic forms of lerociclib. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2038, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We have filed patent applications in the United States, European Patent Office (EPO), Brazil, Canada, China, Colombia, Hong Kong, Egypt, Australia, Brazil, Israel, Japan, South Korea, Mexico, New Zealand, Russia, Indonesia, Sri Lanka, Malaysia, Nigeria, Peru, Philippines, Singapore, Thailand, Vietnam, South Africa, and the regional patent office of the Eurasian Patent Organization (EAPO) and the African Regional Intellectual Property Organization (ARIPO) that cover dosage regimes of lerociclib. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2039, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to certain compositions of trilaciclib. This family has been filed in the United States and has a pending PCT application. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2040, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to the use of our CDK4/6 inhibitors in combination with the inhibitor of microtubule function eribulin for the treatment of cancers. This family has a pending PCT application. The expected year of expiration for this patent

family, where issued, valid and enforceable, is 2039, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to the selection of patients for administration of trilaciclib based on tumor type, chemotherapeutic regimen, and immune factors. This family has a pending PCT application and has been filed in non-PCT countries. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2040, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We also own additional patent families directed to the use of our CDK4/6 inhibitors in combination with various other therapeutic agents for the treatment of cancers harboring specific mutations. The expected year of expiration for these patent families, where issued, valid, and enforceable, is between 2039 and 2040, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own two U.S. patent families directed to the use of our CDK4/6 inhibitors in particular clinical applications. The expected year of expiration for these patent families, where issued, valid, and enforceable, is 2041, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

Rintodestrant Patent Coverage

We have exclusively licensed from University of Illinois, or the University, two patent families that cover rintodestrant and related compounds and their pharmaceutical compositions and use as selective estrogen receptor down-regulators. Selected applications from these families are pending in ARIPO, Australia, Brazil, Canada, China, Eurasia, Europe, Israel, India, Japan, Korea, Mexico, New Zealand, Russia, United States, and South Africa. Three U.S. Patents (U.S. 10,118,910, U.S. 10,377,735, and 10,807,964) have issued from this family. We have also received issued patents in Mexico and South Africa. The expected year of expiration for these patent families, where issued, valid and enforceable, is 2036, without regard to any extensions, adjustments, or restorations of term that may be available under national law. Under the Exclusive License Agreement with the University, we have the right to prosecute the licensed applications, subject to review by the University.

We co-own, along with the University, patent applications filed in the United States, Europe, Australia, Brazil, Canada, China, Israel, India, Japan, South Korea, Mexico, Russia, New Zealand, and the regional patent offices of ARIPO and the EAPO directed to the combination of rintodestrant and related compounds with lerociclib and related compounds for the treatment of estrogen-modulated disorders such as RB-positive breast cancer. We have exclusively licensed the University's rights in this co-owned application. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2038, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We also exclusively own a U.S. application that describes certain compositions of rintodestrant and a U.S. application that describes methods of manufacture of rintodestrant. The expected year of expiration for these patent families, where issued, valid and enforceable, is 2041, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

A number of our pending patent applications covering certain aspects of using our current clinical candidates have not yet issued. As with other biotechnology and pharmaceutical companies, our ability to obtain and maintain a proprietary position on our drug candidates and technologies will depend on our success in obtaining effective patent claims on these pending patents and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future 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.

Any issued patents that we have received or may receive in the future may be challenged, invalidated or circumvented. In addition, because of the extensive time required for clinical development and regulatory review of a drug candidate we may develop, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our clinical candidates. The area of patent and other intellectual property rights in pharmaceuticals is an evolving one with many risks and uncertainties, and third parties may have blocking patents that could be used to prevent us from commercializing our clinical candidates.

Exclusive license for rintodestrant

In November 2016, we entered into a license agreement with the University of Illinois, the University, pursuant to which we obtained an exclusive, worldwide license to make, use, import, sell and offer for sale certain SERDs, including rintodestrant, covered by patent rights owned by the University. The rights licensed to us are for all fields of use. The November 2016 license agreement was amended in March 2017.

Under the terms of the agreement we paid a one-time only, non-refundable upfront fee of $0.5 million, and we are required to pay the University low single-digit royalties on all net sales of products and a share of any sublicensing revenues. We are also obligated to pay annual maintenance fees, which are fully creditable against any royalty payments made by us. We will also be required to pay the University milestone payments of up to an aggregate of $2.6 million related to the initiation and execution of clinical trials and first commercial sale of a product in multiple countries. We are also responsible for any future patent prosecution costs that may arise.

The term of the license agreement will continue on a country-by-country basis until the later of (i) the expiration of the last valid claim within the patent rights covering the product in such country, (ii) the expiration of market exclusivity in such country and (iii) the 10th anniversary of the first commercial sale in such country. The University may terminate the agreement in the event (i) we fail to pay any amount or make any report when required to be made and fail to cure such failure within 30 days after receipt of notice, (ii) we are in breach of any provision of the agreement and fail to remedy such breach within 45 days after receipt of notice, (iii) we make a report to the University under the agreement that is determined to be materially false, (iv) we declare insolvency or bankruptcy or (v) we take any action that causes patent rights or technical information to be subject to any lien or encumbrance and fail to remedy within 45 days of receipt of notice. We may terminate the agreement at any time upon at least 90 days' written notice. Upon expiration or termination of the agreement, all rights revert to the University.

Exclusive license to Nanjing Simcere Dongyuan Pharmaceutical Co., LTD. ("Simcere") for trilaciclib

On August 3, 2020, we entered into a license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., LTD. ("Simcere License") for the development and commercialization of trilaciclib for any indication in humans through parenteral delivery, including intravenous delivery, in China, Hong Kong, Macau, and Taiwan ("Simcere Territory"). Pursuant to the Simcere License, Simcere has been granted an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses to thirteen of our solely-owned patent families in the Simcere Territory. We maintain the exclusive right to prosecute these patent families with consideration of Simcere's comments and suggestions. Where patent applications in the Simcere Territory cover both trilaciclib and lerociclib they are licensed to both Simcere and Genor.

Under the Simcere License, the Company and Simcere share all patent prosecution costs incurred in the Simcere Territory, except that we are solely responsible for costs associated with any adversarial patent prosecution proceeding in the Simcere Territory, including oppositions, reexaminations, invalidations, revocations, nullifications, or cancellation proceedings related to our licensed patent.

Under the Simcere License, we have the sole right in its sole discretion to bring and control any legal action to enforce our licensed patent families against any infringement action in the Simcere Territory, except in the case of infringement relating to i) a G1 patent containing a claim to the composition-of-matter of trilaciclib or ii) a G1 patent that contains claims covering only trilaciclib that arises as a result of making, using, offering to sell, selling or importing of trilaciclib by a third party, in which case we have the first right, but not the obligation, to bring and control any infringement action at its own expense, subject to the consideration of Simcere's reasonable and timely comments. To the extent we decline to bring an action against an infringer under the above described conditions, Simcere has the right, but not the obligation, to bring an infringement action at its own expense.

Exclusive license to EQRx, Inc. for lerociclib

On July 22, 2020, we entered into a license agreement with EQRx, Inc. (the "EQRx License") for the development and commercialization of lerociclib using an oral dosage form to treat any indication in humans. The EQRx, licensed territories are all of the countries and regions of the world, and their territories and possessions, excluding the Genor territory (the "EQRx Territory"). Pursuant to the EQRx License, EQRx has been granted an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to twelve of our solely-owned patent families in the EQRx Territory. We maintain the exclusive right to prosecute these patent families in the EQRx Territory, and EQRx has the right to review and comment on all material patent filings, with the review and comment to be considered by us in good faith.

Under the EQRx License, the Company and EQRx share all patent prosecution costs incurred in the EQRx Territory, except that we are solely responsible for costs associated with any adversarial patent prosecution proceeding in the EQRx Territory, including oppositions, reexaminations, invalidations, revocations, nullifications, interferences, or cancellation proceedings related to our licensed patent families by a third party. We have the sole right in our sole discretion to bring and control any legal action to enforce our licensed patent families against any infringement action in the EQRx Territory, except in the case of infringement relating to a G1

patent that contains claims covering only lerociclib that arises as a result of making, using, offering to sell, selling or importing of a lerociclib by a third party, in which case we have the first right, but not the obligation, to bring and control any infringement action at its own expense, subject to the consideration of EQRX's reasonable and timely comments. To the extent we decline to bring an action against an infringer under the above-described conditions, EQRx has the right, but not the obligation, to bring an infringement action at its own expense.

Exclusive license to Genor Biopharma Co. Inc.. (" Genor") for lerociclib

On June 15, 2020, we entered into a license agreement with Genor Biopharma Co. Inc. ("*Genor* License") for the development and commercialization of lerociclib using an oral dosage form to treat any indication in humans. The Genor licensed territories are in Australia, Bangladesh, China, Hong Kong, India, Indonesia, Macau, Malaysia, Myanmar, New Zealand, Pakistan, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, and Vietnam (the "Genor Territory"). Pursuant to the Genor License, Genor has been granted an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to ten of our solely-owned patent families in the Genor Territory. We maintain the exclusive right to prosecute these patent families in the Genor Territory, and Genor has the right to review and comment on all material patent filings, such review and comment to be considered by us in good faith.

Under the Genor License, the Company and Genor share all patent prosecution costs incurred in the Genor Territory. We are solely responsible for costs associated with any adversarial patent prosecution proceeding in the Genor Territory, including oppositions, reexaminations, invalidations, revocations, nullifications, or cancellation proceedings related to our licensed patent families.

Under the Genor License, we have the sole right in our discretion to bring and control any legal action to enforce our licensed patent families against any infringement action in the Genor Territory, except in the case of i) a G1 patent containing a claim to the composition-of-matter of lerociclib or ii) a G1 patent that contains claims covering only lerociclib that arises as a result of making, using, offering to sell, selling or importing of a lerociclib by a third party, in which case we have the first right, but not the obligation, to bring and control any infringement action at its own expense, subject to the consideration of Genor's reasonable and timely comments. To the extent we decline to bring an action against an infringer under the above-described conditions, Genor has the right, but not the obligation, to bring an infringement action at its own expense.

Exclusive license to ARC Therapeutics

On May 22, 2020, we entered into a global license agreement with ARC for the development and commercialization of a CDK2 inhibitor for all human and veterinary uses. Pursuant to the ARC License, ARC has been granted an exclusive, royalty-bearing, license with the right to grant sublicenses to four of our solely-owned patent families. Under the ARC License, ARC received the exclusive right to prosecute these patent families in its sole discretion, and we have the right to review and comment on all material patent filings, and our review and comments will be considered by ARC in good faith.

Under the ARC License, ARC is solely responsible for all patent prosecution costs. ARC has the first right, but not the obligation, to bring and control any infringement action at its own expense, subject to ARC keeping us reasonably informed. ARC also has the right to name and join us in any infringement action relating to our patents. In the case of a patent certification in connection with an Abbreviated New Drug Application under the U.S. Hatch Waxman Act, or the substantial equivalent in a foreign country, if ARC declines to file a lawsuit, we have the right to bring an infringement action at our own expense.

Trade secrets

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 commercial partners, collaborators, employees, and consultants, and invention assignment agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees, and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government regulation and product approval

FDA approval process

In the United States, pharmaceutical products are subject to extensive regulation by the U.S. Food and Drug Administration, or FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC 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 new drug applications, or NDAs, warning letters, voluntary product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Pharmaceutical product development in the United States typically involves the performance of nonclinical laboratory and animal tests, the submission to the FDA of an investigational new drug application, or IND, which must become effective before clinical testing may commence, and adequate, 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 studies to assess the pharmacokinetic and pharmacodynamic characteristics and potential safety and effectiveness of the product. The conduct of the preclinical tests must comply with certain federal regulations and requirements, including good laboratory practices, or GLP, for any safety testing. 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 nonclinical 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, or placed the proposed clinical trial protocol on hold, 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 qualified investigators. Clinical trials must be conducted: (i) under the supervision of one or more qualified investigators and in compliance with federal regulations, including those encompassing good clinical practice, or GCP, requirements that are meant to protect the rights and welfare of study subjects and to define the roles of clinical trial sponsors, investigators, and monitors, and (ii) under protocols detailing the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol in support of an IND and subsequent protocol amendments must be submitted to the FDA as part of the IND application.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time by imposing a clinical hold 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 subjects. The clinical trial protocol and informed consent information for subjects in clinical trials must also be submitted for review and approval by an institutional review board, or IRB, on behalf of each participating in the clinical trial before the trial commences at that site. An IRB also monitors the trial until completion and may require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements or for safety issues or it may impose other conditions on the clinical investigators or the sponsor of the clinical trial.

Clinical trials to support an NDA for marketing approval are typically conducted in three sequential phases, but the phases may overlap, and in some cases, such as areas of high unmet medical need, NDA approval may be achieved without completing all phases. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence of effectiveness. Phase 2 usually involves clinical trials in a limited patient population to determine the effectiveness of the drug for a particular indication, 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 clinical trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In some cases, the FDA may require two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 clinical trial with other confirmatory evidence may be sufficient in rare instances where the clinical 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 potentially serious outcome, and confirmation of the result in a second clinical trial would be practically or ethically impossible. Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. In addition, post-approval trials, sometimes referred to as "Phase 4" clinical trials, may be conducted after initial marketing approval. These trials are used to gain

additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 clinical trials. The results of Phase 4 clinical trials can confirm the effectiveness of a product candidate and can provide important safety information. Conversely, the results of Phase 4 clinical trials can raise new safety or effectiveness issues that were not apparent during the original review of the product, which may result in product restrictions or even withdrawal of product approval.

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 nonclinical, clinical, and other testing and a compilation of data relating to the product's chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, currently over $2.8 million for an NDA with clinical information, and the manufacturer and/or sponsor under an approved NDA is also subject to an annual program fee, currently over $330,000. These fees are typically increased annually. Fee waivers or reductions are available in certain circumstances.

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. The FDA seeks to review applications for standard review drug products within ten months, and applications for priority review drugs within six months. Priority review can be applied to drugs intended to treat a serious condition and that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists. The review process for both standard and priority reviews may be extended by FDA for three additional months to consider additional, late-submitted information, or information intended to clarify information already provided in the submission in response to FDA review questions.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an external advisory committee, which is 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 typically inspect the facility or the facilities at which the drug is manufactured, unless the facility has recently had an FDA inspection. The FDA also typically inspects the application sponsor. The FDA will not approve the product unless compliance with current good manufacturing practice, or cGMP, requirements is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or additional nonclinical or clinical study information, in order for the FDA to reconsider the application. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw 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. The 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 the accompanying approved prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, in addition to the approved labeling, to help ensure that the benefits of the drug outweigh its risks. A REMS could include communication plans for health care professionals, medication guides for patients, and/or elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, restricted distribution requirements, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS plan. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy as described as postmarketing commitments or requirements included in the approval letter. Once granted, product approvals may be withdrawn if compliance with regulatory requirements and commitments is not maintained or problems are identified following initial marketing.

Disclosure of clinical trial information

Sponsors of clinical trials of certain FDA-regulated products, including prescription drugs, are required to register and disclose certain clinical trial information on a public registry maintained by the U.S. National Institutes of Health (NIH). Information related to the product, patient population, phase of investigation, clinical trial sites and investigator, and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results may be delayed in some cases 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 design and progress of our development programs. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and both NIH and FDA have signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

Data privacy and the protection of personal information

We are subject to laws and regulations governing data privacy and the protection of personal information including health information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which will continue to affect our business. In the United States, we may be subject to state security breach notification laws, state laws protecting the privacy of health and personal information and federal and state consumer protections laws which regulate the collection, use, disclosure and transmission of personal information. These laws overlap and often conflict and each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues for us. If we fail to comply with applicable laws and regulations we could be subject to penalties or sanctions, including criminal penalties. Our customers and research partners must comply with laws governing the privacy and security of health information, including the Health Insurance Portability and Accountability Act of 1996 as amended ("HIPAA") and state health information privacy laws. If we knowingly obtain health information that is protected under HIPAA, called "protected health information", our customers or research collaborators may be subject to enforcement and we may have direct liability for the unlawful receipt of protected health information or for aiding and abetting a HIPAA violation.

State laws protecting health and personal information are becoming increasingly stringent. For example, California has implemented the California Confidentiality of Medical Information Act that imposes restrictive requirements regulating the use and disclosure of health information and other personally identifiable information, and California has recently adopted the California Consumer Privacy Act of 2018 (the CCPA). The CCPA mirrors a number of the key provisions of the EU General Data Protection Regulation (GDPR) described below. The CCPA establishes a new privacy framework for covered businesses by creating an expanded definition of personal information, establishing new data privacy rights for consumers in the State of California, imposing special rules on the collection of consumer data from minors, and creating a new and potentially severe statutory damages framework for violations of the CCPA and for businesses that fail to implement reasonable security procedures and practices to prevent data breaches. Additionally, a new privacy law, the California Privacy Rights Act (CPRA), was approved by California voters in the election on November 3, 2020. The CPRA will modify the CCPA significantly, potentially resulting in further uncertainty, additional costs and expenses in an effort to comply and additional potential for harm and liability for failure to comply. Other states in the US are considering privacy laws similar to CCPA.

The Hatch-Waxman Act and marketing applications for follow-on drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDC Act, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute and also enacted Section 505(b)(2) of the FDC Act. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD. Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug.

Orange book listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent that has claims that cover the applicant's product or method of therapeutic use. 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 ANDA. The ANDA requests permission to market a drug product that has the same active ingredients in the same strengths and dosage form as the RLD and has been shown through bioequivalence testing to be therapeutically equivalent to the RLD. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, nonclinical 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 innovator drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug referenced by the ANDA applicant if the FDA's listing for the generic drug in the Orange Book indicates that it is "therapeutically equivalent" to the RLD.

In contrast, Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. A Section 505(b)(2)

applicant may eliminate the need to conduct certain preclinical or clinical studies, if it can establish that reliance on studies conducted for a previously-approved product is scientifically appropriate. Unlike the ANDA pathway used by developers of bioequivalent versions of innovator drugs, which does not allow applicants to submit new clinical data other than bioavailability or bioequivalence data, the 505(b)(2) regulatory pathway does not preclude the possibility that a follow-on applicant would need to conduct additional clinical trials or nonclinical studies; for example, it may be seeking approval to market a previously approved drug for new indications or for a new patient population that would require new clinical data to demonstrate safety or effectiveness.

When an ANDA applicant submits its application to the FDA, it 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. Moreover, to the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

If the applicant does not challenge the innovator's listed patents, FDA will not approve the ANDA or 505(b)(2) application 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.

An ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Non-Patent Exclusivity

Upon NDA approval of a new chemical entity or NCE, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which time the 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 or a different formulation, are associated with a three-year period of exclusivity. During the exclusivity period, the FDA cannot accept for review any ANDA or 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed on an NCE patent and any time after approval if the application is filed based on a new indication or a new formulation.

The Hatch-Waxman Act also provides three years of data exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving follow-on applications for drugs containing the original active agent. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA or 505(b)(2) NDA may be filed before the expiration of the exclusivity period. Five-year and three-year exclusivity also will not delay the submission or approval of a traditional NDA filed under Section 505(b)(1) of the FDC Act. However, an applicant submitting a traditional NDA would be required to either conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Patent term extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent term extension. The allowable patent term extension is calculated as half of the drug's testing phase—the time between when the IND becomes effective 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 Patent and Trademark Office (PTO) 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.

Pediatric clinical trials and exclusivity

Under the Pediatric Research Equity Act, or PREA, NDAs or certain types of 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 sponsor must submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs. The FDA may grant full or partial waivers, or deferrals, for submission of pediatric assessment data.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or non-patent—for a drug if certain conditions are met, including satisfaction of a pediatric trial(s) agreed with FDA as a Pediatric Written Request. Conditions for pediatric exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric clinical trials, and the applicant agreeing to perform, and reporting on, the requested clinical trials within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to the written request from the FDA for such data. Those data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. Although this is not a patent term extension, it effectively extends the regulatory period during which the FDA cannot approve another application.

Fast track, breakthrough therapy, and priority review designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation, and priority review designation. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, fast track designation is a process designed to facilitate the development, and expedite the review, of drugs to treat serious or life-threatening diseases and fill an unmet medical need. The designation request may be made at the time of IND submission and generally no later than the pre-NDA meeting. The FDA will respond within 60 calendar days of receipt of the request. Priority review, which is requested at the time of NDA submission, is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists, an initial review within six months after filing as compared to a standard review time of ten months. Although fast track designation and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a fast track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides an earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint, which is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. Discussions with the FDA about the feasibility of an accelerated approval typically begin early in the development of the drug in order to identify, among other things, an appropriate endpoint. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials to confirm the appropriateness of the surrogate marker clinical trial.

Another expedited program is that for breakthrough therapy designation, which is designed to expedite the development and review of drugs that are intended to treat a serious condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s). A sponsor may request breakthrough therapy designation at the time that the IND is submitted, or no later than at the end-of-Phase 2 meeting. The FDA will respond to a breakthrough therapy designation request within sixty days of receipt of the request. A drug that receives breakthrough therapy designation is eligible for all fast track designation features, intensive guidance on an efficient drug development program, beginning as early as Phase 1, and commitment from the FDA involving senior managers. Products that are designated as Breakthrough therapies with priority review are often given preclinical or clinical post-marketing requirements or post marketing commitments by the FDA.

Accelerated approval pathway

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval from the FDA and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. The FDA may also grant accelerated approval for such a drug when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval when the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate long-term clinical benefit of a drug.

Discussions with the FDA about the feasibility of an accelerated approval typically begin early in the development of the drug in order to identify, among other things, an appropriate endpoint. The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials to verify and describe the predicted effect on IMM or other clinical endpoint. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. Because the accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit, a product 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 to confirm the predicted clinical benefit of the product during post-marketing studies, would allow the FDA to withdraw approval of the drug. In addition, all promotional materials for product candidates being considered and approved under the accelerated approval program are subject to prior review by the FDA.

Regulation of companion diagnostic devices

If we decide that a diagnostic test would provide useful information for patient selection or if the FDA requires us to develop such a test, we may work with a collaborator to develop an *in vitro* diagnostic, or companion test. The FDA regulates *in vitro* diagnostic tests as medical devices, and the type of regulation to which such a test will be subjected will depend, in part, on a risk assessment by the FDA as well as a determination of whether the test is intended to yield results that would be helpful to know versus one that the FDA or we believe is necessary to know for the safe and effective use of our drugs under development.

The FDA has issued several guidance documents on in vitro companion diagnostic devices in August 2014, which are intended to assist companies developing *in vitro* companion diagnostic devices and companies developing therapeutic products that depend on the use of a specific *in vitro* companion diagnostic for the safe and effective use of the product. The FDA defines an *in vitro* companion diagnostic device, or IVD companion diagnostic device, as a device that provides information that is essential for the safe and effective use of a corresponding therapeutic product, such as when the use of a product is limited to a specific patient subpopulation that can be identified by using the test. The use of an IVD companion diagnostic device with a therapeutic product will be stipulated in the instructions for use in the labeling of both the diagnostic device and the corresponding therapeutic product, including the labeling of any generic equivalents of the therapeutic product. The FDA expects that the therapeutic product sponsor will address the need for an approved or cleared IVD companion diagnostic device in its therapeutic product development plan and that, in most cases, the therapeutic product and its corresponding companion diagnostic will be developed contemporaneously. However, the FDA may decide that it is appropriate to approve such a product without an approved or cleared *in vitro* companion diagnostic device when the drug or therapeutic biologic is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists and the FDA determines that the benefits from the use of a product with an unapproved or uncleared *in vitro* companion diagnostic device are so pronounced as to outweigh the risks from the lack of an approved or cleared *in vitro* companion diagnostic device. The FDA encourages sponsors considering developing a therapeutic product that requires a companion diagnostic to request a meeting with both relevant device and therapeutic product review divisions to ensure that the product development plan will produce sufficient data to establish the safety and effectiveness of both the therapeutic product and the companion diagnostic. Because the FDA's policies on companion diagnostics is set forth only in guidance, this policy is subject to change and is not legally binding.

Post-approval requirements

Following FDA marketing approval of a new prescription drug product, the manufacturer and the approved drug are subject to pervasive and continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting of adverse experiences with the product, product sampling and distribution restrictions, complying with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (i.e., "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. If there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or an NDA supplement, which may require the applicant to develop additional data or conduct additional preclinical studies and clinical trials.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or other enforcement-related letters or clinical holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal health care programs; or mandated modification of promotional materials and labeling and the issuance of corrective information.

Accordingly, COSELA and any future therapeutic candidate manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the therapeutic candidate;
- providing the FDA with updated safety and efficacy information;
- therapeutic sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and
- complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in-patient populations that are not described in the product's approved labeling, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Drug manufacturers and other entities involved in the manufacture and distribution of approved drug products are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMPs and other laws. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the NDA applicant and any third-party manufacturers involved in producing the approved drug product. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of quality control and quality assurance.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or the PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Most recently, the Drug Supply Chain Security Act, or the DSCSA, was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in

the United States, including most biological products. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Europe/Rest of world government regulation

In addition to regulations in the United States, we are and will be subject, either directly or through our distribution partners, to a variety of regulations in other jurisdictions governing, among other things, clinical trials, the privacy of personal data and commercial sales and distribution of our products, if approved.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in non-U.S. countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, or CTA, must be submitted to the competent national health authority and to independent ethics committees in each country in which a company plans to conduct clinical trials. Once the CTA is approved in accordance with a country's requirements, clinical trials may proceed in that country.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country, even though there is already some degree of legal harmonization in the European Union member states resulting from the national implementation of underlying E.U. legislation. In all cases, the clinical trials are conducted in accordance with GCP and other applicable regulatory requirements.

To obtain a marketing license for a new drug, or medicinal product in the European Union, the sponsor must obtain approval of a marketing authorization application, or MAA. The way in which a medicinal product can be approved in the European Union depends on the nature of the medicinal product.

The centralized procedure results in a single marketing authorization granted by the European Commission that is valid across the European Union, as well as in Iceland, Liechtenstein, and Norway. The centralized procedure is compulsory for human drugs that are: (i) derived from biotechnology processes, such as genetic engineering, (ii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, autoimmune and other immune dysfunctions and viral diseases, (iii) officially designated "orphan drugs" (drugs used for rare human diseases) and (iv) advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines. The centralized procedure may at the request of the applicant also be used for human drugs which do not fall within the above mentioned categories if the human drug (a) contains a new active substance which was not authorized in the European Community; or (b) the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation or that the granting of authorization in the centralized procedure is in the interests of patients or animal health at the European Community level.

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application by the European Medicines Agency, or EMA, is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use, or CHMP), with adoption of the actual marketing authorization by the European Commission thereafter. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest from the point of view of therapeutic innovation, defined by three cumulative criteria: the seriousness of the disease to be treated; the absence of an appropriate alternative therapeutic approach, and anticipation of exceptional high therapeutic benefit. In this circumstance, EMA ensures that the evaluation for the opinion of the CHMP is completed within 150 days and the opinion issued thereafter.

The mutual recognition procedure, or MRP, for the approval of human drugs is an alternative approach to facilitate individual national marketing authorizations within the European Union. Basically, the MRP may be applied for all human drugs for which the centralized procedure is not obligatory. The MRP is applicable to the majority of conventional medicinal products, and is based on the principle of recognition of an already existing national marketing authorization by one or more member states. In the MRP, a marketing authorization for a drug already exists in one or more member states of the E.U. and subsequently marketing authorization applications are made in other European Union member states by referring to the initial marketing authorization. The member state in which the marketing authorization was first granted will then act as the reference member state. The member states where the marketing authorization is subsequently applied for act as concerned member states. After a product assessment is completed by the reference member state, copies of the report are sent to all member states, together with the approved summary of product characteristics, labeling and package leaflet. The concerned member states then have 90 days to recognize the decision of the reference member state and the summary of product characteristics, labeling and package leaflet. National marketing authorizations within individual member states shall be granted within 30 days after acknowledgement of the agreement

Should any member state refuse to recognize the marketing authorization by the reference member state, on the grounds of potential serious risk to public health, the issue will be referred to a coordination group. Within a timeframe of 60 days, member states shall, within the coordination group, make all efforts to reach a consensus. If this fails, the procedure is submitted to an EMA scientific committee for arbitration. The opinion of this EMA committee is then forwarded to the Commission, for the start of the decision-making process. As in the centralized procedure, this process entails consulting various European Commission Directorates General and the Standing Committee on Human Medicinal Products or Veterinary Medicinal Products, as appropriate.

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

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

Europe - Data Privacy

On May 25, 2018, the European General Data Protection Regulation, or GDPR, went into effect, implementing a broad data protection framework that expanded the scope of EU data protection law, including to non-EU entities that process, or control the processing of, personal data relating to individuals located in the EU, including clinical trial data. The GDPR sets out a number of requirements that must be complied with when handling the personal data of European Union-based data subjects including: providing expanded disclosures about how their personal data will be used; higher standards for organizations to demonstrate that they have obtained valid consent or have another legal basis in place to justify their data processing activities; the obligation to appoint data protection officers in certain circumstances; new rights for individuals to be "forgotten" and rights to data portability, as well as enhanced current rights (e.g. access requests); the principal of accountability and demonstrating compliance through policies, procedures, training and audit; and a new mandatory data breach regime. In particular, medical or health data, genetic data and biometric data where the latter is used to uniquely identify an individual are all classified as "special category" data under the GDPR and afforded greater protection and require additional compliance obligations. Further, EU member states have a broad right to impose additional conditions—including restrictions—on these data categories. This is because the GDPR allows EU member states to derogate from the requirements of the GDPR mainly in regard to specific processing situations (including special category data and processing for scientific or statistical purposes). As the EU states continue to reframe their national legislation to harmonize with the GDPR, we will need to monitor compliance with all relevant EU member states' laws and regulations, including where permitted derogations from the GDPR are introduced.

We will also be subject to evolving EU laws on data export, if we transfer data outside the EU to ourselves or third parties outside of the EU. The GDPR only permits exports of data outside the EU where there is a suitable data transfer solution in place to safeguard personal data (e.g. the European Union Commission approved Standard Contractual Clauses). On July 16, 2020, the Court of Justice of the European Union or the CJEU, issued a landmark opinion in the case *Maximilian Schrems vs. Facebook* (Case C-311/18), called *Schrems II.* This decision calls into question certain data transfer mechanisms as between the EU member states and the US. The CJEU is the highest court in Europe and the *Schrems II* decision heightens the burden on data importers to assess U.S. national security laws on their business and future actions of EU data protection authorities are difficult to predict. Consequently, there is some risk of any data transfers from the European Union being halted. If we have to rely on third parties to carry out services for us, including processing personal data on our behalf, we are required under GDPR to enter into contractual arrangements to help ensure that these third parties only process such data according to our instructions and have sufficient security measures in place. Any security breach or non-compliance with our contractual terms or breach of applicable law by such third parties could result in enforcement actions, litigation, fines and penalties or adverse publicity and could cause customers to lose trust in us, which would have an adverse impact on our reputation and business. Any contractual arrangements requiring the transfer of personal data from the EU to us in the United States will require greater scrutiny and assessments as required under *Schrems II* and may have an adverse impact on cross-border transfers of personal data, or increase costs of compliance. The GDPR provides an enforcement authority to impose large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. We will be subject to the GDPR when we have a European Union presence or "establishment" (e.g., EU based subsidiary or operations), when conducting clinical trials with EU based data subjects, whether the trials are conducted directly by us or through a vendor or partner, or offering approved products or services to EU-based data subjects, regardless of whether involving a EU based subsidiary or operations.

Pharmaceutical Coverage, Pricing, and Reimbursement

Sales of our products that are approved by the FDA will depend, in part, on the extent to which the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate

from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved, and it is time consuming and expensive to seek reimbursement from third-party payors. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by third-party 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. In the U.S., third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but they also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. Accordingly, one third-party payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product.

In addition, the containment of healthcare costs has become a priority of federal and state governments and the prices of therapeutics have been a focus in this effort. The United States government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis. Moreover, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical products. Similar challenges to obtaining coverage and reimbursement for the pharmaceutical products apply to companion diagnostics.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of our product candidate to currently available therapies (so called health technology assessment, or HTA) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various E.U. member states, and parallel distribution (arbitrage between low-priced and high-priced member states), can further reduce prices. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates that are approved for commercial marketing and distribution. Historically, therapeutic candidates launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Other Healthcare Laws and Regulations

As we are commercializing COSELA and may commercialize other product candidates, we are subject to additional healthcare statutory and regulatory requirements and enforcement by federal government and the states and foreign governments in the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of COSELA and any other product candidates for which we obtain marketing approval. Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval.

Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The federal Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the federal Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- The federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalty laws, prohibit, among other things, knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the U.S. government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. Actions under these laws may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. The federal government uses these laws, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of products for unapproved uses and other allegedly unlawful sales and marketing practices;

- The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal, civil and criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- The Physician Payments Sunshine Act, enacted as part of the Affordable Care Act of 2010, among other things, imposes reporting requirements on manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare, Medicaid, or the Children's Health Insurance Program to report, on an annual basis, to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, chiropractors and, beginning in 2022 for payments and other transfers of value provided in the previous year, certain advanced non-physician health care practitioners), teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations impose specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities, which include certain healthcare providers, health plans, and healthcare clearinghouses, 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 HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions;

- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers;

- State laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the

Physician Payments Sunshine Act, as well as state and local laws that require the registration of pharmaceutical sales representatives; and

- State laws and foreign laws and regulations (particularly European Union laws regarding personal data relating to individuals based in Europe) that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Moreover, in November 2020, the Department of Health and Human Services ("DHHS") finalized significant changes to the regulations implementing the Anti-Kickback Statute, as well as the Physician Self-Referral Law (Stark Law) and the civil monetary penalty rules regarding beneficiary inducements, with the goal of offering the healthcare industry more flexibility and reducing the regulatory burden associated with those fraud and abuse laws, particularly with respect to value-based arrangements among industry participants. As noted below under "Healthcare Reform," however, those final rules may be potentially overturned under the Congressional Review Act following the change in control of the legislative and executive branches in January 2021.

Ensuring that our current and future business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. It is possible that governmental authorities may conclude that our business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including monetary damages, fines, disgorgement, imprisonment, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, reputational harm, diminished profits and future earnings, or additional reporting requirements if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with any of these laws, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Healthcare Reform and potential changes to drug and healthcare laws

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product and therapeutic candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product and therapeutic candidates that obtain marketing approval. The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product and therapeutic candidates. 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 otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations. Moreover, 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.

For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, was enacted in March 2010 and has had a significant impact on the health care industry in the U.S. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to biopharmaceutical products, the ACA, among other things, addressed 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, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program. Additionally, on December 20, 2019, President Trump signed the Further Consolidated Appropriations Act for 2020 into law (P.L. 116-94) that includes a piece of bipartisan legislation called the Creating and Restoring Equal Access to Equivalent Samples Act of 2019 or the "CREATES Act." The CREATES Act aims to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic product developers access to samples of brand products. Because generic product developers need samples to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic products. To remedy this concern, the CREATES Act establishes a private cause of action that permits a generic product developer to sue the brand manufacturer to compel it to furnish the necessary samples on "commercially reasonable, market-based terms." Whether and how generic product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on future competition for COSELA or any of our other future commercial products are unknown.

As another example, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drugs and biological products covered under Medicare Part B report the product's average sales price, or ASP, to DHHS beginning on January 1, 2022, subject to enforcement via civil money penalties.

Since its enactment, there have been executive, judicial and Congressional challenges to certain aspects of the ACA and we expect there will be additional challenges and amendments to the ACA in the future. Members of the US Congress have indicated that they may continue to seek to modify, repeal or otherwise invalidate all, or certain provisions of, the ACA. For example, the Tax Cuts and Jobs Act, or TCJA, was enacted in 2017 and, among other things, removed penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, commonly referred to as the "individual mandate." In December 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate was a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the TCJA, the remaining provisions of the ACA were invalid and the law in its entirety was unconstitutional. In December 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional but remanded the case back to the District Court to determine whether other reforms enacted as part of the ACA but not specifically related to the individual mandate or health insurance could be severed from the rest of the ACA so as not to be declared invalid as well. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case and allocated one hour for oral arguments, which occurred on November 10, 2020. A decision from the Supreme Court is expected to be issued in spring 2021. It is unclear how this litigation and other efforts to repeal and replace the ACA will impact the implementation of the ACA, the pharmaceutical industry more generally, and our business. Complying with any new legislation or reversing changes implemented under the ACA could be time-intensive and expensive, resulting in a material adverse effect on our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA that affect health care expenditures. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through 2030 unless additional Congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, which was signed into law on March 27, 2020 and was designed to provide financial support and resources to individuals and businesses affected by the COVID-19 pandemic, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030, in order to offset the added expense of the 2020 cancellation. The 2021 Consolidated Appropriations Act was subsequently signed into law on December 27, 2020 and extends the CARES Act suspension period to March 31, 2021.

Moreover, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. DHHS, has solicited feedback on some of various measures intended to lower drug prices and reduce the out of pocket costs of drugs and implemented others under its existing authority. For example, in May 2019, DHHS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified a DHHS policy change that was effective January 1, 2019. As part of the Trump Administration's so-called "Blueprint" to lower drug prices, DHHS and FDA also released on July 31, 2019 their Safe Importation Action Plan proposing two different pathways for the importation of foreign drug products. One pathway focuses on the importation of certain drugs from Canada, which required the agencies to go through notice-and-comment rulemaking, while the second pathway allows manufacturers to distribute their drugs manufactured abroad and was released as agency policy in an FDA guidance document first issued in December 2019. FDA's notice of proposed rulemaking to implement a system whereby state governmental entities could lawfully import and distribute prescription drugs sourced from Canada was published at the end of December 2019 and in September 2020, the rulemaking was finalized by FDA. Those new regulations became effective on November 30, 2020, although the impact of such future programs is uncertain, in part because lawsuits have been filed challenging the government's authority to promulgate them. The final regulations may also be vulnerable to being overturned by a joint resolution of disapproval from Congress under the procedures set forth in the Congressional Review Act, which could be applied to regulatory actions taken by the Trump Administration on or after August 21, 2020 (i.e., in the last 60 days of legislative session of the 116th Congress). Congress and the executive branch have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs, making this area subject to ongoing uncertainty. In addition, the probability of success of other policies enacted over the final months of the Trump Administration and their impact on the U.S. prescription drug marketplace is unknown. There are likely to be political and legal challenges associated with implementing these reforms as they are currently envisioned, and the January 20, 2021 transition to a new Democrat-led presidential administration created further uncertainty. Following his inauguration, President Biden took immediate steps to order a regulatory freeze on all pending substantive executive actions in order to permit incoming department and agency heads to review whether questions of fact, policy, and law may be implicated and to determine how to proceed.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmaceutical benefit managers (PBMs) and other members of the health care and pharmaceutical supply chain, an important decision that may lead to further and more aggressive efforts by states in this area.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, including COSELA and any future products for which we secure marketing approval.

Human Capital

As of December 31, 2020, we had 122 full-time employees, including 57 in research and development and 65 in general and administrative functions. Of these full-time employees, 35 had an MD, PhD or PharmD. We have no collective bargaining agreements with our employees, and we have not experienced any work stoppages. We expect headcount growth to continue for the foreseeable future, particularly as we continue to develop our products and commercialize COSELA. We consider our relations with our employees to be good.

Diversity and Inclusion

Diversity and inclusion are an important part of our culture. We seek to build a diverse and inclusive workplace where we can leverage our collective cognitive and other diversity. In 2020, we conducted pay equity analysis and we determined that we have pay equity across gender and race for people in similar jobs, accounting for factors such as role, experience, education and level. We also

have a Culture Committee comprised of employees across departments, who focus on employee engagement and other initiatives throughout the year.

Compensation and Benefits

We offer competitive compensation to attract and retain the best people. Our total compensation package includes market-competitive salary, bonuses, and equity. We offer full-time employees equity at the time of hire and through annual equity grants because we want them to consider themselves to have an ownership stake in the company and to be committed to our long-term success. We offer a wide range of benefits across areas such as health, family, finance, community, and time off, including healthcare and wellness benefits, a 401(k) plan, access to legal services, family leave, and paid time off.

Protection and Support of our Employees During the COVID-19 Pandemic

In response to the COVID-19 pandemic, we put in place the following safety measures for our employees, patients, healthcare professionals, and suppliers to limit exposure and protect the health of those we employ and serve. These measures included, but were not limited to, we substantially restricted travel, supplied personal protective equipment to employees, limited access to our headquarters and asked most of our staff to work remotely. On short notice, we transitioned most of our employees to working remotely and added bandwidth and VPN capacity to our infrastructure. In addition, we continued to enhance our cybersecurity protections. As a company, we supported our employees by maintaining base compensation throughout the year, and our year-end practices around merit, bonus and equity were not impacted. We continue to build a strong supportive culture around values of patients first, integrity, respect and collaboration. Our efforts to develop our culture will last far beyond this pandemic.

Available Information

Our internet address is www.g1therapeutics.com. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the Investors section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the Securities and Exchange Commission, or the SEC. The information found on our website is not part of this or any other report we file with, or furnish to, the SEC.

In addition, the SEC maintains an internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. Our filings with the SEC may be accessed through the SEC's website at http://www.sec.gov.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information in this Annual Report, including our financial statements and related notes, before investing in our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. If any of the following risks occur, our business, operating results and prospects could be materially harmed. In that event, the price of our common stock could decline, and you could lose part or all of your investment.

Summary Risk Factors

Below is a summary of the principal risk factors in each risk category that could adversely affect our business, operations, and financial results.

Risks related to the commercialization of our product candidates

- We depend almost entirely on the commercial success of COSELA.
- COSELA may fail to achieve the degree of market acceptance for commercial success.
- We face substantial competition.
- COSELA may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies.
- We may not be able to effectively sell or market our product candidates, if approved, or generate product revenues.
- Product liability lawsuits against us could cause us to incur substantial liabilities.
- If we or BI fail to adequately perform under the Co-Promotion Agreement, our business would be adversely affected.
- If we violate the guidelines pertaining to promotion and advertising we may be subject to disciplinary action.
- Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Risks related to development of our product candidates:

- Initial success in our ongoing clinical trials may not be indicative of results obtained when these trials are completed.
- If we are unable to successfully develop and commercialize our product candidates, our business will be materially harmed.
- Our development of a CDK4/6 to decrease the incidence of chemotherapy-induced myelosuppression may never lead to a marketable product.
- Delays in the enrollment of patients in clinical trials, may delay or prevent our plans.
- We may incur additional costs or experience delays in completing the development and may ultimately be unable to obtain the approval of our product candidates.

Risks related to our financial position and need for additional capital:

- We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- Our limited operating history may make it difficult for you to evaluate the success of our business.
- We will need substantial additional funding.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights.

Risks related to marketing approval of our product candidates:

- If we are not able to obtain, or if there are delays in obtaining, required marketing approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.
- Our product candidates may cause undesirable side effects that could delay or prevent their marketing approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.
- Any product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Risks related to our dependence on third parties

- We rely on, and expect to continue to rely on, third parties to conduct our clinical trials for our product candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain marketing approval for or commercialize our product candidates, and our business could be substantially harmed.
- We have entered into license agreements for lerociclib, a license agreement for the development of COSELA in greater China, and intend to continue to use third-party collaborators to help us develop and commercialize any new products, and our ability to commercialize such products could be impaired or delayed if these collaborations are unsuccessful.
- We contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

Risks related to our intellectual property

- If we are unable to obtain and maintain intellectual property protection for our technology and products, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired and, if we infringe the valid patent rights of others, we may be prevented from making, using or selling our products or may be subject to damages or penalties.
- Some intellectual property may have been discovered through government funded programs and thus may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.
- We may become involved in administrative adversarial proceedings in the U.S. PTO or in the patent offices of foreign countries brought by a third party to attempt to cancel or invalidate our patent rights, which could be expensive, time consuming and cause a loss of patent rights.
- We may have to file one or more lawsuits in court to prevent a third party from selling a product or using a product in a manner that infringes our patent, which could be expensive, time consuming and unsuccessful, and ultimately result in the loss of our proprietary market.

Risks related to employee matters, managing growth and other risks related to our business

- We currently have a limited number of employees, and our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- We expect to potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.
- We face risks related to health epidemics and outbreaks, including the novel coronavirus (COVID-19), which could significantly disrupt our preclinical studies and clinical trials.

Risks related to our common stock

- The price of our common stock may be volatile and fluctuate substantially.
- Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.
- Our certificate of incorporation includes a forum selection clause, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us.

For a more complete discussion of the material risks facing our business, see below.

Risks related to the commercialization of our product candidates

We depend almost entirely on the commercial success of COSELA. There is no assurance that the launch of COSELA in the U.S. will occur on our anticipated timing. There is no assurance that our commercialization efforts in the U.S. with respect to COSELA will be successful or that we will be able to generate revenues at the levels or within the timing we expect or at the levels or within the timing necessary to support our goals.

To date, we have not generated any revenues from the sale of COSELA. COSELA was approved by the FDA in February 2021 but is not yet commercially available. We plan to make COSELA available in the U.S. in March 2021. There is no assurance that the launch of COSELA will occur on the timing we anticipate. We may encounter delays or hurdles related to our launch that affect timing.

Our business currently depends heavily on our ability to successfully commercialize COSELA in the U.S. to treat patients with ES-SCLC. We may never be able to successfully commercialize COSELA or meet our expectations with respect to revenues. We have never marketed, sold or distributed for commercial use any pharmaceutical product. There is no guarantee that the infrastructure, systems, processes, policies, personnel, relationships and materials we have built in anticipation of the launch and commercialization of COSELA in the U.S. will be sufficient for us to achieve success at the levels we expect. Additionally, healthcare providers may not accept a new treatment paradigm for patients with ES-SCLC. We may also encounter challenges related to reimbursement of COSELA, even if we have positive early indications from payors, including potential limitations in the scope, breadth, availability, or amount of reimbursement covering COSLEA. Similarly, healthcare settings or patients may determine that the financial burdens of treatment are not acceptable. Our results may also be negatively impacted if we have not adequately sized our field teams or our physician segmentation and targeting strategy is inadequate or if we encounter deficiencies or inefficiencies in our infrastructure or processes. Any of these issues could impair our ability to successfully commercialize COSELA or to generate substantial revenues or profits or to meet our expectations with respect to the amount or timing of revenue or profits. Any issues or hurdles related to our commercialization efforts may materially adversely affect our business, results of operations, financial condition and prospects. There is no guarantee that we will be successful in our launch or commercialization efforts with respect to COSELA.

Our COSELA commercialization efforts may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Our COSELA commercialization efforts may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If COSELA or our other product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of COSELA and our other product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the timing of our receipt of any marketing approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the efficacy and safety and potential advantages and disadvantages compared to alternative treatments;
- the prevalence and severity of any side effects associated with our products;
- the indications for which our products are approved;
- adverse publicity about our products or favorable publicity about competing products;
- the approval of other products for the same indications as our products;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the success of our physician education programs;
- the strength of our marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement, including patient cost-sharing programs such as copays and deductibles; and
- any restrictions on the use of our products together with other medications.

If COSELA and any other product we commercialize fails to achieve market acceptance, it could have a material and adverse effect on our business, financial condition, results of operation and prospects.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. COSELA competes with (a) existing growth factor support treatments, and (b) multiple approved drugs or drugs that may be approved in the future for indications for which we may develop COSELA. If rintodestrant is approved, it would compete with (a) the approved intramuscular SERD, fulvestrant, being marketed by AstraZeneca, (b) if approved, other oral SERDs in development by Radius Health, Genentech, AstraZeneca, Sanofi, Eli Lilly and Zentalis; and (c) multiple approved drugs or drugs that may be approved in the future for indications for which we may develop rintodestrant.

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 products that we may develop. Our competitors also may obtain FDA or other marketing approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market and/or slow our marketing approval. Some of the important competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price and the availability of reimbursement from government and other third-party payors.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to commercialize COSELA and our other product candidates, such drugs may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product candidate, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product candidate in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and reimbursement for these product candidates and related treatments will be available from government authorities, private health insurers and other organizations. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs are generally covered and paid for in the United States, but have not been approved for reimbursement in certain European countries. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of payments for particular drugs. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We cannot be sure that coverage will be available for any product candidate that we commercialize and, if coverage is available, the level of payments. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

In addition to CMS and private payors, professional organizations such as the National Comprehensive Cancer Network and the American Society of Clinical Oncology can influence decisions about reimbursement for new medicines by determining standards of care. In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of our products.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs 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 drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

If we are unable to establish effective sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to effectively sell or market our product candidates, if approved, or generate product revenues.

We have limited infrastructure for the sale, marketing or distribution of drugs. To achieve commercial success for COSELA or any future approved product candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any drug launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so when needed or on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates that receive marketing approval or any such commercialization may experience delays or limitations. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our business, results of operations, financial condition and prospects will be materially adversely affected.

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

We face an inherent risk of product liability exposure related to the evaluation of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;

- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to successfully commercialize any products that we may develop.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. 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 Co-Promotion Agreement with Boehringer Ingelheim Pharmaceuticals, Inc. or BI, is important to our business. If we or BI fail to adequately perform under the Co-Promotion Agreement, or if we or BI terminate the Co-Promotion Agreement, the commercialization of COSELA and our business would be adversely affected.

The Co-Promotion Agreement is important to our business, and our ability to fully commercialize COSELA in the United States is dependent upon this agreement.

Under the terms of the Co-Promotion Agreement, BI will provide salesforce engagements for COSELA within the United States and Puerto Rico utilizing BI's own sales and marketing personnel. BI will hire and maintain, and be solely responsible for, its own personnel conducting the promotion services described in the Co-Promotion Agreement, including ensuring that such personnel adhere to certain guidelines and practices with respect to the promotion of COSELA. The Company will lead marketing, market access, and medical engagement initiatives under the Co-Promotion Agreement. The Company will also be responsible for the costs of maintaining regulatory approval of, manufacturing, supplying and distributing COSELA, and will prepare and control the content of COSELA marketing and training materials, subject to review and feedback by BI.

Subject to early termination, the Co-Promotion Agreement will expire on the third anniversary of the first commercial sale. Subject to specified notice periods and specified limitations, either party may terminate the Co-Promotion Agreement in the event of (i) uncured material breach by the other party, (ii) COSELA not having obtained regulatory approval from the FDA by September 30, 2021, (iii) withdrawal of COSELA from the market by the Company as a result of a decision by the FDA or a material safety concern; (iv) the bankruptcy, insolvency, dissolution or winding up of the other party, or (v) for convenience (which termination right, in the case of BI, may only be exercised six months after first commercial sale). In addition, the Company may terminate the Co-Promotion Agreement if the Company receives feedback from a regulatory authority that the Company reasonably believes indicates that COSELA is unlikely to receive regulatory approval. BI may also terminate the Co-Promotion Agreement if the first commercial sale has not occurred by September 30, 2021 or upon a change of control of the Company.

Termination of the Co-Promotion Agreement could cause significant delays and disruption to our commercialization efforts for COSELA. If the Co-Promotion Agreement is terminated, we may need to seek additional financing to support our commercialization efforts or find another third party to enter into a new collaboration agreement. Any alternative collaboration could also be on less favorable terms to us. If the Co-Promotion Agreement is terminated our business would be adversely affected.

If we or any of our current or future partners violate the guidelines pertaining to promotion and advertising of COSELA or any of our other product candidates, if approved, we or they may be subject to disciplinary action by the FDA's Office of Prescription Drug Promotion (OPDP) or other regulatory authorities.

The FDA's Office of Prescription Drug Promotion (OPDP), is responsible for reviewing prescription drug advertising and promotional labeling to ensure that the information contained in these materials is not false or misleading. There are specific disclosure requirements, and the applicable regulations mandate that advertisements cannot be false or misleading or omit material facts about the product. Prescription drug promotional materials must present a fair balance between the drug's effectiveness and the risks associated with its use. Most warning letters from OPDP cite inadequate disclosure of risk information.

OPDP prioritizes its actions based on the degree of risk to the public health, and often focuses on newly introduced drugs and those associated with significant health risks. There are two types of letters that OPDP typically sends to companies that violate its drug advertising and promotional guidelines: untitled letters and warning letters. In the case of an untitled letter, OPDP typically alerts the drug company of the violation and issues a directive to refrain from future violations, but does not typically demand other corrective action. A warning letter is typically issued in cases that are more serious or where the company is a repeat offender. Although we have not received any such letters from OPDP, we or any of our current or future partners may inadvertently violate OPDP's guidelines in the future and be subject to an OPDP untitled letter or warning letter, which may have a negative impact on our business.

Our relationships with customers and third-party payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

As we are commercializing COSELA and may commercialize other product candidates, we are subject to additional healthcare statutory and regulatory requirements and enforcement by federal government and the states and foreign governments in the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of COSELA and any other product candidates for which we obtain marketing approval. Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid; a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal false claims laws impose criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; in addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal physician payment transparency requirements, sometimes referred to as the “Sunshine Act” under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to the Centers for Medicare & Medicaid Services, or CMS, information related to payments and other transfers of value to physicians and teaching hospitals and the ownership and investment interests of physicians and their immediate family members in such manufacturers;
- HIPPA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouses as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers;
- some 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 and may 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 also govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. It is possible that governmental authorities may conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Because COSELA received accelerated approval by the FDA, we must still comply with post-approval development and regulatory requirements to maintain that approval and, if we fail to do so, FDA could withdraw its approval of COSELA, which would lead to substantially lower revenues.

For drugs granted accelerated approval, the FDA typically requires post-marketing confirmatory trials to evaluate the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence. As a condition of the accelerated approval of COSELA, we are required to (i) conduct a study in a sufficient number of adult patients with extensive stage-small cell lung cancer undergoing chemotherapy to evaluate the impact of COSELA on disease progression or survival in patients with chemotherapy-induced myelosuppression treated with a platinum/etoposide-containing regimen or topotecan-containing regimen with at least 2 years of follow-up (ii) conduct an in vitro metabolism study and CYP phenotyping study at clinically relevant concentrations to appropriately determine major metabolic pathway for COSELA. Characterize the formation of the major circulating metabolite of trilaciclib, M8, using the purified M8 compound with a validated bioanalytical method), (iii) conduct an in vitro Drug-Drug Interaction (DDI) study to evaluate the major circulating metabolite of COSELA, M8, as an inhibitor for major CYP enzymes and drug transporters, and (iv) conduct a clinical trial to evaluate the effect of hepatic impairment on the pharmacokinetics and safety of COSELA.

The FDA may withdraw approval of a product candidate approved under the accelerated approval pathway if, for example, the trial required to verify the predicted clinical benefit of our product candidate fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Risks related to development of our product candidates

Initial success in our ongoing clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials.

We are currently evaluating our product candidates in clinical trials. There can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results.

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

We have invested substantially all of our efforts and financial resources identifying and developing our CDK4/6 inhibitor product candidates, COSELA and our oral SERD product candidate, rintodestrant. Our ability to generate product revenues will depend on the successful development and eventual commercialization of COSELA and our other product candidates. In 2020, we did not generate any revenues from sales of any drugs. Each of our product candidates will require additional development, management of development and manufacturing activities, marketing approval in multiple jurisdictions, obtaining manufacturing supply, commercialization activities, substantial investment and significant marketing efforts before we generate any revenues from drug sales.

We have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

- build and maintain robust sales, distribution and marketing capabilities, either on our own or in collaboration with strategic partners;
- gain acceptance for our product candidates, if approved, by patients, the medical community and third-party payors;

- compete effectively with other therapies;
- execute development activities for our product candidates, including successful enrollment in and completion of clinical trials;
- obtain required marketing approvals for the development and commercialization of our product candidates;
- obtain and maintain patent and trade secret protection and regulatory exclusivity for our product candidates and ensure that we do not infringe the valid patent rights of third parties;
- protect, leverage and expand our intellectual property portfolio;
- establish and maintain clinical and commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical and commercial manufacturing;
- obtain and maintain healthcare coverage and adequate reimbursement;
- maintain a continued acceptable safety profile for our product candidates following approval, if approved;
- develop and maintain any strategic relationships;
- enforce and defend intellectual property rights and claims; and
- manage our spending as costs and expenses increase due to preclinical development, clinical trials, marketing approvals and commercialization.

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

Our development of COSELA, a CDK4/6 to decrease the incidence of chemotherapy-induced myelosuppression is novel, unproven and rapidly evolving.

COSELA is a short-acting intravenous CDK4/6 inhibitor. The use of a CDK4/6 inhibitor to decrease the incidence of chemotherapy-induced myelosuppression is a novel approach and we believe that we are the only company currently developing a CDK4/6 inhibitor for this patient population. Even though COSELA has demonstrated positive results in clinical trials for small cell lung cancer, we may not succeed in demonstrating safety and efficacy of COSELA in additional indications.

Advancing COSELA creates significant challenges for us, including:

- obtaining marketing approval for multiple indications, as the FDA and other regulatory authorities have limited experience with commercial development of a CDK4/6 inhibitor for this type of use;
- educating medical personnel regarding the potential safety benefits, as well as the challenges, of incorporating our product candidates into their treatment regimens; and
- establishing sales and marketing capabilities to gain market acceptance of a novel therapy.

If we experience delays or difficulties in the enrollment of patients in clinical trials, development of our product candidates may be delayed or prevented, which would have a material adverse effect on our business.

Identifying and qualifying patients to participate in clinical trials for our product candidates is critical to our success. In particular, because we are initially focused on patients with diseases with genetically defined tumors, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials. Patient enrollment may be affected by many factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the clinical trial in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the availability of competing therapies and clinical trials; and
- the proximity and availability of clinical trial sites for prospective patients.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical trials may be delayed or terminated. Any delays in completing our clinical trials will increase our costs, delay or prevent our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and prospects significantly.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and may experience delays in obtaining, or ultimately be unable to obtain, the approval of our product candidates.

The risk of failure in drug development is high. Before obtaining marketing approval from regulatory authorities for the sale of any of our product candidates, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical trials are expensive, difficult to design and implement and can take several years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the clinical trial process. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates. Clinical trials may be delayed, suspended or prematurely terminated because costs are greater than we anticipate or for a variety of reasons, such as:

- delay or failure in reaching agreement with the FDA or a comparable foreign regulatory authority on a trial design that we are able to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delays in reaching, or failure to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inability, delay, or failure in identifying and maintaining a sufficient number of trial sites, many of which may already be engaged in other clinical programs;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial;
- delay or failure in having subjects complete a trial or return for post-treatment follow-up;
- clinical sites and investigators deviating from the clinical protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- failure to initiate or delay of or failure to complete a clinical trial as a result of an IND being placed on clinical hold by the FDA, or for other reasons;
- lack of adequate funding to continue a clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials and increased expenses associated with the services of our CROs and other third parties;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators, or a Data Safety Monitoring Board, or DSMB, if one is used for our clinical trials, may require that we suspend or terminate our clinical trials for various reasons, including noncompliance with regulatory requirements, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, or a finding that the participants are being exposed to unacceptable health risks;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient;
- the FDA or other regulatory authorities may require us to submit additional data or impose other requirements before permitting us to initiate a clinical trial; or
- there may be changes in governmental regulations or administrative actions.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval for our product candidates. Further, the FDA may disagree with our clinical trial design and our interpretation of data from clinical trials or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials.

If we are required to conduct additional clinical trials or other studies of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other studies, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval for our product candidates at all;
- 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 that would reduce the potential market for our products or inhibit our ability to successfully commercialize our products;
- be subject to additional post-marketing restrictions and/or requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in preclinical and clinical development or receiving the requisite marketing approvals. We do not know whether any of our preclinical studies or clinical trials will need to be restructured or will be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Risks related to our financial position and need for additional capital

We have incurred significant operating losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

We have incurred significant operating losses since our inception. We incurred net losses of $99.3 million for the year ended December 31, 2020, $122.4 million for the year ended December 31, 2019, and $85.3 million for the year ended December 31, 2018. As of December 31, 2020, we had an accumulated deficit of $436.1 million. Our product candidates span a range from development to commercialization, and it may be several years, if ever, before we become profitable. To date, we have financed our operations through sales of our preferred and common stock, license agreements and debt. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially as we:

- support our commercialization efforts for COSELA;
- continue development of our product candidates, including additional clinical trials;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- increase our sales, marketing and distribution infrastructure to commercialize COSELA and any other products for which we may obtain marketing approval;
- achieve market acceptance for COSELA and any other of our product candidates in the medical community and with third-party payors;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel;
- enter into collaboration arrangements, if any, for the development of our product candidates or in-license other products and technologies;
- achieve milestones requiring payment under our in-licensing programs;
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts; and
- incur increased costs as a result of operating as a public company.

Because of the numerous risks and uncertainties associated with developing and commercializing pharmaceutical drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. In addition, our expenses could increase beyond expectations if we are required by the FDA or foreign regulatory agencies, to perform studies and clinical trials in addition to those that we currently anticipate for COSELA, or if there are any delays in our or our partners completing clinical trials or the development of any of our product candidates.

To become and remain profitable, we must develop and commercialize products with significant market potential. This will require us to be successful in a range of challenging activities, including the following:

- completing clinical trials of our product candidates that meet their clinical endpoints;
- obtaining marketing approval for our product candidates;
- manufacturing, marketing and selling those products for which we may obtain marketing approval; and
- achieving market acceptance of our product candidates in the medical community and with third-party payors.

We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our discovery and preclinical development efforts, expand our business or continue our operations and may require us to raise additional capital that may dilute your ownership interest. A decline in the value of our company could also cause you to lose all or part of your investment.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Biopharmaceutical drug development is a highly speculative undertaking and involves a substantial degree of risk. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies, and conducting clinical trials of trilaciclib, rintodestrant and lerociclib. We have not yet demonstrated our ability to successfully complete large-scale, pivotal clinical trials, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Typically, it takes several years to develop one new drug from the time it is discovered to when it is available for treating patients. In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities and continuing to develop products. We may not be successful in such a transition.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be compelled to delay, reduce or eliminate our product development programs or commercialization efforts.

The development of pharmaceutical drugs is a capital-intensive venture. We expect our expenses to continue to increase along with our ongoing activities, particularly as we support commercial activities and conduct larger-scale clinical trials of, and seek marketing approval for, our product candidates. For example, we expect to incur significant COSELA commercialization expenses related to product sales, marketing, manufacturing and distribution. We may also need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our product candidates or otherwise expand more rapidly than we presently anticipate. Furthermore, we have incurred, and expect to continue to incur, additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our clinical programs, development efforts or any future commercialization efforts.

As of December 31, 2020, we had $207.3 million in cash and cash equivalents. We believe that, based upon our current operating plan, our existing capital resources will be sufficient to fund our anticipated operations for greater than 12 months from the date of filing this Annual Report. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing commercialization expenses, research and development, and other corporate activities. Because the length of time and activities associated with successful commercialization and research and development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for commercialization and development of any approved product candidates. In addition, our future capital requirements will depend on many factors, and could increase significantly as a result of many factors, including:

- the costs of commercialization activities, including product sales, marketing, manufacturing and distribution of COSELA and any of our future product candidates for which we receive marketing approval;
- the scope, progress, results and costs of development, laboratory testing and clinical trials for our product candidates;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- the extent to which we enter into non-exclusive, jointly funded clinical research collaboration arrangements, if any, for the development of our product candidates in combination with other companies' products;
- our ability to establish collaboration arrangements for the development of our product candidates on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our license agreement and any collaboration agreements into which we may enter, if any;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the extent to which we acquire or in-license product candidates and technologies, such as rintodestrant, and the terms of such in-licenses;
- revenue received from commercial sales of COSELA and any future product candidates; and

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

Conducting studies and clinical trials is a time-consuming, expensive and uncertain process that can take years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, COSELA and our future product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that may not be commercially available for some time, if ever. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize COSELA and our other product candidates. Volatility in the financial markets have generally made equity and debt financing more difficult to obtain and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue the commercialization of COSELA or any one or more of our research or development programs or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity financings, debt financings, collaborations, strategic alliances and licensing arrangements. The sale of additional equity or convertible debt securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights, limitations on declaring dividends and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through collaborations, strategic alliances or licensing arrangements with third parties, and we could be required to do so at an earlier stage than otherwise would be desirable. In connection with any such collaborations, strategic alliances or licensing arrangements, we may be required to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates, grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves, or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

Our level of indebtedness and debt service obligations could adversely affect our financial condition and may make it more difficult for us to fund our operations.

We have entered into a loan and security agreement with Hercules Capital, Inc. for up to $100.0 million of debt under a term loan, or the Hercules Loan Agreement. The maturity date of the Hercules Loan Agreement is June 1, 2024. As of December 31, 2020, the Company has borrowed $20.0 million under the Hercules Loan Agreement. The Company’s obligations under the Hercules Loan Agreement are secured by a blanket lien on substantially all of the Company’s assets, including a security interest in the intellectual property.

This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have important negative consequences, including the fact that we will need to repay our indebtedness by making payments of interest and principal, which will reduce the amount of money available to finance our operations, our commercialization efforts, our research and development efforts and other general corporate activities.

If we were to become unable to pay, when due, the principal of, interest on, or other amounts due in respect of, our indebtedness, our financial condition would be adversely affected. Further, under the Hercules Loan Agreement, we are subject to certain restrictive covenants that, among other things, subject to exceptions, restrict the Company’s ability to do the following things: declare dividends or redeem or repurchase equity interests; incur additional liens; make loans and investments; incur additional indebtedness; engage in mergers, acquisitions, and asset sales; transact with affiliates; undergo a change in control; and add or change business locations. If we breach any of these restrictive covenants or are unable to pay our indebtedness under the Hercules Loan Agreement when due, this could result in a default under the Hercules Loan Agreement. In such event, Hercules may elect (after the expiration of any applicable notice or grace periods) to declare all outstanding borrowings, together with accrued and unpaid interest and other amounts payable

under the Hercules Loan Agreement, to be immediately due and payable. Any such occurrence would have an adverse impact on our financial condition.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and the amount of the liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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 other 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 discovery, preclinical development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks related to marketing approval of our product candidates

If we are not able to obtain, or if there are delays in obtaining, required marketing approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current good manufacturing practice, or cGMP, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by FDA and other regulatory authorities, requirements regarding the distribution of samples to physicians and recordkeeping. Before we can commercialize any of our product candidates, each such product candidate must be approved by the FDA pursuant to a new drug application, or NDA, in the United States, by the European Medicines Agency, or EMA, pursuant to a marketing authorization application, or MAA, in the European Union, and by similar regulatory authorities outside the United States prior to commercialization.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes several years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have limited experience in planning and conducting the clinical trials required for marketing approvals, and we expect to rely on third-party contract research organizations, or CROs, to assist us in this process. Obtaining marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process, and in many cases the inspection of manufacturing facilities by the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies or clinical trials. Our product candidates could be delayed in receiving, or fail to receive, marketing approval for many reasons, including the following:

- the FDA or comparable 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 comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission to obtain marketing approval in the United States or elsewhere;
- third-party manufacturers or our clinical or commercial product candidates may be unable to meet the FDA's cGMP requirements or similar requirements of foreign regulatory authorities; and
- the approval requirements or policies of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

In addition, even if we were to obtain approval, regulatory authorities may approve our product candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

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

Undesirable side effects caused by our product candidates could cause us or the FDA or other regulatory authorities to interrupt, delay or halt our clinical trials and could result in more restrictive labels or the delay or denial of marketing approval by the FDA or other regulatory authorities of our product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. In addition to this, the drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates (or any other similar drugs) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such product candidates from the marketplace after they are approved;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates, if approved, and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

COSELA and any other product candidate for which we obtain marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Commercialization activities for COSELA, and any other product candidate, such as the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. The FDA or a comparable foreign regulatory authority may also impose requirements

for costly post-marketing preclinical studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products, and if we promote COSELA or any other of our products beyond their approved indications, we may be subject to enforcement actions or prosecution arising from that off-label promotion. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay marketing approval of our product candidates. 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, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and certain disabled people and introduced a reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this law provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this law and future laws could decrease the coverage and price that we will receive for any approved products. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Therefore, any limitations in reimbursement that results from the MMA may result in reductions in payments from private payors.

In March 2010, the ACA became law. The ACA is a sweeping law 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 ACA of importance to our potential product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service Act's pharmaceutical pricing program;
- new requirements to report financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; 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 several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to bring more transparency to drug pricing, reduce the costs of drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Although any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Also, the FDA recently issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries as a means to lower drug prices.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we will receive for any approved product. Any reduction in payments from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals, if any, of our product candidates, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing conditions and other requirements.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets. In order to market and sell our products in the European Union and many other jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and economic areas and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by FDA. Additionally, a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the marketing approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials. Obtaining foreign marketing approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. If we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;

- longer lead times for shipping;
- language barriers for technical training;
- reduced or no protection on pharmaceutical products or their use in some foreign countries;
- the unwillingness of courts in some foreign jurisdictions to enforce patents even when valid and infringed in that country;
- the possibility of pre-grant or post-grant review proceedings in certain foreign countries that allow a petitioner to hold up patent rights for an extended period or permanently by challenging the patent filing at the patent office of that country;
- the possibility of a compulsory license issued by a foreign country that allows a third-party company or a government to manufacture, use or sell our products with a government-set low royalty to us;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

Risks related to our dependence on third parties

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

We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or otherwise support clinical trials for our product candidates. We expect to rely heavily on these parties for performance of clinical trials for our product candidates. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards.

We, our investigators, and our CROs will be required to comply with regulations, including good clinical practice, or GCP, and other related requirements for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials and their rights are protected. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any drugs in clinical development. The FDA enforces GCPs through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we, our investigators or our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be called into question and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before considering our marketing applications for approval. We cannot assure you that, upon inspection, the FDA will determine that any of our future clinical trials will comply with GCPs.

In addition, our clinical trials must be conducted with product candidates produced under cGMPs. Our failure or the failure of our investigators or CROs to comply with these requirements may require us to repeat clinical trials, which would delay the marketing approval process and could also subject us to enforcement action. We also are required to register certain clinical trials and post the results of such completed clinical trials involving product candidates for which we receive marketing approval on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Although we intend to design the clinical trials for our product candidates, CROs will administer all of the clinical trials. As a result, many important aspects of our development programs, including their conduct and timing, will be outside of our direct control. Our reliance on third parties to conduct future clinical trials will also result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed;
- make errors in the design, management or retention of our data or data systems; and/or
- form relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If the CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development, marketing approval and commercialization of our product candidates may be delayed, we may not be able to obtain marketing approval and commercialize our product candidates, or our development program may be materially and irreversibly harmed. If we are unable to rely on clinical data collected by our

CROs, we could be required to repeat, extend the duration of, or increase the size of any clinical trials we conduct, and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials such CROs are associated with may be extended, delayed or terminated, and we may not be able to obtain marketing approval for or successfully commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We have entered into license agreements for lerociclib, a license agreement for the development of COSELA in greater China, and intend to continue to use third-party collaborators to help us develop and commercialize any new products, and our ability to commercialize such products could be impaired or delayed if these collaborations are unsuccessful.

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

We have entered into license agreements with third-parties, and may continue to selectively pursue strategic collaborations, for the development and commercialization of our products. For example, (i) in June 2020, we entered into a license agreement with Genor Biopharma Co. Inc., for the development and commercialization of lerociclib in the Asia-Pacific region (excluding Japan); (ii) in July 2020, we and EQRx entered into license agreement pursuant to which we have granted EQRx the exclusive rights to develop and commercialize lerociclib in the U.S., Europe, Japan and all other global markets, excluding the Asia-Pacific region (except Japan); and (iii)in August 2020, we entered into a license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd, for the development and commercialization of COSELA in Greater China.

In our third-party collaborations, we are dependent upon the success of the collaborators to perform their responsibilities with continued cooperation. Our collaborators may not cooperate with us or perform their obligations under our agreements with them. We cannot control the amount and timing of our collaborators' resources that will be devoted to performing their responsibilities under our agreements with them. Our collaborators may choose to pursue alternative therapies in preference to those being developed in collaboration with us. The development and commercialization of our product candidates will be delayed if collaborators fail to conduct their responsibilities in a timely manner or in accordance with applicable regulatory requirements or if they breach or terminate their collaboration agreements with us. Disputes with our collaborators could also impair our reputation or result in development delays, decreased revenues, and litigation expenses.

We face significant competition in seeking additional appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs and market conditions generally. The proposed collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate drug revenue.

In addition, any collaboration that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Any such collaboration may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration or integration costs, write-down of assets or goodwill or impairment charges, increased amortization expenses and difficulty and cost in facilitating the collaboration.

Lastly, disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

We contract with third parties for the manufacture of COSELA and our other product candidates for preclinical studies, clinical trials, and commercial supply This reliance on third parties increases the risk that we will not have sufficient quantities of COSELA and our other product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities. We rely, and expect to continue to rely, on third parties for the manufacture of COSELA and our other product candidates for preclinical studies, clinical trials, and commercial supply of COSELA and our other product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

The facilities used to manufacture COSELA and our other product candidates (drug substance and drug product) must be approved by the FDA (and comparable foreign regulatory authority depending on where marketing authorizations are filed) before marketing authorizations are approved. Often, but not always, these inspections are triggered by marketing authorization submissions. We are completely dependent on our contract manufacturers for compliance with current Good Manufacturing Practices (cGMPs) in connection with the manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and to the regulatory requirements of the FDA or comparable foreign regulatory authority, then we will not be able to use the products produced at their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or comparable foreign regulatory authority finds that these facilities do not comply with cGMP, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Further, our failure, or the failure of our third party manufacturers, to comply with these or other applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of our product candidates.

We may be unable to establish any agreements with third-party manufacturers or do so on acceptable terms. Even if we are able to establish agreements with third party manufacturers, reliance on third party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

COSELA and our other product candidates and any other drugs that we may develop may compete with other product candidates and approved drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development, marketing approval, or commercialization efforts. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacements.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or drugs may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

We, or our third-party manufacturers, may be unable to successfully scale-up manufacturing of COSELA or our other product candidates in sufficient quality and quantity, which would delay or prevent us from developing COSELA or our other product candidates and commercializing approved products.

In order to conduct large-scale clinical trials of COSELA and our other product candidates, or successfully commercialize COSELA, we will need to manufacture them in large quantities. We, or any of our manufacturing partners, may be unable to successfully increase the manufacturing capacity COSELA or for any of our other product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any manufacturing partners, are unable to successfully scale up the manufacture COSELA or our other product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

The third parties upon which we rely for the supply of the drug substance, and drug products are our sole sources of supply and have limited capacity, and the loss of any of these suppliers could harm our business.

Some drug substances and drug products for our product candidates are supplied to us from single source suppliers with limited capacity. Our ability to successfully develop our product candidates, and to ultimately supply our commercial drugs in quantities sufficient to meet the market demand, depends in part on our ability to obtain the drug substances and drug products in accordance with cGMP requirements and in sufficient quantities for clinical trials and commercialization. It is possible that our suppliers of drug substance or drug product which are not dual-sourced could, for any reason, cease their operations.

We do not know whether our suppliers will be able to meet our demand, either because of the nature of our agreements with those suppliers, our limited experience with those suppliers or our relative importance as a customer to those suppliers. It may be difficult for us to assess their ability to timely meet our demand in the future based on past performance. While our suppliers have generally met our demand for their products on a timely basis in the past, they may subordinate our needs in the future to their other customers.

For all of our product candidates, we intend to identify and qualify additional manufacturers to provide drug substances and drug products ideally prior to submission of an NDA to the FDA and/or an MAA to the EMA. Establishing additional or replacement suppliers for drug substances and drug products for our product candidates, if required, may not be accomplished quickly. If we are able to find a replacement supplier, such replacement supplier would need to be qualified, or we may have to perform comparative studies comparing the drug product from a new manufacturer to the product used in any completed clinical trials. All of this may require additional regulatory approval, which could result in further delay. While we seek to maintain adequate inventory of drug substance and drug product for our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such drug substance and drug product from alternate sources at acceptable prices in a timely manner could impede, delay, limit, or prevent our development efforts, which could harm our business, results of operations, financial condition, and prospects.

Risks related to our intellectual property

If we are unable to obtain and maintain intellectual property protection for our technology and products, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired and, if we infringe the valid patent rights of others, we may be prevented from making, using or selling our products or may be subject to damages or penalties.

Our success depends in large part on our ability to obtain and maintain patents in the United States and other countries that adequately protect our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and in foreign countries that cover our novel product candidates and their uses, pharmaceutical formulations and dosages, and processes for the manufacture of them. Our patent portfolio currently includes both patents and patent applications.

The patent prosecution process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may choose not to seek patent protection for certain innovations and may choose not to pursue patent protection in certain jurisdictions. Under the laws of certain jurisdictions, patents or other intellectual property rights may be unavailable or limited in scope. It is also possible that we will fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

We currently solely own or exclusively license our patents and patent applications and we have the right to control the prosecution of the in-licensed patent applications. In the future, we may choose to in-license additional patents or patent applications from third

parties that we conclude are useful or necessary for our business goals. We may not have the right to control the preparation, filing, prosecution or maintenance of such patent applications. Therefore, if we do license additional patents or patent applications in the future, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The U.S. Patent and Trademark Office, or U.S. PTO, recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, became effective on March 16, 2013. The Leahy-Smith Act also created certain new administrative adversarial proceedings, discussed below. It is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

The U.S. Supreme Court has issued opinions in patent cases in the last few years that many consider may weaken patent protection in the United States, either by narrowing the scope of patent protection available in certain circumstances, holding that certain kinds of innovations are not patentable or generally otherwise making it easier to invalidate patents in court. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the U.S. PTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and in other countries. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Likewise, a court could uphold and enforce a third-party patent that it rules we have infringed, which would subject us to damages or prevent us from making, using or selling our products.

During patent prosecution in the United States and in most foreign countries, a third party can submit prior art or arguments to the reviewing patent office to attempt to prevent the issuance of a competitor’s patent. For example, our pending patent applications may be subject to a third-party pre-issuance submission of prior art to the U.S. PTO or an Observation in Europe. Such submission may convince the receiving patent office not to issue the patent. In addition, if the breadth or strength of protection provided by our patents and patent applications is reduced by such third-party submission, it could affect the value of our resulting patent or dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

The risks described here pertaining to our patents and other intellectual property rights also apply to any intellectual property rights that we may license in the future, and any failure to obtain, maintain and enforce these rights could have a material adverse effect on our business. In some cases, we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain and enforce the

licensed patents. Any inability on our part to adequately protect or defend our intellectual property may have a material adverse effect on our business, operating results and financial position.

Some intellectual property may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.

Many of our intellectual property rights were generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we fail to disclose the invention to the government or fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

We may become involved in administrative adversarial proceedings in the U.S. PTO or in the patent offices of foreign countries brought by a third party to attempt to cancel or invalidate our patent rights, which could be expensive, time consuming and cause a loss of patent rights.

The Leahy-Smith Act created for the first time new procedures to challenge issued patents in the United States, including post-grant review and *inter partes* review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with a priority date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for *inter partes* review can be filed immediately following the issuance of a patent if the patent was filed prior to March 16, 2013. A petition for *inter partes* review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with a priority date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of challenge, whereas *inter partes* review proceedings can only be brought to raise a challenge based on published prior art. These administrative adversarial actions at the U.S. PTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts, use a lower burden of proof than used by U.S. federal courts. The U.S. PTO issued a Final Rule on November 11, 2018, announcing that it will now use the same claim construction currently used in the U.S. federal courts to interpret patent claims, which is the plain and ordinary meaning of words used. If any of our patents are challenged by a third party in such a U.S. patent office proceeding, there is no guarantee that we will be successful in defending the patent, which would result in a loss of the challenged patent right to us. Further, even if a U.S. federal court or PTAB rules that a patent owned by us is valid and enforceable, if the other venue takes a contrary position, the patent is considered invalid and not enforceable. Therefore, a party seeking to invalidate a patent owned by us in the United States has the procedural advantage of two alternative venues.

Opposition or invalidation procedures are also available in most foreign countries. Many foreign authorities, such as the authorities at the European Patent Office, have only post-grant opposition proceedings, however, certain countries, such as India, have both pre-grant and post-grant opposition proceedings. These procedures have been used frequently against pharmaceutical patents in foreign countries. For example, in some foreign countries, these procedures are used by generic companies to hold up an innovator's patent rights as a means to allow the generic company to enter the market. This activity is particularly prevalent in India, China and South America and may become more prevalent in Africa and other parts of Asia as certain countries reach more established economies. If any of our patents are challenged in a foreign opposition or invalidation proceeding, we could face significant costs to defend our patents, and we may not be successful. Uncertainties resulting from the initiation, continuation or loss of such proceedings could have a material adverse effect on our ability to compete in the market place. Further, in many foreign jurisdictions, the losing party must pay the attorneys' fees of the winning party, which can be substantial.

We may have to file one or more lawsuits in court to prevent a third party from selling a product or using a product in a manner that infringes our patent, which could be expensive, time consuming and unsuccessful, and ultimately result in the loss of our proprietary market.

Because competition in our industry is intense, competitors may infringe or otherwise violate our issued patents, patents of our licensors or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement lawsuits, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could be significant. 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.

Because our CDK 4/6 inhibitor candidates are small molecules, after commercialization they will be subject in the United States to the patent litigation process of the Hatch Waxman Act, which allows a generic company to submit an Abbreviated New Drug Application, or ANDA, to the FDA to obtain approval to sell our drug using bioequivalence data only. Under the Hatch Waxman Act, we will have the opportunity to list all of our patents that cover our drug product or its method of use in the FDA's compendium of "Approved Drug Products with Therapeutic Equivalence Evaluation," sometimes referred to as the FDA's Orange Book. A generic company can submit an ANDA to the FDA four years after our drug approval because our drug products candidates, COSELA and lerociclib, would be deemed new chemical entities. The submission of the ANDA by a generic company is considered a technical act of patent infringement. The generic company can certify that it will wait until the natural expiration date of our listed patents to sell a generic version of our product or can certify that one or more of our listed patents are invalid, unenforceable, or not infringed. If the latter, we will have 45 days to bring a patent infringement lawsuit against the generic company. This will initiate a challenge to one or more of our Orange Book listed patents based on arguments from the generic company that either our patent is invalid, unenforceable or not infringed. Under the Hatch Waxman Act, if a lawsuit is brought, the FDA is prevented from issuing a final approval on the generic drug until the earlier of seven-and-a-half years from our drug approval or a final decision of a court holding that our asserted patent claims are invalid, unenforceable or not infringed. If we do not properly list our relevant patents in the Orange Book, or timely file a lawsuit in response to a certification from a generic company under an ANDA, or if we do not prevail in the resulting patent litigation, we can lose our proprietary market, which can rapidly become generic. Further, even if we do correctly list our relevant patents in the Orange Book, bring a lawsuit in a timely manner and prevail in that lawsuit, it may be at a very significant cost to us of attorneys' fees and employee time and distraction over a long period. Further, it is common for more than one generic company to try to sell an innovator drug at the same time, and so we may be faced with the cost and distraction of multiple lawsuits. We may also determine it is necessary to settle the lawsuit in a manner that allows the generic company to enter our market prior to the expiration of our patent or otherwise in a manner that adversely affects the strength, validity or enforceability of our patent.

A number of pharmaceutical companies have been the subject of intense review by the U.S. Federal Trade Commission or a corresponding agency in another country based on how they have conducted or settled drug patent litigation, and certain reviews have led to an allegation of an anti-trust violation, sometimes resulting in a fine or loss of rights. We cannot be sure that we would not also be subject to such a review or that the result of the review would be favorable to us, which could result in a fine or penalty.

The U.S. Federal Trade Commission, or FTC, has brought a number of lawsuits in federal court in the past few years to challenge Hatch Waxman ANDA litigation settlements between innovator companies and generic companies as anti-competitive. The FTC has taken an aggressive position that anything of value is a payment, whether money is paid or not. Under their approach, if an innovator as part of a patent settlement agrees not to launch or delay launch of an authorized generic during the 180-day period granted to the first generic company to challenge an Orange Book listed patent covering an innovator drug, or negotiates a delay in entry without payment, the FTC may consider it an unacceptable reverse payment. The biopharmaceutical industry argues that such agreements are rational business decisions to dismiss risk and are immune from antitrust attack if the terms of the settlement are within the scope of the exclusionary potential of the patent. In 2013, the U.S. Supreme Court, in a five-to-three decision in *FTC v. Actavis, Inc.* rejected both the biopharmaceutical industry's and FTC's arguments with regard to so-called reverse payments, and held that whether a "reverse payment" settlement involving the exchange of consideration for a delay in entry is subject to an anticompetitive analysis depends on five considerations: (a) the potential for genuine adverse effects on competition; (b) the justification of payment; (c) the patentee's ability to bring about anticompetitive harm; (d) whether the size of the payment is a workable surrogate for the patent's weakness; and (e) that antitrust liability for large unjustified payments does not prevent litigating parties from settling their lawsuits, for example, by allowing the generic to enter the market before the patent expires without the patentee's paying the generic. Furthermore, whether a reverse payment is justified depends upon its size, its scale in relation to the patentee's anticipated future litigation costs, its independence from other services for which it might represent payment, as was the case in *Actavis*, and the lack of any other convincing justification. The Court held that reverse payment settlements can potentially violate antitrust laws and are subject to the standard antitrust rule-of-reason analysis, with the burden of proving that an agreement is unlawful on the FTC and leaving to lower courts the structuring of such rule of reason analysis. If we are faced with drug patent litigation, including Hatch Waxman litigation with a generic company, we could be faced with such an FTC challenge based on that activity, including how or whether we settle the case, and even if we strongly disagree with the FTC's position, we could face a significant expense or penalty.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights covering our products and technology, including inter parties review proceedings before the U.S. PTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. For example, we are aware that many companies, universities and institutions, including competitors, have filed patent applications and received issued patents in our general areas of CDK 4/6 inhibitors and SERD compounds and their uses in methods of treatment and combinations with other drugs as well as their processes of manufacture. If we are found to infringe a third party's intellectual property rights, we could be required to litigate the validity or enforceability of the third-party asserted patent, which may be expensive, time-consuming and distracting to the company, and which litigation we may lose. We may, instead of litigating, seek to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and therefore we only file for patent protection in selected countries. The requirements for patentability may differ in certain countries, particularly in developing countries. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, Europe, India, China and certain other countries do not allow patents for methods of treating the human body. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions that do not favor patent protection on drugs. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own drugs and, further, may export otherwise infringing drugs to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These drugs may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in the major markets for our product candidates, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

A number of foreign countries have stated that they are willing to issue compulsory licenses to patents held by innovator companies on approved drugs to allow the government or one or more third party companies to sell the approved drug without the permission of the innovator patentee where the foreign government concludes it is in the public interest. India, for example, has used such a procedure to allow domestic companies to make and sell patented drugs without innovator approval. There is no guarantee that patents covering any of our drugs will not be subject to a compulsory license in a foreign country, or that we will have any influence over if or how such a compulsory license is granted. Further, Brazil allows its regulatory agency ANVISA to participate in deciding whether to grant a drug patent in Brazil, and patent grant decisions are made based on several factors, including whether the patent meets the requirements for a patent and whether such a patent is deemed in the country's interest. In addition, several other countries have created laws that make it more difficult to enforce drug patents than patents on other kinds of technologies. Further, under the treaty on the Trade-Related Aspects of Intellectual Property, or TRIPS, as interpreted by the Doha Declaration, countries in which drugs are manufactured are required to allow exportation of the drug to a developing country that lacks adequate manufacturing capability. Therefore, our drug markets in the United States or foreign countries may be affected by the influence of current public policy on patent issuance, enforcement or involuntary licensing in the healthcare area.

In addition, in November 2015, members of the World Trade Organization, or the WTO, which administers TRIPS, voted to extend the exemption against enforcing pharmaceutical drug patents in least developed countries until 2033. We currently have no patent applications filed in least developed countries, and our current intent is not to file in these countries in the future, at least in part due to this WTO pharmaceutical patent exemption.

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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the U.S. PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. 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 and 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. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we fail to comply with our obligations under the license agreement with the University of Illinois, we could lose license rights that are necessary for developing and commercializing rintodestrant.

Our exclusive license with the University of Illinois, or the University, for technology relating to rintodestrant imposes various development, commercialization, royalty payment, diligence and other obligations on us. Specifically, we are required to:

- pay the University a minimum annual fee and potential milestone payments;
- pay the University low single-digit royalties on all net sales of products and a share of any sublicensing revenues;
- use commercially reasonable efforts to bring products to market;
- provide financial reports to the University;
- file, prosecute, defend and maintain patent rights; and
- indemnify the University against certain claims and maintain insurance coverage.

If we breach any of these obligations, the University may have the right to terminate the license, which would result in our being unable to develop, manufacture and sell products that are covered by the licensed technology, including rintodestrant, or in a competitor’s gaining access to the licensed technology.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee’s former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be

self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We seek to protect our confidential proprietary information, in part, by entering into confidentiality and invention or patent assignment agreements with our employees and consultants, however, we cannot be certain that such agreements have been entered into with all relevant parties. Moreover, to the extent we enter into such agreements, 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 inside and outside the United States 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, or those to whom they communicate it, 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.

Risks related to employee matters, managing growth and other risks related to our business

We currently have a limited number of employees, and our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are a clinical development company, and, as of December 31, 2020, had only 122 employees, which includes seven executive officers. We are highly dependent on the commercialization, research and development, clinical, and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, obtain marketing approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We may encounter difficulties in managing our growth, which could disrupt our operations.

To manage our anticipated expansion, we must continue to implement and improve our managerial, operational and financial systems, and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these growth activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. The expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product candidates. If our management is unable to effectively manage our expected expansion, our expenses may increase more than expected, our ability to

generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future expansion of our company.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The global financial crisis at the end of the last decade caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as that global financial crisis, could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business, and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We face risks related to health epidemics and outbreaks, including the novel coronavirus (COVID-19), which could significantly disrupt our preclinical studies and clinical trials.

In December 2019, a novel strain of coronavirus (COVID-19) surfaced in Wuhan, China and in March 2020, in an effort to halt the outbreak of COVID-19, the United States, along with many other countries, placed significant restrictions on travel and many businesses have announced extended closures which could adversely impact our operations. Such government-imposed precautionary measures have been relaxed in certain countries or states, but there is no assurance that more strict measures will be put in place again due to a resurgence in COVID-19 cases. The duration and the geographic impact of the business disruption and related financial impact resulting from the COVID-19 pandemic cannot be reasonably estimated at this time and our business could be adversely impacted by the effects of the COVID-19 pandemic.

The enrollment of patients in current and future clinical trials may be slower due to the outbreak of COVID-19. In addition, we rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our nonclinical studies and clinical trials, and the outbreak may affect their ability to devote sufficient time and resources to our programs. We also rely on third party suppliers and contract manufacturers to produce the drug product we utilize in our clinical trials. Although we do not anticipate significant supply chain delays or shortages as a result of the COVID-19 pandemic at this time, the outbreak may cause delays in delivery of APIs and drug product. Temporary closure of our facilities, or facilities at which our clinical trials or nonclinical studies are conducted, or restrictions on the ability of our employees, clinicians or patients enrolled in our trials to travel could adversely affect our operations and our ability to conduct and complete our nonclinical studies and clinical trials. As a result of the foregoing factors, the expected timeline for data readouts of our clinical trials may be negatively impacted, which would adversely affect our business.

The COVID-19 pandemic also presents a number of challenges for our emerging commercial business, including, among others, the impact due to travel limitations and government-mandated work-from-home or shelter-in-place orders, potential decreased product demand due to reduced numbers of in-person meetings with prescribers and patient visits with physicians, possible delay in cancer treatments with chemotherapy as well as increased unemployment resulting in lower new prescriptions.

In addition, the FDA's ability to engage in routine regulatory and oversight activities, such as the review and clearance or approval of new products, may be affected by the COVID-19 pandemic. The FDA and other regulatory authorities may have slower response times or be under-resourced. If the global health concerns continue to disrupt or prevent the FDA or other regulatory authorities from conducting their regular reviews, inspections, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our marketing applications, clinical trial authorizations, or other regulatory submissions, which could have a material adverse effect on our business.

The full extent to which COVID-19 impacts our business will depend on future developments, including, but not limited to, the ultimate severity and scope of the pandemic, the pace at which governmental and private travel restrictions and public concerns about public gatherings will ease, the rate at which historically large increases in unemployment rates will decrease, if at all, and whether, and the speed with which the economy recovers, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of COVID-19 and the actions to treat or contain COVID-19 or to otherwise limit its impact.

Our business and operations could suffer in the event of system failures.

We utilize information technology systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects.

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from cyber-attack, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Furthermore, we have little or no control over the security measures and computer systems of our third-party CROs and other contractors and consultants. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

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

We are exposed to the risk that our employees, principal investigators, CROs and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violate the regulations of the FDA and other regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities; healthcare fraud and abuse laws and regulations in the United States and abroad; or laws that require the reporting of financial information or data accurately. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. 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. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, 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.

We may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on specific product candidates. As a result, we may 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. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We may acquire businesses or drugs, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses 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 drugs resulting from a strategic alliance or acquisition that 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 to justify the transaction.

We or the third parties upon which we depend may be adversely affected by earthquakes, pandemics, or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes, pandemics such as the COVID-19 (coronavirus), or other natural disasters could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Risks related to our common stock

The price of our common stock may be volatile and fluctuate substantially.

The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results of preclinical and clinical trials of our product candidates, including COSELA, rintodestrant and lerociclib;
- results of clinical trials of our competitors' products;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated fluctuations in our financial condition and operating results;
- publication of research reports by securities analysts about us or our competitors or our industry;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, collaborations, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- the passage of legislation or other regulatory developments in the United States and other countries affecting us or our industry;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other stockholders;
- speculation in the press or investment community;
- announcement or expectation of additional financing efforts;
- changes in accounting principles;
- changes in the structure of healthcare payment systems;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities;
- changes in market conditions for pharmaceutical and biopharmaceutical stocks;
- changes in general market, industry and economic conditions; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market has experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our by-laws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board of directors were considered beneficial by some stockholders. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least two-thirds of the voting power of all of the then-outstanding shares of capital stock that would be entitled to vote generally in the election of directors to amend or repeal specified provisions of our certificate of incorporation or by-laws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our certificate of incorporation includes a forum selection clause, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any stockholder to bring (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, or employees to us or to our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or by-laws, or (iv) any action asserting a claim governed by the internal affairs doctrine; in all cases subject to the court's having personal jurisdiction over the indispensable parties named as defendants. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the foregoing provisions. This forum selection provision in our certificate of incorporation may limit our stockholders' ability to obtain a favorable judicial forum for disputes with us. It is also possible that, notwithstanding the forum selection clause included in our certificate of incorporation, a court could rule that such a provision is inapplicable or unenforceable.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market 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. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located in Research Triangle Park, North Carolina, where we lease approximately 60,000 square feet of laboratory and office space. This lease on our corporate headquarters commenced in September 2019 and expires on September 30, 2027. None of our leases are material to our business operations. We believe our facility is adequate for our current needs and that suitable additional or substitute space would be available if needed.

Item 3. Legal Proceedings.

We are not currently subject to any material pending legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock has traded on the Nasdaq Global Select Market under the symbol "GTHX" since May 17, 2017. Prior to that time, there was no public market for our common stock.

Holders

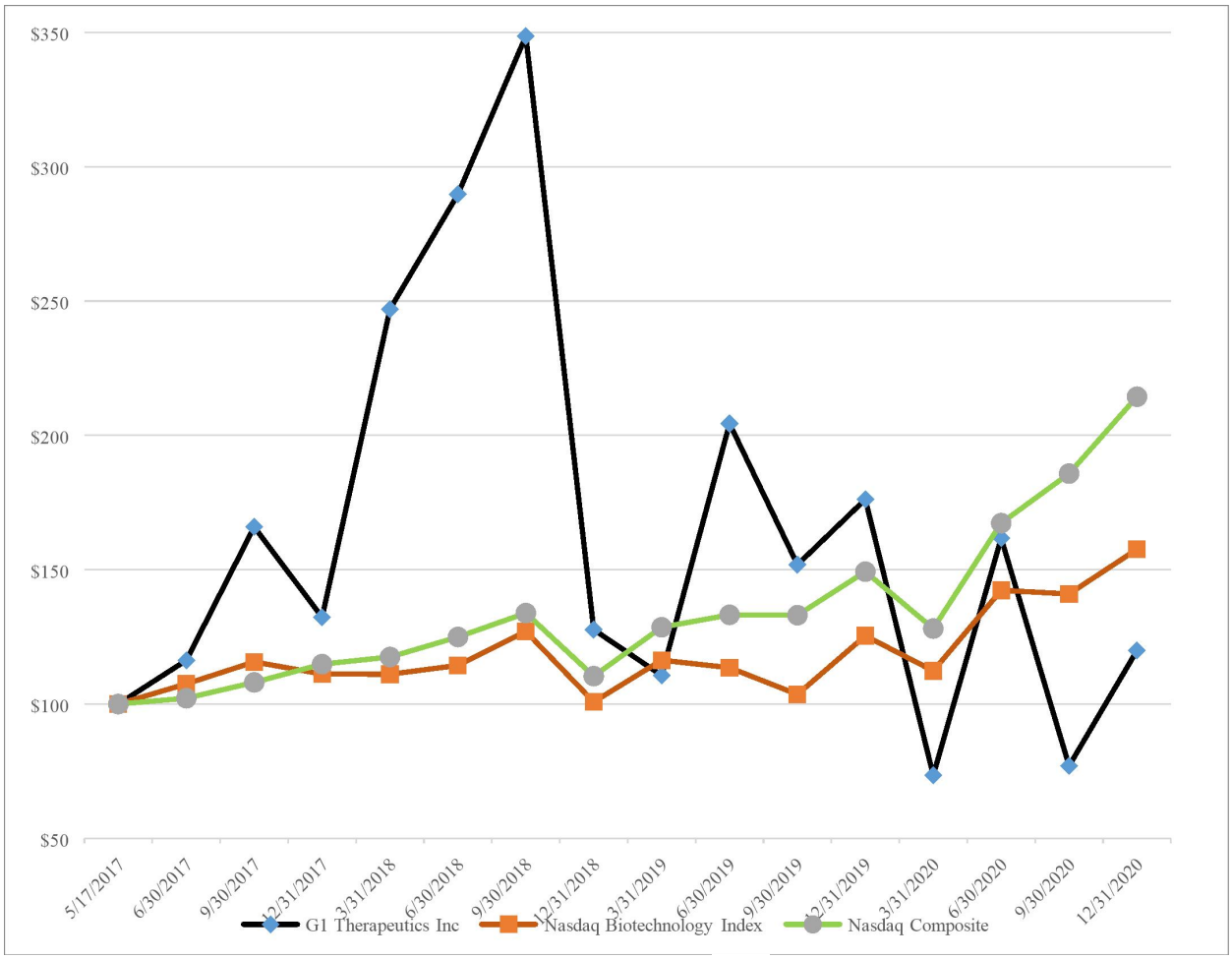
As of February 22, 2021, there were approximately 10 stockholders of record of our common stock. Holders of record are defined as those stockholders whose shares are registered in their names in our stock records and do not include beneficial owners of common stock whose shares are held in the names of brokers, dealers or clearing agencies.

Stock Performance Graph

This performance graph is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing by us under the Securities Act of 1933 or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. The stock price performance shown on the graph is not necessarily indicative of future price performance.

Comparison of Cumulative Total Return

Among G1 Therapeutics, Inc., the Nasdaq Biotechnology Index and the Nasdaq Composite Index



The above graph measures the change in a $100 investment in our common stock from May 17, 2017 (the date our common stock commenced trading on the Nasdaq Global Select Market) through December 31, 2020. Our relative performance is then compared with the Nasdaq Composite Index and the Nasdaq Biotechnology Index.

Recent Sales of Unregistered Securities

None.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference from Item 12 of Part III of this Annual Report.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our equity securities during the fiscal year 2020.

Item 6. Selected Financial Data.

You should read the following selected financial data together with the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our audited financial statements and accompanying notes included in this Annual Report. We have derived the statement of operations data for the years ended December 31, 2020, 2019 and 2018 and the balance sheet data as of and December 31, 2020 and 2019 from our audited financial statements included elsewhere in this Annual Report. The statement of operations data for the year ended December 31, 2017 and 2016 and the balance sheet data as of December 31, 2018, 2017 and 2016 is derived from audited financial statements that are not included in this Annual Report. Our historical results are not necessarily indicative of results that should be expected in the future.

	Year Ended December 31,				
	2020	2019	2018	2017	2016
	(in thousands except share and per share amounts)				
Statements of Operations Data:					
License revenue	$ 45,285	$ —	$ —	$ —	$ —
Operating expenses:					
Research and development	73,271	89,002	70,683	53,881	25,161
General and administrative	68,490	40,039	18,603	7,087	5,230
Total operating expenses	141,761	129,041	89,286	60,968	30,391
Loss from operations	(96,476)	(129,041)	(89,286)	(60,968)	(30,391)
Other income (expenses):					
Interest income	952	6,579	3,998	891	200
Interest expense	(1,778)	—	—	—	—
Other income (expenses)	(542)	15	—	(3)	(18)
Change in fair value of warrant liability	—	—	—	(41)	(82)
Total other income (expense), net	(1,368)	6,594	3,998	847	100
Loss before income taxes	(97,844)	(122,447)	(85,288)	(60,121)	(30,291)
Income tax expense	1,410	—	—	—	—
Net loss	(99,254)	(122,447)	(85,288)	(60,121)	(30,291)
Accretion of redeemable convertible preferred stock(1)	—	—	—	(4,757)	(4,405)
Net loss attributable to common shareholders	(99,254)	(122,447)	(85,288)	(64,878)	(34,696)
Basic and diluted net loss per share(2)	$ (2.62)	$ (3.27)	$ (2.56)	$ (3.57)	$ (23.33)
Weighted average shares outstanding, basic and diluted(2)	37,878,026	37,499,256	33,316,719	18,197,970	1,486,986

	Year Ended December 31,				
	2020	2019	2018	2017	2016
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 207,306	$ 269,208	$ 369,290	$ 103,812	$ 47,305
Working capital(3)	192,949	251,234	357,771	92,957	42,276
Total assets	228,552	284,831	371,270	105,171	48,212
Redeemable convertible preferred stock	—	—	—	—	107,580
Total stockholders' equity/(deficit)	177,351	255,527	358,820	93,388	(64,993)

(1) Subsequent to our initial public offering in May 2017, our redeemable convertible preferred stock was converted to common stock and no further accretion has been recorded.

(2) See Note 11 to our financial statements appearing elsewhere in this Annual Report for further details on the calculation of basic and diluted net loss per share applicable to common stockholders.

(3) We define working capital as current assets less current liabilities.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes included elsewhere in this Annual Report. This discussion contains forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a commercial-stage biopharmaceutical company focused on the development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. Our first approved product by the U.S. Food and Drug Administration (FDA), COSELA™ (trilaciclib), is the first and only therapy indicated to proactively help protect bone marrow from the damage of chemotherapy and is the first innovation in managing myeloprotection in decades. COSELA was developed from a technology platform that targets key cellular pathways including transient arrest of the cell cycle at G1, prior to the beginning of DNA replication. Our therapies are designed to improve outcomes for patients across multiple oncology indications.

We shall use "COSELA" when we are referring our FDA approved drug and "trilaciclib" when we are referring to our development of COSELA for additional indications.

Product Pipeline

We are advancing two clinical stage programs. Trilaciclib is a first-in-class therapy designed to help protect against chemotherapy-induced myelosuppression. Trilaciclib helps protect HSPCs in bone marrow by transiently inhibiting CDK4/6 leading to a temporary arrest of susceptible host cells during chemotherapy in ES-SCLC patients. This reduces the duration and severity of neutropenia and other myelosuppressive consequences of chemotherapy. In addition, trilaciclib activates and enhances the immune system response driving increased anti-tumor efficacy, which we continue to explore in clinical trials.

On February 12, 2021, COSELA was approved by the FDA to decrease the incidence of chemotherapy-induced myelosuppression in adult patients treated with a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive stage small cell lung cancer (ES-SCLC). We are also exploring potential use of trilaciclib in a variety of tumors, including colorectal cancer (CRC), triple negative breast cancer (TNBC), neoadjuvant breast cancer, non-small cell lung cancer (NSCLC), and bladder cancer.

Rintodestrant is an oral selective estrogen receptor degrader (SERD) for the treatment of ER+ breast cancer. In 2020, we out-licensed global rights to lerociclib, an internally discovered and differentiated oral CDK4/6 inhibitor designed to enable more effective combination treatment strategies across multiple oncology indications. We also have intellectual property focused on cyclin-dependent kinase targets.

G1 Therapeutics Product Pipeline

Candidate	Indication	Status	Development & Commercialization Rights (all indications)
trilaciclib	Extensive-stage small cell lung cancer (ES-SCLC)	COSELA (trilaciclib) Approved by FDA	G1 Therapeutics owns all global development and commercial rights across all indications, with the exception of Greater China (Simcere)
	Colorectal cancer (CRC)	Registrational trial (initiated in 2020)	
	1L/2L Triple negative breast cancer (TNBC)	Registrational trial (initiating in 1H 2021)	
	2L/3L Non-small cell lung cancer (NSCLC)	Phase 2 trial (initiating in 1H 2021)	
	1L Bladder cancer	Phase 2 trial (initiating in 1H 2021)	
	Neoadjuvant breast cancer (I-SPY 2 TRIAL™)	Phase 2 trial (initiated in 2020)	
rintodestrant	ER+, HER2- breast cancer	Phase 2a (initiated in 2019)	G1 - Global
lerociclib	Multiple	Clinical Stage	EQRx: Global and Japan (ex. Asia Pacific) Genor Biopharma: Asia Pacific (ex. Japan)

Trilaciclib helps protect HSPCs in bone marrow by transiently inhibiting CDK4/6 leading to a temporary arrest of susceptible host cells during chemotherapy in ES-SCLC patients. This reduces the duration and severity of neutropenia and other myelosuppressive consequences of chemotherapy. In addition, trilaciclib has demonstrated immune system response enhancement which we are exploring in clinical trials to show increased anti-tumor efficacy.

Trilaciclib, a transient IV CDK4/6 inhibitor, is a novel therapeutic approach which is given before chemotherapy that temporarily blocks progression through the cell cycle. This provides two benefits. First, it proactively helps protect HSPCs in bone marrow leading to preservation of neutrophils, erythrocytes, and platelets (called myeloprotection) which reduces the occurrences and severity of neutropenia and other myelosuppressive consequences of chemotherapy. This myeloprotection benefit has been conclusively proven in double-blind placebo-controlled clinical trials in extensive-stage small cell lung cancer. Second, trilaciclib activates and enhances the immune system response driving increased anti-tumor efficacy, which we are exploring in clinical trials. Our randomized clinical trials have demonstrated that trilaciclib can provide myeloprotection benefits and has the potential to improve survival as a result of its anti-tumor efficacy benefit.

Chemotherapy is an effective and important weapon against cancer. However, chemotherapy does not differentiate between healthy cells and cancer cells and kills both, including important stem cells in the bone marrow (hematopoietic stem and progenitor cells, or HSPCs) that produce white blood cells, red blood cells and platelets, and immune cells. This chemotherapy-induced bone marrow damage is known as myelosuppression. When white blood cells, red blood cells and platelets become depleted, chemotherapy patients are at increased risk of infection, experience anemia and fatigue, and are at increased risk of bleeding. Myelosuppression often requires the administration of rescue interventions such as growth factors and blood or platelet transfusions and may also result in chemotherapy dose delays and reductions. Immune cell damage may decrease the ability of the immune system to fight the cancer, as well as infection.

In preclinical studies, administration of trilaciclib prior to chemotherapy has been shown to induce transient cell-cycle arrest of HSPCs, helps protect HSPCs from chemotherapy-induced damage, preserve bone marrow and immune system function, helps protect against bone marrow exhaustion, improve complete blood counts (CBC) recovery, prevent myeloid skewing and consequent lymphopenia, and enhance T-cell effector function in the tumor microenvironment.

Following evaluation of trilaciclib in a Phase 1 trial in healthy volunteers, we initiated two Phase 1b/2 trials in patients with ES-SCLC; one in a first line setting (in combination with carboplatin/etoposide) and the other in a second-/third-line setting (in combination with topotecan). Enrollment in both trials has been completed and preliminary data from the open label Phase 1b segment were reported in 2016 and 2017. In the Phase 1b segments of these two trials, we treated 51 patients with over 250 cycles of trilaciclib and chemotherapy. There were no episodes of febrile neutropenia – one of the most common adverse consequences of these chemotherapy regimens. Further, there were no drug-related serious adverse events reported during the Phase 1b segments of these two trials. There were some adverse events reported involving fatigue and cytopenias, but those adverse events were less severe and less frequent than those generally reported in trials involving the use of chemotherapy alone.

Based on these encouraging preliminary data, we advanced both SCLC trials into the randomized, placebo-controlled, double-blind Phase 2 segment. Enrollment in the first-line SCLC Phase 2 trial was completed in the second quarter of 2017 and positive multilineage myeloprotection results were reported in March 2018, with additional data reported at the European Society for Medical Oncology (ESMO) 2018 Congress and published in Annals of Oncology in 2019. Enrollment in the second-/third-line SCLC Phase 2 trial was completed in the second quarter of 2018, with positive multilineage myeloprotection data reported in the fourth quarter of 2018 and full data presented at an oral session at the American Society of Clinical Oncology (ASCO) 2019 Annual Meeting. These data were also published in Advances in Therapy (Hart *et al.*) in 2020.

Our third trial in SCLC was initiated in 2017, as part of our non-exclusive collaboration with Genentech, with the goal of exploring the use of trilaciclib in combination with chemotherapy and a checkpoint inhibitor. The trial was a randomized, placebo-controlled, double-blind Phase 2 trial of trilaciclib in combination with Tecentriq® (atezolizumab)/carboplatin/etoposide in first-line SCLC patients. We completed enrollment in February 2018 and reported positive multilineage myeloprotection data in November 2018. Additional data, including myeloprotection and anti-tumor efficacy findings (as measured by overall survival, or "OS"), were reported at the 2019 ESMO Congress. and featured in a concurrent publication in The Lancet Oncology

All three SCLC trials demonstrated that trilaciclib, when added to standard of care chemotherapy or chemotherapy/checkpoint inhibitor regimens, decreases the incidence of clinically significant chemotherapy-induced myelosuppression. The FDA granted Breakthrough Therapy Designation for trilaciclib based on myeloprotection data from our three randomized, double-blind, placebo-controlled SCLC clinical trials, as well as safety data collected across all completed and ongoing clinical trials. The Breakthrough Therapy program is designed to expedite development and review of drugs intended for serious or life-threatening conditions. In August 2020, the FDA accepted our New Drug Application (NDA) for trilaciclib in SCLC, granting Priority Review with a Prescription Drug User Fee Act (PDUFA) action date of February 15, 2021. Discussions with European regulatory authorities have indicated existing data is sufficient to support a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for trilaciclib for myeloprotection in SCLC, which we plan to pursue in collaboration with a partner.

On February 12, 2021, COSELA was approved by the FDA to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC). We expect COSELA to be commercially available through G1's specialty pharmacy partner network in early March. COSELA is administered intravenously as a 30-minute infusion completed within 4 hours prior to the start of chemotherapy and is the first and only FDA-approved therapy that helps proactively deliver multilineage myeloprotection to patients with extensive-stage small cell lung cancer being treated with chemotherapy. The approval of COSELA is based on data from three randomized, placebo-controlled trials that showed patients receiving COSELA prior to chemotherapy had clinically meaningful and statistically significant reduction in the duration and severity of neutropenia, reduction of red blood cell transfusions, as well as improvements in other myeloprotection measures, compared to patients receiving chemotherapy without COSELA.

In June 2020, we entered into a three-year co-promotion agreement for COSELA™ (trilaciclib) in the United States and Puerto Rico with Boehringer Ingelheim. The agreement is limited to support for SCLC. Under the terms of the agreement, we will book revenue in the United States and Puerto Rico and retain development and commercialization rights to trilaciclib. We will lead marketing, market access and medical engagement initiatives; Boehringer Ingelheim will lead sales force engagements.

In August 2020, we entered into an exclusive license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd ("Simcere") for development and commercialization rights for trilaciclib in all indications in Greater China (mainland China, Hong Kong, Macau and Taiwan). Under the terms of the agreement, we received an upfront payment of $14.0 million and will be eligible to receive up to $156.0 million in development and commercial milestone payments. Simcere will also pay us tiered low double-digit royalties on annual net sales of trilaciclib in Greater China. As part of the agreement, Simcere will participate in global clinical trials of trilaciclib and the companies will be responsible for all development and commercialization costs in their respective territories.

We are also executing on our tumor-agnostic strategy to evaluate the potential benefits of trilaciclib to patients with other tumors that are treated with chemotherapy. We have two on-going trials: a pivotal 1L colorectal cancer (CRC) study and a Phase 2 neoadjuvant breast cancer (I-SPY 2). We intend to initiate a pivotal study in mTNBC (including 1L and 2L patients) and have two additional Phase 2 studies: a 2L/3L non-small cell lung cancer (NSCLC) trial in post-checkpoint patients and a 1L bladder cancer trial with chemotherapy and a checkpoint inhibitor. These studies across treatment settings and tumor types will evaluate trilaciclib's dual benefits in both multi-lineage myeloprotection and anti-tumor efficacy.

Pivotal 1L Colorectal Cancer (CRC)

We enrolled the first patient in a randomized, placebo-controlled registrational trial of trilaciclib in colorectal cancer (CRC) in the first quarter of 2021. CRC is a large indication commonly treated with 5-FU-based chemotherapy. We have extensive preclinical research demonstrating myeloprotection and potential efficacy in 5-FU-based regimens with trilaciclib. Our ongoing 1L CRC trial is with FOLFOXIRI, which is the most efficacious chemo regimen in this tumor but is also highly myelosuppressive. By reducing the toxicity of FOLFOXIRI, we believe we will significantly expand its use in CRC and potentially improve overall survival.

1L/2L Metastatic Triple-Negative Breast Cancer (mTNBC)

In 2017, we initiated a randomized Phase 2 trial of trilaciclib in patients with first-/second-/third-line metastatic triple-negative breast cancer (mTNBC) receiving gemcitabine and carboplatin. Enrollment was completed in the second quarter of 2018. At the 2018 SABCS, we presented preliminary trilaciclib data demonstrating improvement in progression-free survival (PFS). In September 2019, we presented updated data demonstrating significant improvement in OS (preliminary). Though the trial did not meet the primary myeloprotection endpoints, patients receiving trilaciclib were able to receive approximately 50% more cycles of chemotherapy, without additional hematological toxicity. These data were presented at the 2019 ESMO Congress and were concurrently published in The Lancet Oncology. Updated safety and efficacy data from this trial were presented at the 2020 SABCS. Data included that compared to GC alone (Group 1), OS was improved in both trilaciclib arms (Groups 2 and 3) (Group 2: HR=0.31, p=0.0016; Group 3: HR=0.40, p=0.0004). Median OS was 12.6 months in Group 1, not reached for Group 2, and 17.8 months in Group 3. The median OS for Groups 2 and 3 combined was 19.8 months (HR=0.37, p<0.0001). OS findings in patients receiving trilaciclib were consistent with previously-reported data from this trial. The median OS for GC alone (Group 1, 12.6 months) was consistent with the previous trial findings and historical data. Patients with both PD-L1-positive and PD-L1-negative tumors treated with trilaciclib and GC demonstrated improvement in OS compared to patients receiving GC alone, with the PD-L1-positive subset achieving statistically significant improvement. Further, data from T cell clonality analyses suggest that administering trilaciclib prior to chemotherapy enhanced immune system function. These compelling Phase 2 data supported the potential effectiveness of trilaciclib in mTNBC. We expect to initiate a randomized, placebo-controlled registrational trial in in 1L patients and 2L post-checkpoint patients with mTNBC in the first half of 2021. TNBC is a difficult and aggressive tumor to treat with many new therapies only effective in certain subpopulations

Phase 2 Neoadjuvant Breast Cancer (I-SPY 2)

In January 2020, we announced that trilaciclib will be included in a new randomized, investigational treatment arm for the ongoing I-SPY 2 TRIAL™ for neoadjuvant treatment of locally advanced breast cancer. The trial, initiated in the second quarter of 2020 and run by the non-profit Quantum Leap Healthcare Collaborative, is designed to rapidly screen promising experimental treatments and identify those most effective in specific patient subgroups based on molecular characteristics (biomarker signatures). This trial will generate myeloprotection and anti-tumor efficacy data across the different subtypes of breast cancer.

2L/3L Non-Small Cell Lung Cancer (NSCLC)

Evaluating trilaciclib in 2L/3L NSCLC (post-checkpoint setting) will provide us with meaningful data in an area of high unmet with a large patient population. NSCLC is a known immunogenic tumor which may provide trilaciclib an opportunity to increase anti-tumor efficacy through its distinct mechanism even after checkpoint inhibitors have failed. There is also a high complementary commercial fit with our initial SCLC indication.

1L Bladder Cancer

We intend to initiate a 1L bladder cancer trial in the first half of 2021 with chemotherapy and a checkpoint inhibitor. There is a strong rationale to evaluate trilaciclib in 1L bladder cancer: (1) bladder is a known immunogenic tumor proven to be responsive to chemotherapy; (2) the most common chemotherapy regimen used in 1L bladder is gemcitabine and platinum, which is similar to the chemotherapy regimen in our TNBC study (gemcitabine and carboplatin) where we showed significant OS benefits; and (3) we have observed synergistic benefits combining trilaciclib with checkpoints.

Rintodestrant: Our differentiated oral SERD

Rintodestrant is an oral SERD which we plan to initially develop as a monotherapy and in combination with CDK4/6 inhibitors, initially Ibrance® (palbociclib), for the treatment of ER+, HER2- breast cancer. Based on compelling preclinical efficacy and safety data, we filed an Investigational New Drug application (IND) with the FDA in the fourth quarter of 2017. In 2018, we initiated a Phase 1b (dose escalation/dose expansion) clinical trial in ER+, HER2- breast cancer. Preliminary data from the Phase 1 portion of

this trial were presented at the 2019 ESMO Congress, showing that rintodestrant was well tolerated and demonstrated evidence of anti-tumor activity in heavily pre-treated patients. The mature monotherapy data were presented at the 2020 SABCS, confirming the safety and efficacy results of the preliminary analysis. Based on those results we advanced an 800 mg dose of rintodestrant into a 40-patient Phase 2 combination trial with palbociclib, a CDK4/6 inhibitor. We completed enrollment of patients in this trial in October 2020 and expect to disclose initial safety and efficacy data in the second quarter of 2021. If the Phase 2 data are promising, we will seek to partner rintodestrant. Palbociclib is being provided under a non-exclusive clinical supply agreement that we signed with Pfizer in February 2020.

Lerociclib: Our differentiated CDK4/6 inhibitor for patients with CDK4/6-dependent tumors

Lerociclib is a differentiated oral CDK4/6 inhibitor being developed for use in combination with other targeted therapies in multiple oncology indications. In 2020, we entered into separate, exclusive agreements with EQRx, Inc. (rights for U.S., Europe, Japan and all markets outside Asia-Pacific) and Genor Biopharma Co. Inc. (rights for Asia-Pacific, excluding Japan) for the development and commercialization of lerociclib in all indications. Combined, these agreements provided $26.0 million in upfront payments, along with sales-based royalties, and the opportunity for up to $330.0 million in potential milestone payments. EQRx, Inc. and Genor Biopharma Co. Inc. are responsible for all costs related to the development and commercialization of lerociclib in their respective territories.

Coronavirus (COVID-19) impact on operations

We have implemented business continuity plans to address the COVID-19 pandemic and minimize disruptions to ongoing operations. Enrollment of patients in current and future clinical trials may be impacted by COVID-19. We do not anticipate significant supply chain delays or shortages as a result of the COVID-19 pandemic. COVID-19 travel limitations and government-mandated work-from-home or shelter-in-place orders, may reduce the number of in-person meetings with prescribers and fewer patient visits with physicians, potentially resulting in fewer new prescriptions.

We established a COVID-19 response team which continually monitors the impact of COVID-19 on our operations. The COVID-19 response team manages our workplace protocols that governs our employees use of our office. To mitigate the impact of COVID-19 on our business, we put in place the following safety measures for our employees, patients, healthcare professionals, and suppliers to limit exposure: we substantially restricted travel, supplied personal protective equipment to employees, limited access to our headquarters and asked most of our staff to work remotely. In addition, we transitioned most of our employees to working remotely and added bandwidth and VPN capacity to our infrastructure. We will continue to monitor the impact of COVID-19 on our operations and report to our Board regularly on the progress of our response to the COVID-19 outbreak.

Financial Overview

Since our inception in 2008, we have devoted substantially all of our resources to synthesizing, acquiring, testing and developing our product candidates, including conducting preclinical studies and clinical trials and providing general and administrative support for these operations as well as securing intellectual property protection for our product candidates. As of February 2021, COSELA is our only product approved for sale. COSELA has not generated any revenues from product sales in 2020. We expect COSELA to start generating revenue in the first quarter of 2021. We recorded $45.3 million of license revenue for the year ended December 31, 2020, and $0 million of revenue for the years ended December 31, 2019. To date, we have financed our operations primarily through the sale of equity securities, our loan agreement with Hercules Capital, Inc., and licensing arrangements. Under our licensing arrangements, we are eligible to receive certain development and sales-based milestones. Our ability to earn these milestones and the timing of achieving these milestones is primarily dependent upon the outcome of the licensee’s activities and is uncertain at this time.

As of December 31, 2020, we had cash and cash equivalents of $207.3 million. Since inception, we have incurred net losses. Our net losses were $99.3 million, $122.4 million and $85.3 million for the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $436.1 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs, our commercial launch preparations, and from general and administrative expenses associated with our operations. We expect to continue to incur significant expenses and increasing operating losses. We expect our research and development, commercial activities, and general and administrative expenses will continue to increase in connection with our ongoing and future activities as we:

- continue development of our product candidates, including initiating additional clinical trials of trilaciclib and rintodestrant;
- identify and develop new product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- grow our sales, marketing and distribution infrastructure to commercialize COSELA and any future products for which we may obtain marketing approval;

- achieve market acceptance of our product candidates in the medical community and with third-party payors;
- maintain, expand and protect our intellectual property portfolio;
- hire additional personnel;
- enter into collaboration arrangements, if any, for the development of our product candidates or in-license other products and technologies;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- continue to incur increased costs as a result of operating as a public company.

License agreement with the University of Illinois - Rintodestrant

In November 2016, and as amended in March 2017, we entered into a license agreement with the Board of Trustees of the University of Illinois, or the University. Pursuant to the license agreement, as amended, the University licensed patent rights to the Company, with rights to sublicense, to make, have made, use, import, sell and offer for sale SERDs, including rintodestrant, covered by certain patent rights owned by the University. The rights licensed to us are exclusive, worldwide, non-transferable rights, for all fields of use. Under the terms of the agreement, as amended, we paid a one-time only, non-refundable upfront fee of $0.5 million, and are required to pay the University low single-digit royalties on all net sales of products and a share of any sublicensing revenues. We are also obligated to pay annual maintenance fees, which are fully creditable against any royalty payments made by us. In addition, the Company may also be required to pay the University milestone payments of up to an aggregate of $2.6 million related to the initiation and execution of clinical trials, with payments made for the initial dosing for each phase of the clinical trials, as well as the first commercial sale of a product in another country. To date, the Company has made milestone payments totaling $0.6 million, of which $0 was incurred during 2020. We will also be responsible for any future patent prosecution costs that may arise. See “Business—Intellectual Property—Exclusive License for rintodestrant.”

Components of our Results of Operations

Revenues

To date, we have not generated any revenues from the sale of products. Our revenues have been derived from our license agreements.

We entered into an exclusive license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd (“Simcere”) in August 2020 and granted them the rights to develop and commercialize trilaciclib in Greater China (mainland China, Hong Kong, Macau, and Taiwan) (the “Simcere Territory”). We received an upfront payment of $14.0 million (less applicable withholding taxes of $1.4 million) in September 2020. This was recognized in December 2020 when we transferred the license and related technology know-how. We have the potential to receive $156.0 million upon reaching development and commercial milestones, and receive tiered low double-digit royalties on annual net sales of trilaciclib in the Simcere Territory.

We entered into an exclusive license agreement with EQRx, Inc. (“EQRx”) in July 2020 and granted them the rights to develop and commercialize lerociclib in the U.S., Europe, Japan and all other global markets, excluding the Asia-Pacific region (except Japan) (the “EQRx Territory”). We received an upfront payment of $20.0 million in August 2020. This was recognized as revenue in September 2020 when we transferred the license and related technology and know-how. We have the potential to receive $290.0 upon reaching development and commercial milestones, and receive tiered royalties ranging from mid-single digits to mid-teens based on annual net sales of lerociclib in the EQRx Territory.

We entered into an exclusive license agreement with Genor Biopharma Co. Inc. (“Genor”) in June 2020 and granted them the rights to develop and commercialize lerociclib in the Asia-Pacific Region, excluding Japan (the “Genor Territory”). We received an upfront payment of $6.0 million in July 2020. This was recognized as revenue in September 2020 when we transferred the license and related technology and know-how. We have the potential to receive $40.0 million upon reaching development and commercial milestones, and receive tiered royalties ranging from high single to low double-digits based on annual net sales of lerociclib in the Genor Territory.

We entered into an exclusive license agreement with ARC Therapeutics, LLC (“ARC”) in May 2020. The Company granted ARC an exclusive, worldwide, royalty-bearing license of its CDK2 inhibitor compounds in exchange for an upfront payment and equity in ARC with a total value of approximately $2.1 million, which resulted in the recognition of related party revenue. The Company is entitled to receive additional milestone payments and sales-based royalties, and has right of first negotiation to re-acquire these assets.

Operating expenses

We classify our operating expenses into two categories: research and development and general and administrative expenses. Personnel costs, including salaries, benefits, bonuses and stock-based compensation expense, comprise a significant component of each of these expense categories. We allocate expenses associated with personnel costs based on the nature of work associated with these resources.

Research and Development Expenses

The largest component of our total operating expenses since inception has been research and development activities, including the preclinical and clinical development of our product candidates.

Research and development costs are expensed as incurred. Our research and development expense primarily consists of:

- salaries and personnel-related costs, including bonuses, benefits and any stock-based compensation, for our scientific personnel performing or managing out-sourced research and development activities;
- costs incurred under agreements with contract research organizations and investigative sites that conduct preclinical studies and clinical trials;
- costs related to manufacturing pharmaceutical active ingredients and drug products for preclinical studies and clinical trials;
- costs related to upfront and milestone payments under in-licensing agreements;
- fees paid to consultants and other third parties who support our product candidate development;
- other costs incurred in seeking regulatory approval of our product candidates; and
- allocated facility-related costs and overhead.

The successful development of our product candidates is highly uncertain. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. Accordingly, we expect research and development costs to increase significantly for the foreseeable future as programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. We are also unable to predict when, if ever, material net cash inflows will commence from our product candidates to offset these expenses. Our expenditures on current and future preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors including:

- the scope, rate of progress, and expenses of our ongoing as well as any additional clinical trials and other research and development activities;
- future clinical trial results;
- achievement of milestones requiring payments under our in-licensing agreements;
- uncertainties in clinical trial enrollment rates or drop-out or discontinuation rates of patients;
- potential additional studies requested by regulatory agencies;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.

We track research and development expenses on a program-by-program basis only for clinical-stage product candidates. Preclinical research and development expenses and chemical manufacturing research and development expenses are not assigned or allocated to individual development programs. In 2020, we had two clinical-stage product candidates, trilaciclib and rintodestrant.

General and administrative expenses

General and administrative expenses consist of personnel costs, allocated expenses and other expenses for outside professional services, including legal, audit and accounting services. Personnel costs consist of salaries, bonuses, benefits and stock-based compensation. Other general and administrative expenses include facility-related costs not otherwise allocated to research and development expense, professional fees, pre-commercialization costs, expenses associated with obtaining and maintaining patents and costs of our information systems. We anticipate that our general and administrative expenses will continue to increase in the future as we increase our headcount to support our continued research and development and commercialization of COSELA.

We expect to continue to incur additional general and administrative expenses in 2020 as we support continued research and development activities and support our operations in a public company environment, including expenses related to compliance with

the rules and regulations of the SEC and Nasdaq, additional insurance expenses, and expenses related to investor relations activities, commercialization costs and other administration and professional services.

Total other income (expense), net

Total other income (expense), net consists of interest income earned on cash and cash equivalents and interest expenses incurred under our loan and security agreement with Hercules.

Income taxes

To date, we have not been required to pay U.S. federal or state income taxes because we have not generated taxable income. Income tax expense recognized in 2020 related to the foreign withholding taxes incurred as a result of the upfront payment received from the Simcere license agreement entered into during the quarter.

Critical accounting policies and significant judgments and estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of our 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 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.

While our significant accounting policies are more fully described in the notes to our financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our financial statements and understanding and evaluating our reported financial results.

Revenue Recognition

For elements of those arrangements that we determine should be accounted for under ASC 606, *Revenue from Contracts with Customers* (“ASC 606”), we assess which activities in our license or collaboration agreements are performance obligations that should be accounted for separately and determine the transaction price of the arrangement, which includes the assessment of the probability of achievement of future milestones and other potential consideration. For arrangements that include multiple performance obligations, such as granting a license or performing manufacturing or research and development activities, we allocate the transaction price based on the relative standalone selling price and recognize revenue that is allocated to the respective performance obligation when (or as) control is transferred to the customer and the performance obligation is satisfied. Accordingly, we develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. These key assumptions may include revenue forecasts, clinical development timelines and costs, discount rates and probabilities of clinical and regulatory success.

Licenses of Intellectual Property

If a license to the Company’s intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue associated with the bundled performance obligation. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of progress and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes developmental and regulatory milestone payments, the Company evaluates whether the achievement of each milestone specifically relates to the Company’s efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. The Company evaluates each milestone to determine when and how much of the milestone to include in the transaction price. The Company first estimates the amount of the milestone payment that the Company could receive using either the expected value or the most likely amount approach. The Company primarily uses the most likely

amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, the Company considers whether any portion of that estimated amount is subject to the variable consideration constraint (that is, whether it is probable that a significant reversal of cumulative revenue would not occur upon resolution of the uncertainty). The Company updates the estimate of variable consideration included in the transaction price at each reporting date which includes updating the assessment of the likely amount of consideration and the application of the constraint to reflect current facts and circumstances.

Royalties

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

Accrued research and development expenses

As part of the process of preparing our financial statements, we estimate and accrue research and development expenses, including external clinical study costs associated with clinical trial activities. The process involves reviewing contracts and purchase orders, identifying services that have been provided on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual costs.

Costs for clinical trial activities are recognized based on an evaluation of our vendors' progress towards completion of specific tasks, using data such as patient enrollment, clinical site activations or information provided to us by our vendors regarding their actual costs incurred. Payments for these activities are based on the terms of individual contracts and payment timing may differ significantly from the period in which the services were performed. We determine accrual estimates through reports from and discussions with applicable personnel and outside service providers as to the progress or state of completion of trials, or the services completed. Our estimates of accrued external clinical study costs as of each balance sheet date are based on the facts and circumstances known at the time.

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

Stock-based compensation

We account for stock-based compensation awards in accordance with Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options, to be recognized in the statement of operations based on their fair values. Our stock-based compensation awards have historically consisted of stock options.

We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant. 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 generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. We account for forfeitures as they occur, rather than estimating forfeitures as of the date of grant.

We recorded non-cash stock-based compensation expense of $18.8 million, $16.4 million and $10.2 million for the years ended December 31, 2020, 2019 and 2018, respectively.

We calculate the fair value of stock options using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of subjective assumptions, including the expected volatility of our common stock, the assumed dividend yield, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options, and the fair value of the underlying common stock on the date of grant. In applying these assumptions, we considered the following factors:

- we do not have sufficient history to estimate the volatility of our common stock; we calculate expected volatility based on reported data for selected similar publicly traded companies for which the historical information is available as we do not have sufficient history to estimate volatility using only our common stock; in 2019, we began incorporating our historical stock price in conjunction with selected similar publicly traded companies; we plan to continue to use the guideline peer group volatility information until the historical volatility of our common stock is sufficient to measure expected volatility for future option grants;
- the assumed dividend yield of zero is based on our expectation of not paying dividends for the foreseeable future;
- our estimates of expected term used in the Black-Scholes option-pricing model were based on the estimated time from the grant date to the date of exercise;
- we determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant; and
- we account for forfeitures as they occur, rather than estimating forfeitures as of an award's grant date.

See "Note 9 – Stock-Based compensation" to the accompanying audited financial statements included in Item 15 of this Annual Report for the weighted average assumptions used in the Black-Scholes option-pricing model for awards granted in the years ended December 31, 2020, 2019 and 2018.

Prior to our initial public offering, the fair value of our common shares underlying our stock options was estimated on each grant date by our board of directors. In order to determine the fair value of our common shares underlying granted stock options, our board of directors considered, among other things, timely valuations of our common shares prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

Given the absence of a public trading market for our common shares, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common shares, including (1) our business, financial condition and results of operations, including related industry trends affecting our operations; (2) our forecasted operating performance and projected future cash flows; (3) the illiquid nature of our common shares; (4) liquidation preferences and other rights and privileges of our common shares; (5) market multiples of our most comparable public peers and (6) market conditions affecting our industry. Since our IPO, our board of directors has determined the fair value of each common share underlying share-based awards based on the closing price of our common shares as reported by the Nasdaq on the date of grant.

Income taxes

We recognize deferred income taxes for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. We periodically evaluate the positive and negative evidence bearing upon the ability to realize our deferred tax assets. Based upon the weight of the available evidence, which includes historical operating performance, reported cumulative net losses since inception and difficulty in accurately forecasting our future results, we maintained a full valuation allowance on the net deferred tax assets for all periods presented. We intend to maintain a full valuation allowance on the U.S. deferred tax assets for the foreseeable future until sufficient positive evidence exists to support reversal of the valuation allowance.

At December 31, 2020, the Company has federal net operating loss carryforwards ("NOLs") of approximately $373.1 million, which are available to offset future taxable income. Of the $373.1 million available, $95.4 million will begin to expire in 2029. The remaining $277.6 million has an indefinite carryforward period. Under the Tax Cuts and Jobs Act ("Tax Act"), federal NOLs arising after December 31, 2017 may be carried forward indefinitely. However, for NOLs arising after December 31, 2017, NOL carryforwards will be limited to 80% of taxable income. Our NOLs generated in 2017 and in prior years will not be subject to the 80% limitation under the Tax Act. In addition, we had state net operating loss carryforwards totaling approximately $379.8 million, which are available to offset future state taxable income. State net operating losses begin to expire in 2024. Because we had incurred cumulative net operating losses since inception, all tax years remain open to examination by U.S. federal and state income tax authorities. As of December 31, 2020, we also had federal research and development (R&D) credit carryforwards of approximately $14.0 million available to offset future income tax which begin to expire in 2035.

Our ability to utilize net operating losses and research and development credit carryforwards may be substantially limited due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the Code), as well as similar state provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change," as defined by Section 382 of the Code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percent of the outstanding stock of a company by certain stockholders or public groups.

In April 2019, we completed an evaluation study as to whether an "ownership change" had occurred and determined that the limitation would be approximately $8.0 million on federal net operating loss carryforwards, $1.2 million on state net operating loss carryforwards, and $0.1 million on R&D tax credit carryforwards. The carryforward amounts reported above have already been reduced for these limitations. We continue to maintain a valuation allowance on the remaining NOLs as we believe that it is more likely than not that all of the deferred tax asset associated with the NOLs will not be realized regardless of whether an "ownership change" has occurred.

Results of operations

Comparison of the year ended December 31, 2020 and December 31, 2019

	Year Ended December 31,		Change
	2020	2019	$
	(in thousands)		
License revenue	$ 45,285	$ —	$ 45,285
Operating Expenses:			
Research and Development	73,271	89,002	(15,731)
General and Administrative	68,490	40,039	28,451
Total operating expenses	141,761	129,041	12,720
Loss from Operations	(96,476)	(129,041)	32,565
Other income (expense):			
Interest income	952	6,579	(5,627)
Interest expense	(1,778)	—	(1,778)
Other income (expense)	(542)	15	(557)
Total other income (expense), net	(1,368)	6,594	(7,962)
Loss before income taxes	(97,844)	(122,447)	24,603
Income tax expense	1,410	—	1,410
Net Loss	$ (99,254)	$ (122,447)	$ 23,193

Revenue

Revenue was $45.3 million and $0 for the years ended December 31, 2020 and December 31, 2019 respectively. The revenue for the year ended December 31, 2020 was primarily related to $42.1 million in revenue recognized from the Simcere, EQRx, Genor and ARC upfront payments under the respective license agreements following the transfer of the related technology and know-how which occurred during the period. We also recognized $1.3 million for clinical trial costs and $0.4 million in patent costs to be reimbursed by EQRx, Genor, and Simcere. Additionally, we recognized $1.3 million in revenue for existing inventory transfers to EQRx and Genor which occurred during the fourth quarter of 2020.

Research and development

Research and development expenses were $73.3 million for the year ended December 31, 2020 as compared to $89.0 million for the year ended December 31, 2019. The decrease of $15.7 million, or -18%, was primarily due to a decrease of $10.2 million in our clinical program costs due to a decrease in spend for ongoing clinical trials of $5.7 million and decrease of $5.9 million related to a regulatory filing expense of $2.9 million incurred in 2019 and reimbursed in 2020, partially offset by an increase in personnel costs of $1.4 million. The decrease of $1.3 million in costs for manufacturing of active pharmaceutical ingredient and drug product to support our clinical trials, as well as a decrease in research and development expenses was also due to a decrease of $4.2 million in external costs related to discovery and preclinical development. The following table summarizes our research and development expenses allocated to trilaciclib, rintodestrant, lerociclib, and unallocated research and development expenses for the periods indicated:

	Year Ended December 31,	
	2020	2019
	(in thousands)	
Clinical Expenses—trilaciclib	$ 34,292	$ 36,196
Clinical Expenses—rintodestrant	7,005	8,334
Clinical Expenses—lerociclib	6,092	13,041
Chemical Manufacturing and Development	22,040	23,364
Discovery and Pre-clinical Expenses	3,842	8,067
Total Research and Development Expenses	$ 73,271	$ 89,002

General and administrative

General and administrative expenses were $68.5 million for the year ended December 31, 2020 as compared to $40.0 million for the year ended December 31, 2019. The increase of $28.5 million, or 71%, was due to an increase of $6.8 million in personnel related costs due to increased headcount, of which $1.7 million related to non-cash stock compensation expense, an increase of $15.8 million in pre-commercialization activities, an increase of $2.0 million in medical affairs costs related to trilaciclib, an increase of $0.8 million in information technology systems and related expenses, and an increase of $3.1 million professional services, insurance, and other administrative costs.

Total other income (expense), net

Total other income, net was $(1.4) million for the year ended December 31, 2020 as compared to $6.6 million for the year ended December 31, 2019. The decrease in income of $8.0 million was primarily driven by a lower balance of money market funds due to cash used in operating activities and changes in interest rates during the year ended December 31, 2020 as compared to the year ended December 31, 2019, interest expense on loan payable, and loss on disposal of fixed assets.

Income tax expense

Income tax expense was $1.4 million for the year ended December 31, 2020 as compared to $0 for the year ended December 31, 2019. The increase was related to the foreign withholding taxes incurred as a result of the upfront payment received from the Simcere license agreement entered into in 2020.

Comparison of the year ended December 31, 2019 and December 31, 2018

	Year Ended December 31,		Change
	2019	2018	$
	(in thousands)		
License revenue	$ —	$ —	$ —
Operating Expenses:			
Research and Development	89,002	70,683	18,319
General and Administrative	40,039	18,603	21,436
Total operating expenses	129,041	89,286	39,755
Loss from Operations	(129,041)	(89,286)	(39,755)
Other income (expense):			
Interest income	6,579	3,998	2,581
Interest expense	—	—	—
Other income (expense)	15	—	15
Total other income (expense), net	6,594	3,998	2,596
Loss before income taxes	(122,447)	(85,288)	(37,159)
Income tax expense	—	—	—
Net Loss	$ (122,447)	$ (85,288)	$ (37,159)

Revenue

Revenue was $0 for the years ended December 31, 2019 and December 31, 2018.

Research and development

Research and development expenses were $89.0 million for the year ended December 31, 2019 as compared to $70.7 million for the year ended December 31, 2018. The increase of $18.3 million, or 26%, was primarily due to an increase of $11.8 million in our clinical program costs which reflects increased costs in our ongoing clinical trials, increased headcount-related expenses to support these trials, and costs associated with seeking regulatory approval for our product candidates. The increase in research and development expenses was also due to an increase of $6.0 million in costs for manufacturing of active pharmaceutical ingredient and drug product to support our clinical trials, as well as an increase of $0.5 million in external costs related to discovery and preclinical development. The following table summarizes our research and development expenses allocated to trilaciclib, rintodestrant, lerociclib and unallocated research and development expenses for the periods indicated:

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Clinical Expenses—trilaciclib	$ 36,196	$ 35,116
Clinical Expenses—rintodestrant	8,334	2,251
Clinical Expenses—lerociclib	13,041	8,383
Chemical Manufacturing and Development	23,364	17,323
Discovery and Pre-clinical Expenses	8,067	7,610
Total Research and Development Expenses	$ 89,002	$ 70,683

General and administrative

General and administrative expenses were $40.0 million for the year ended December 31, 2019 as compared to $18.6 million for the year ended December 31, 2018. The increase of $21.4 million, or 115%, was due to an increase of $8.1 million in personnel related costs due to increased headcount, of which $5.2 million related to non-cash stock compensation expense, an increase of $5.5 million in pre-commercialization activities, an increase of $3.1 million in medical affairs costs related to trilaciclib, an increase of $1.6 million in information technology systems and related expenses, and an increase of $3.1 million professional services, insurance, and other administrative costs.

Total other income (expense), net

Total other income, net was $6.6 million for the year ended December 31, 2019 as compared to $4.0 million for the year ended December 31, 2018. The increase of $2.6 million was due to additional interest income earned on a higher balance of cash and cash equivalents during the year ended December 31, 2019 as compared to the year ended December 31, 2018.

Liquidity and Capital Resources

We have incurred cumulative losses and negative cash flows from operations since our inception in 2008. We incurred net losses of $99.3 million for the year ended December 31, 2020, $122.4 million for the year ended December 31, 2019, and $85.3 million for the year ended December 31, 2018. As of December 31, 2020, we had an accumulated deficit of $436.1 million.

As of December 31, 2020, we had cash and cash equivalents of $207.3 million. To date, we have funded our operations primarily through proceeds from our initial public offering, our follow-on stock offerings, our debt agreement with Hercules Capital, and proceeds from our license agreements. Under our licensing arrangements, we are eligible to receive certain development and sales-based milestones. Our ability to earn these milestones and the timing of achieving these milestones is primarily dependent upon the outcome of the licensee's activities and are uncertain at this time.

Follow-on offering

On March 12, 2018, we closed an underwritten public offering of 3,910,000 shares of common stock at a public offering price of $29.50 per share, including 510,000 shares of common stock issued upon exercise by the underwriters of their option to purchase additional shares. The gross proceeds from the offering were $115.3 million and net proceeds were $107.9 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

At-the-market offering

On June 15, 2018, we entered into a sales agreement for "at the market offerings" with Cowen and Company, LLC ("Cowen"), which allows us to issue and sell shares of common stock pursuant to a shelf registration statement for total gross sales proceeds of up to $125.0 million from time to time through Cowen, acting as our agent. Between June 18, 2018 and August 2, 2018, we sold 752,008 shares of common stock pursuant to this agreement resulting in $36.1 million in net proceeds, realizing $12.1 million in the second quarter and the remaining $24.0 million by August 2, 2018.

Between January 14, 2021 and February 9, 2021, we sold 3,513,027 shares of common stock pursuant to this agreement resulting in $86.4 million in net proceeds. As of February 9, 2021, we have used the entirety of the remaining availability under the sales agreement with Cowen.

Follow-on offering

On September 21, 2018, we closed an underwritten public offering of 3,450,000 shares of common stock at a public offering price of $60.00 per share, including 450,000 shares of common stock issued upon exercise by the underwriters of their option to purchase additional shares, pursuant to a shelf registration statement. The gross proceeds from the offering were $207.0 million and net proceeds were $194.9 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

Loan and Security Agreement with Hercules

On May 29, 2020, we entered into a loan and security agreement with Hercules Capital, Inc. ("Hercules") under which Hercules has agreed to lend us up to $100.0 million, to be made available in a series of tranches, subject to specified conditions. We borrowed $20.0 million at loan closing. The term of the loan is approximately 48 months, with a maturity date of June 1, 2024. No principal payments are due during an interest-only period, commencing on the initial borrowing date and continuing through June 1, 2022. The interest only period may be extended through January 1, 2023 upon satisfaction of certain milestones. Following the interest only period, we will repay the principal balance and interest of the advances in equal monthly installments through June 1, 2024.

Cash flows

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

	Year Ended December 31,		
	2020	2019	2018
	(in thousands)		
Net cash used in operating activities	$ (83,742)	$ (99,571)	$ (74,307)
Net cash provided/used in investing activities	152	(2,716)	(709)
Net cash provided by financing activities	21,688	2,705	340,494
Net change in cash, cash equivalents and restricted cash	$ (61,902)	$ (99,582)	$ 265,478

Net cash used in operating activities

During the year ended December 31, 2020, net cash used in operating activities was $83.7 million, which consisted of a net loss of $99.3 million, a decrease in net operating assets and liabilities of $4.0 million, and a decrease in non-cash equity interest of $0.9 million, partially offset by non-cash stock compensation expense of $18.8 million, $0.6 million of depreciation expense, $0.6 million in amortization of debt issuance costs, $0.3 million loss on disposal of fixed assets, and $0.2 million of non-cash interest expense.

During the year ended December 31, 2019, net cash used in operating activities was $99.6 million, which consisted of a net loss of $122.4 million, partially offset by non-cash stock compensation expense of $16.4 million, working capital adjustments of $6.0 million and $0.4 million of depreciation expense.

During the year ended December 31, 2018, net cash used in operating activities was $74.3 million, which consisted of a net loss of $85.3 million, partially offset by non-cash stock compensation expense of $10.2 million, working capital adjustments of $0.6 million and $0.2 million of depreciation expense.

Net cash used in investing activities

Net cash provided by investing activities was $0.2 million for the year ended December 31, 2020, which represented proceeds from the disposal of property and equipment.

Net cash used in investing activities was $2.7 million and $0.7 million for the years ended December 31, 2019 and 2018, respectively. Net cash used in investing activities represented purchases of property and equipment, primarily associated with laboratory equipment and leasehold improvements for new office space.

Net cash provided by financing activities

During the year ended December 31, 2020, net cash provided by financing activities was $21.7 million, which consisted of $2.3 million in net proceeds from the exercise of stock options and $20.0 million in proceed from our loan agreement with Hercules, partially offset by $0.6 million in payments related to debt issuances costs.

During the year ended December 31, 2019, net cash provided by financing activities was $2.7 million in net proceeds from the exercise of stock options.

During the year ended December 31, 2018, net cash provided by financing activities was $340.5 million, consisting of $338.7 million of net proceeds from our public offerings, after deducting cash paid for underwriting discounts and commissions and other expenses, and $1.8 million of proceeds from the exercise of stock options.

Operating capital requirements and plan of operations

To date, we have not generated any revenue from product sales. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of and seek regulatory approvals for our product candidates, and begin to commercialize COSELA. We are subject to all of the risks inherent in the development of new products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We expect to incur additional costs associated with operating as a public company and we anticipate that we will need substantial additional funding in connection with our continuing operations.

We believe that our existing cash and cash equivalents will be sufficient to fund our projected cash needs for greater than 12 months following the filing of this Annual Report.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of nonclinical development, laboratory testing and clinical trials for our product candidates;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- the extent to which we enter into non-exclusive, jointly funded clinical research collaboration arrangements, if any, for the development of our product candidates in combination with other companies' products;
- our ability to establish such collaborative co-development arrangements on favorable terms, if at all;
- the achievement of milestones or occurrence of other developments that trigger payments under our license agreement and any collaboration agreements into which we enter;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the extent to which we acquire or in-license product candidates and technologies, such as rintodestrant, and the terms of such in-licenses;
- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- revenue, if any, received from commercial sales of our product candidates; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Until such time, if ever, as we can generate substantial revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds except for amounts included under our licensing arrangements and the loan agreement with Hercules. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations, Commitments and Contingencies

Our principal commitments consist of obligations under our clinical trial commitments, consulting fees, operating lease commitments and long-term debt obligations. The following table summarizes these contractual obligations as of December 31, 2020:

	Payments due by period				
	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More Than 5 Years
	(in thousands)				
Contractual Obligations:					
Operating lease obligations(1)	$ 11,529	$ 1,657	$ 3,337	$ 3,404	$ 3,131
Long-term debt obligation, including interest and end of term charge (2)	$ 27,125	1,957	17,530	7,638	-
Total contractual obligations(3)	$ 38,654	$ 3,614	$ 20,867	$ 11,042	$ 3,131

(1) Represents future minimum lease payments under the non-cancelable lease for our headquarters in Research Triangle Park, NC and our former headquarters in Research Triangle Park, NC. The lease for the new office space commenced in September 2019 for approximately 60,000 square feet of laboratory space and office space in Research Triangle Park, NC. The lease will expire in September 2027, with the Company having the option to renew for an additional 5 years. The lease for our former headquarters will expire in December 2022. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) Amounts in the table reflect payments due for our loan agreement under an arrangement with Hercules for $20.0 million. The amounts in the table above reflect interest-only payments through June 1, 2022 with payments on principal beginning thereafter. For purposes of the table above, interest payments were calculated using an annual interest rate of 9.65%, which was the interest rate in effect as of December 31, 2020. Additionally, the table above includes a payment due upon maturity of the loan of $2.1 million. See Note 7 of the financial statements for further discussion of the Hercules loan agreement.

(3) We enter into agreements in the normal course of business with contract research organizations (CROs) for clinical trials and with vendors for preclinical studies and other services and products for operating purposes which are cancelable at any time by us, generally upon 30-60 days prior written notice. As of December 31, 2020, we have several on-going clinical studies in various stages. Under agreements with various CROs and clinical study sites, we incur expenses related to clinical studies of our product candidates and potential other clinical candidates. The timing and amounts of these disbursements are contingent upon the services rendered or as expenses are incurred by the CROs or clinical trial sites. Therefore, we cannot estimate the potential timing and amount of these payments and they have been excluded from the table above. Also, the above amounts exclude potential payments to be made under our license agreement for rintodestrant with the University of Illinois that are based on the progress of rintodestrant, as these payments are not determinable.

(4) Effective on October 22, 2019, we entered into a Product Agreement with Patheon Manufacturing Services, LLC as issued under the Master Manufacturing Services Agreement dated August 27, 2019 to manufacture and supply trilaciclib for commercial production. The initial term of the agreement is effective until December 31, 2024. If the annual volume of product ordered does not meet a specified amount, a true-up payment to this minimum will be due at the end of the applicable year. This minimum purchase amount was excluded from the table above as the conditions of the committed amount make it undeterminable at this time.

(5) The Company entered into a three-year co-promotion agreement in the United States and Puerto Rico with Boehringer Ingelheim Pharmaceuticals, Inc., or BI, in June 2020. Under the terms of the agreement, we will record revenue in the United States and Puerto Rico and retain development and commercialization rights to trilaciclib. We will lead marketing, market access and medical engagement initiatives; BI will lead sales force engagements. The agreement is limited to promotional support in the U.S. for the initial extensive stage small cell lung cancer indication.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Recent Accounting Pronouncements

See Note 2 to our financial statements included elsewhere in this report regarding the impact of certain recent accounting pronouncements on our 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. We had cash and cash equivalents of $207.3 million as of December 31, 2020, which consists of deposits in banks, including checking accounts, money market accounts and certificates of deposit. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant.

We also have exposure to market risk on our loan agreement with Hercules Capital, Inc. Our loan agreement accrues interest from its date of issue at a variable interest rate equal to the greater of either (i) (a) the prime rate as reported in The Wall Street Journal, plus (b) 6.40%, and (ii) 9.65%. As of December 31, 2020, $20.0 million was outstanding under the loan agreement with Hercules.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Inflation generally affects us by increasing our cost of labor. We do not believe that inflation had a material effect on our business financial condition or results of operations three and twelve months ended December 31, 2020.

Item 8. Financial Statements and Supplementary Data.

The financial statements of G1 Therapeutics, Inc. are provided in Part IV, Item 15 in this Annual Report.

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

Not Applicable.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and Exchange Act of 1934 is (i) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (ii) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure.

As of December 31, 2020, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934). Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgement in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of December 31, 2020, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Controls Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f) and 15d-15(f). Under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on our evaluation under the framework in *Internal Control—Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2020.

The effectiveness of our internal control over financial reporting as of December 31, 2020, has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report, which is included in this Annual Report on Form 10-K.

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 from the Company's Proxy Statement for the 2021 Annual Meeting of Stockholders, which will be filed with the SEC within 120 days after the end of our 2020 fiscal year pursuant to Regulation 14A for our 2021 Annual Meeting of Stockholders (the "Proxy Statement"), under the captions "Management and Corporate Governance" and "Code of Conduct and Ethics.

Item 11. Executive Compensation.

The information required by this item is incorporated herein by reference from the Proxy Statement under the captions "Executive Officer and Director Compensation," "Compensation Discussion and Analysis," "Compensation Committee Report," and "Management and Corporate Governance – Compensation Committee Interlocks and Insider Participation."

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 from the Proxy Statement, under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information."

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

The information required by this item is incorporated herein by reference from the Proxy Statement, under the captions "Management and Corporate Governance" and "Certain Relationships and Related Person Transactions."

Item 14. Principal Accounting Fees and Services.

The information required by this item is incorporated herein by reference from the Proxy Statement under the caption "Independent Registered Public Accounting Firm"

PART IV

Item 15. Exhibits, Financial Statement Schedules.

The following documents are filed as part of this Annual Report:

(a) *Financial Statements*.

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(b) *Financial Statement Schedules*.

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

(c) *Exhibits.*

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of G1 Therapeutics, Inc., dated as of May 22, 2017, filed as Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on May 26, 2017 (File No. 001-38096), and incorporated herein by reference.
3.2	Amended and Restated Bylaws of G1 Therapeutics, Inc., dated as of May 22, 2017, filed as Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed on May 26, 2017 (File No. 001-38096), and incorporated herein by reference.
4.1	Specimen Common Stock Certificate, filed as Exhibit 4.1 to the Registrant's Second Amendment to the Registration Statement on Form S-1 filed on May 8, 2017 (File No. 333-217285), and incorporated herein by reference.
4.2	Description of Securities of the Registrant.
4.3	Second Amended and Restated Registration Rights Agreement, dated as of April 27, 2016, by and among the Registrant and the Stockholders listed therein, filed as Exhibit 4.6 to the Registrant's Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference.
10.1**	Exclusive License Agreement, dated November 23, 2016, by and between the Registrant and The Board of Trustees of the University of Illinois, filed as Exhibit 10.11 to the Registrant's Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference.
10.2**	Amendment No. 1 to Exclusive License Agreement, dated March 24, 2017, by and between the Registrant and The Board of Trustees of the University of Illinois, filed as Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference.

10.3**	Loan and Security Agreement, by and between the Registrant and Hercules Capital, Inc., dated May 29, 2020, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 filed on August 5, 2020 (File No. 001-38096), and incorporated herein by reference.
10.4**	Co-Promotion Agreement by and between the Registrant and Boehringer Ingelheim Pharmaceuticals, Inc., dated June 29, 2020, filed as Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 filed on August 5, 2020 (File No. 001-38096), and incorporated herein by reference.
10.5*	2011 Equity Incentive Plan, dated March 3, 2011, as amended; First Amendment effective August 27, 2011; Second Amendment effective October 8, 2013; Third Amendment effective February 4, 2015; Fourth Amendment effective December 10, 2015; Fifth Amendment effective April 27, 2016; and Sixth Amendment effective November 7, 2016, filed as Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference.
10.6*	Amended and Restated 2017 Employee, Director and Consultant Equity Plan, filed as Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 filed on August 8, 2018 (File No. 001-38096), and incorporated herein by reference.
10.7*	G1 Therapeutics, Inc. 2021 Inducement Equity Incentive Plan.
10.8*	Form of Indemnification Agreement, filed as Exhibit 10.1 to the Registrant's Second Amendment to the Registration Statement on Form S-1 filed on May 8, 2017 (File No. 333-217285), and incorporated herein by reference.
10.9*	Non-Employee Director Compensation Policy, filed as Exhibit 10.13 to the Registrant's Second Amendment to the Registration Statement on Form S-1 filed on May 8, 2017 (File No. 333-217285), and incorporated herein by reference.
10.10*	Scientific, Clinical, and Regulatory Advisor Agreement, by and between the Registrant and Seth A. Rudnick, M.D., effective July 1, 2020, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 filed on August 5, 2020 (File No. 001-38096), and incorporated herein by reference.
10.11*	Employment Agreement by and between Registrant and John E. Bailey, Jr. dated September 29, 2020, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed on November 4, 2020 (File No. 001-38096), and incorporated herein by reference.
10.12*	Senior Advisor Agreement between Registrant and John E. Bailey, Jr. dated September 29, 2020, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed on November 4, 2020 (File No. 001-38096), and incorporated herein by reference.
10.13*	Employment Agreement by and between the Registrant and Mark Avagliano, dated as of July 29, 2019, filed as Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 filed on August 7, 2019 (File No. 001-38096), and incorporated herein by reference.
10.14*	Employment Agreement by and between the Registrant and Soma Gupta dated March 12, 2020, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020 filed on May 6, 2020 (File No. 001-38096), and incorporated herein by reference.
10.15*	Employment Agreement by and between the Registrant and James S. Hanson, dated as of June 25, 2018, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 filed on August 8, 2018 (File No. 001-38096), and incorporated herein by reference.

10.16*	Employment Agreement, by and between the Registrant and Rajesh K. Malik, M.D., dated July 1, 2014, as amended; First Amendment effective May 5, 2017, filed as Exhibit 10.5 to the Registrant's Second Amendment to the Registration Statement on Form S-1 filed on May 8, 2017 (File No. 333-217285), and incorporated herein by reference; and Second Amendment effective June 12, 2019, filed as Exhibit 10.2 to the Registrant's Form 8-K filed on June 13, 2019 (File No. 001-38096), and incorporated herein by reference.
10.17*	Amended and Restated Employment Agreement by and between the Registrant and Jennifer K. Moses dated May 8, 2019, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 filed on May 9, 2019 (File No. 001-38096), and incorporated herein by reference.
10.18*	Employment Agreement by and between the Registrant and Terry Murdock, dated as of August 1, 2017, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 filed on November 8, 2017 (File No. 001-38096) incorporated herein by reference; and First Amendment effective June 12, 2019, filed as Exhibit 10.3 to the Registrant's Form 8-K filed on June 13, 2019 (File No. 001-38096), and incorporated herein by reference.
10.19*	Executive Employment Agreement, by and between the Registrant and Mark A. Velleca, M.D., Ph.D., dated May 19, 2014, as amended; First Amendment effective February 1, 2015; Second Amendment effective May 10, 2016; and Third Amendment effective May 5, 2017, filed as Exhibit 10.4 to the Registrant's Second Amendment to the Registration Statement on Form S-1 filed on May 8, 2017 (File No. 333-217285), and incorporated herein by reference.
10.20*	Senior Advisor Agreement between Registrant and Mark A. Velleca, M.D., Ph.D. dated September 29, 2020, filed as Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed on November 4, 2020 (File No. 001-38096), and incorporated herein by reference.
21.1	Subsidiaries of the Registrant, filed as Exhibit 21.1 to the Registrant's Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference.
23.1	Consent of PricewaterhouseCoopers LLP.
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. § 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. § 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document

101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)XBRL Taxonomy Extension Presentation Linkbase Document

* Management contract or compensatory plan or arrangement.

** Confidential treatment has been requested for portions of this exhibit. These portions have been omitted and have been filed separately with the U.S. Securities and Exchange Commission.

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.

G1 THERAPEUTICS, INC.

Date: February 24, 2021

By: /s/ John E. Bailey, Jr.
John E. Bailey, Jr.
President and Chief Executive Officer

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.

Name	Title	Date
/s/ John E. Bailey, Jr. **John E. Bailey, Jr.**	President, Chief Executive Officer and Director (Principal Executive Officer)	February 24, 2021
/s/ Jennifer K. Moses **Jennifer K. Moses**	Chief Financial Officer (Principal Financial and Accounting Officer)	February 24, 2021
/s/ Fredric N. Eshelman **Fredric N. Eshelman, Pharm.D.**	Director	February 24, 2021
/s/ Willie A. Deese **Willie A. Deese**	Director	February 24, 2021
/s/ Glenn P. Muir **Glenn P. Muir**	Director	February 24, 2021
/s/ Garry A. Nicholson **Garry A. Nicholson**	Director	February 24, 2021
/s/ Seth A. Rudnick **Seth A. Rudnick, Ph.D.**	Director	February 24, 2021
/s/ Cynthia L. Schwalm **Cynthia L. Schwalm**	Director	February 24, 2021
/s/ Mark A. Velleca **Mark A. Velleca, M.D., Ph.D.**	Director	February 24, 2021

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of G1 Therapeutics, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying balance sheets of G1 Therapeutics, Inc. (the "Company") as of December 31, 2020 and 2019, and the related statements of operations, of redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows for each of the three years in the period ended December 31, 2020, including the related notes (collectively referred to as the "financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Change in Accounting Principle

As discussed in Note 6 to the financial statements, the Company changed the manner in which it accounts for leases in 2019.

Basis for Opinions

The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's financial statements and on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the financial statements 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. 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.

Critical Audit Matters

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

Accrued External Clinical Study Costs

As described in Notes 2 and 5 to the financial statements, management estimated and accrued research and development expenses including external clinical study costs associated with clinical trial activities. The Company's accrued external clinical study costs were $5.7 million as of December 31, 2020. The process of estimating and accruing expenses involved reviewing contracts and purchase orders, identifying services that have been provided on the Company's behalf, and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual cost. Costs for clinical trial activities were estimated based on an evaluation of the vendors' progress towards completion of specific tasks, using data such as patient enrollment, clinical site activations or information provided by vendors regarding their actual costs incurred. Management determined accrual estimates through reports from and discussion with applicable personnel and outside service providers as to the progress or state of completion of trials, or the services completed.

The principal considerations for our determination that performing procedures relating to accrued external clinical study costs is a critical audit matter are the significant judgment by management in estimating the costs incurred to date, specifically progress towards completion of specific tasks. This in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating audit evidence relating to cost estimates made by management to establish accrued external clinical study costs.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the financial statements. These procedures included testing the effectiveness of controls relating to the completeness and accuracy of accrued external clinical study costs. These procedures also included, among others, (i) testing management's process for estimating accrued external clinical study costs, (ii) evaluating the appropriateness of the method used by management to develop the estimate, (iii) evaluating the reasonableness of significant assumptions, including progress towards completion of specific tasks and the associated cost incurred for services when the Company has not yet been invoiced or otherwise notified of the actual cost, and (iv) testing the completeness and accuracy of underlying data used in the model.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
February 24, 2021

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

G1 Therapeutics, Inc.
Balance Sheets
(in thousands, except share and per share amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets		
Cash and cash equivalents	$ 207,306	$ 269,208
Restricted cash	63	63
Accounts Receivable	237	—
Prepaid expenses and other current assets	8,786	1,732
Total current assets	216,392	271,003
Property and equipment, net	2,482	3,538
Restricted cash	437	437
Operating lease assets	8,026	9,853
Other assets	1,215	—
Total assets	$ 228,552	$ 284,831
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 3,572	$ 3,684
Accrued expenses	16,486	15,403
Deferred revenue	237	—
Other current liabilities	3,148	682
Total current liabilities	23,443	19,769
Loan payable	19,893	—
Operating lease liabilities	7,865	9,535
Total liabilities	51,201	29,304
Stockholders' equity		
Common stock, $0.0001 par value, 120,000,000 shares authorized as of December 31, 2020 and December 31, 2019, respectively; 38,140,756 and 37,638,260 shares issued as of December 31, 2020 and December 31, 2019, respectively; 38,114,090 and 37,611,594 shares outstanding as of December 31, 2020 and December 31, 2019, respectively	4	4
Treasury stock, 26,666 shares	(8)	(8)
Additional paid-in capital	613,462	592,384
Accumulated deficit	(436,107)	(336,853)
Total stockholders' equity	177,351	255,527
Total liabilities and stockholders' equity	$ 228,552	$ 284,831

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

G1 Therapeutics, Inc.
Statements of Operations
(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2020	2019	2018
License revenue	$ 45,285	$ —	$ —
Operating expenses			
Research and development	73,271	89,002	70,683
General and administrative	68,490	40,039	18,603
Total operating expenses	141,761	129,041	89,286
Loss from operations	(96,476)	(129,041)	(89,286)
Other income (expense):			
Interest income	952	6,579	3,998
Interest expense	(1,778)	—	—
Other income (expense)	(542)	15	—
Total other income (expense), net	(1,368)	6,594	3,998
Loss before income taxes	$ (97,844)	$ (122,447)	$ (85,288)
Income tax expense	1,410	—	—
Net loss	$ (99,254)	$ (122,447)	$ (85,288)
Net loss per share, basic and diluted	$ (2.62)	$ (3.27)	$ (2.56)
Weighted average common shares outstanding, basic and diluted	37,878,026	37,499,256	33,316,719

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

G1 Therapeutics, Inc.
Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share amounts)

	Common stock		Treasury stock		Additional paid-in	Accumulated	Total stock-holders'
	Shares	Amount	Shares	Amount	capital	deficit	equity
Balance at December 31, 2017	**28,420,511**	**$ 3**	**(26,666)**	**$ (8)**	**$ 222,511**	**$ (129,118)**	**$ 93,388**
Public offering (Follow-on Financings)	7,360,000	1	—	—	303,521	—	303,522
Public offering (ATM)	752,008	—	—		36,068		36,068
Exercise of common stock options	736,273	—	—	—	1,797	—	1,797
Stock-based compensation	—	—	—	—	10,225	—	10,225
Stock financing costs	—	—	—	—	(892)	—	(892)
Net loss during year	—	—	—	—	—	(85,288)	(85,288)
Balance at December 31, 2018	**37,268,792**	**$ 4**	**(26,666)**	**$ (8)**	**$ 573,230**	**$ (214,406)**	**$ 358,820**
Exercise of common stock options	369,468	—	—	—	2,705	—	2,705
Stock-based compensation	—	—	—	—	16,449	—	16,449
Net loss during year	—	—	—	—	—	(122,447)	(122,447)
Balance at December 31, 2019	**37,638,260**	**$ 4**	**(26,666)**	**$ (8)**	**$ 592,384**	**$ (336,853)**	**$ 255,527**
Exercise of common stock options	502,496	—	—	—	2,308	—	2,308
Stock-based compensation	—	—	—	—	18,770	—	18,770
Net loss during year	—	—	—	—	—	(99,254)	(99,254)
Balance at December 31, 2020	**38,140,756**	**$ 4**	**(26,666)**	**$ (8)**	**$ 613,462**	**$ (436,107)**	**$ 177,351**

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

G1 Therapeutics, Inc.
Statements of Cash Flows
(amounts in thousands)

	Year Ended December 31,		
	2020	**2019**	**2018**
Cash flows from operating activities			
Net loss	$ (99,254)	$ (122,447)	$ (85,288)
Adjustments to reconcile net loss to net cash used in operating activities			
Stock-based compensation	18,770	16,449	10,225
Depreciation and amortization	582	356	175
Loss on disposal of fixed assets	322	—	8
Amortization of debt issuance costs	615	—	—
Non-cash interest expense	166	—	—
Non-cash equity interest, net	(867)	—	—
Change in operating assets and liabilities			
Accounts Receivable	(237)	—	—
Prepaid expenses and other assets	(5,545)	(219)	113
Accounts payable	(244)	248	(1,002)
Accrued expenses and other liabilities	1,713	6,042	1,446
Deferred revenue	237	—	—
Deferred rent	—	—	16
Net cash used in operating activities	(83,742)	(99,571)	(74,307)
Cash flows from investing activities			
Proceeds from disposal of property and equipment	152	—	—
Purchases of property and equipment	—	(2,716)	(709)
Net cash provided/used in investing activities	152	(2,716)	(709)
Cash flows from financing activities			
Proceeds from stock options exercised	2,308	2,705	1,797
Proceeds from loan agreement	20,000	—	—
Payments of debt issuance costs	(620)	—	—
Proceeds from public offering, net of underwriting fees and commissions	—	—	339,589
Payment of public offering costs	—	—	(892)
Net cash provided by financing activities	21,688	2,705	340,494
Net change in cash, cash equivalents and restricted cash	(61,902)	(99,582)	265,478
Cash, cash equivalents and restricted cash			
Beginning of period	269,708	369,290	103,812
End of period	$ 207,806	$ 269,708	$ 369,290
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 997	$ —	$ —
Non-cash investing and financing activities			
Upfront project costs and other current assets in accounts payable and accrued expenses	132	43	107
Purchases of equipment in accounts payable and accrued expenses	-	41	100
Operating lease liabilities arising from obtaining right-of-use asset	-	8,947	-

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

1. Description of Business

G1 Therapeutics, Inc. (the "Company") is a commercial-stage biopharmaceutical company based in Research Triangle Park, North Carolina focused on the development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. Our first FDA-approved product, COSELA™ (trilaciclib) is the first and only therapy indicated to proactively help protect bone marrow from the damage of chemotherapy and is first innovation in managing myelosuppression in decades. The Company was incorporated on May 19, 2008 in the state of Delaware.

The Company is advancing two clinical-stage programs. Our lead compound trilaciclib is a first-in-class therapy designed to help protect against chemotherapy-induced myelosuppression. Trilaciclib helps protect HSPCs in bone marrow by transiently inhibiting CDK4/6 leading to a temporary arrest of susceptible host cells during chemotherapy in ES-SCLC patients. This reduces the duration and severity of neutropenia and other myelosuppressive consequences of chemotherapy. In addition, trilaciclib activates and enhances the immune system response driving increased anti-tumor efficacy, which we continue to explore in clinical trials. We are developing trilaciclib in a variety of tumors, including small cell lung cancer (SCLC), colorectal cancer (CRC), metastatic triple negative breast cancer (mTNBC), neoadjuvant breast cancer, non-small cell lung cancer (NSCLC) and bladder cancer. Rintodestrant is an oral selective estrogen receptor degrader (SERD) for the treatment of estrogen receptor-positive (ER+) breast cancer. In 2020, the Company out-licensed global rights to lerociclib, an internally discovered and differentiated oral CDK4/6 inhibitor designed to enable more effective combination treatment strategies across multiple oncology indications, including ER+, HER2-negative (HER2-) breast cancer. The Company also has intellectual property focused on cyclin-dependent kinase targets.

Trilaciclib, a transient IV CDK4/6 inhibitor, is a novel therapeutic approach which is given before chemotherapy that temporarily blocks progression through the cell cycle. This provides two benefits. First, it proactively helps protect HSPCs in bone marrow leading to preservation of neutrophils, erythrocytes, and platelets (called myeloprotection) which reduces the occurrences and severity of neutropenia and other myelosuppressive consequences of chemotherapy. This myeloprotection benefit has been conclusively proven in double-blind placebo-controlled clinical trials in extensive-stage small cell lung cancer. Second, trilaciclib activates and enhances the immune system response driving increased anti-tumor efficacy, which we are exploring in clinical trials.

On February 12, 2021, COSELA (trilaciclib) for injection was approved by the U.S. Food and Drug Administration (FDA) to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive stage small cell lung cancer (ES-SCLC). COSELA is expected to be commercially available through G1's specialty pharmacy partner network in early March. COSELA is administered intravenously as a 30-minute infusion completed within 4 hours prior to the start of chemotherapy and is the first FDA-approved therapy to provide proactive, multilineage protection from chemotherapy-induced myelosuppression. The approval of COSELA is based on data from three randomized, placebo-controlled trials that showed patients receiving COSELA prior to chemotherapy had clinically meaningful and statistically significant reduction in the duration and severity of neutropenia, reduction of red blood cell transfusions, as well as improvements in other myeloprotection measures, compared to patients receiving chemotherapy without COSELA.

In June 2020, the Company entered into a three-year co-promotion agreement for COSELA in the United States and Puerto Rico with Boehringer Ingelheim. The agreement is limited to support SCLC. Under the terms of the agreement, the Company will book revenue in the United States and Puerto Rico and retain development and commercialization rights to trilaciclib. The Company will lead marketing, market access and medical engagement initiatives; Boehringer Ingelheim will lead sales force engagements. In addition, discussions with European regulatory authorities have indicated existing data is sufficient to support a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for trilaciclib for myeloprotection in SCLC, which the Company plans to pursue in collaboration with a partner.

In August 2020, the Company entered into an exclusive license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd ("Simcere") for development and commercialization rights for trilaciclib in all indications in Greater China (mainland China, Hong Kong, Macau and Taiwan). Under the terms of the agreement, the Company received an upfront payment of $14.0 million in September 2020 and will be eligible to receive up to $156.0 million in development and commercial milestone payments. Simcere will also pay the Company tiered low double-digit royalties on annual net sales of trilaciclib in Greater China. As part of this agreement, Simcere will participate in global clinical trials of trilaciclib and the companies will be responsible for all development and commercialization costs in their respective territories.

We are also executing on our tumor-agnostic strategy to evaluate the potential benefits of trilaciclib to patients with other tumors that are treated with chemotherapy. We have two on-going trials: a pivotal 1L colorectal cancer (CRC) study and a Phase 2 neoadjuvant breast cancer (I-SPY 2). We intend to initiate another pivotal study in mTNBC (including 1L and 2L patients) and have two additional Phase 2 studies: a 2L/3L non-small cell lung cancer (NSCLC) trial in post-checkpoint patients and a 1L bladder cancer trial with chemotherapy and a checkpoint inhibitor. These studies across treatment settings and tumor types will evaluate trilaciclib's dual benefits in both multi-lineage myeloprotection and anti-tumor efficacy.

The Company is developing rintodestrant, an oral SERD, as a monotherapy and in combination with CDK4/6 inhibitors, initially Ibrance® (palbociclib), for the treatment of ER+ breast cancer. In 2018, the Company initiated a Phase 1/2a (dose escalation/dose expansion) clinical trial in ER+, HER2- breast cancer. Preliminary data from the Phase 1 potion of this trial were presented at the 2019 ESMO Congress, showing that rintodestrant was well tolerated and demonstrated evidence of anti-tumor activity in heavily pre-treated patients. The mature monotherapy data were presented at the 2020 San Antonio Breast Cancer Symposium (SABCS) conference, confirming the safety and efficacy results of the preliminary analysis. Based on these findings the Company advanced an 800 mg dose of rintodestrant into a 40-patient Phase 2 combination trial with palbociclib, a CDK4/6 inhibitor. The Company has completed enrollment of patients in this trial, and expects to disclose initial safety and efficacy data in the second quarter of 2021. Palbociclib is being provided under a non-exclusive clinical supply agreement that was signed with Pfizer in February 2020. We will evaluate partnering options for rintodestrant following the data read-out from our combination study.

Lerociclib is a differentiated oral CDK4/6 inhibitor being developed for use in combination with other targeted therapies in multiple oncology indications. In 2020, the Company entered into separate, exclusive agreements with EQRx, Inc. (rights for U.S., Europe, Japan and all markets outside Asia-Pacific) and Genor Biopharma Co. Inc. (rights for Asia-Pacific, excluding Japan) for the development and commercialization of lerociclib in all indications. Combined, these agreements provide $26.0 million in upfront payments to the Company, and the opportunity for up to $330.0 million in potential milestone payments, plus sales-based royalties. EQRx, Inc. and Genor Biopharma Co. Inc. are responsible for all costs related to the development and commercialization of lerociclib in their respective territories.

The Company's financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. As of December 31, 2020, the Company had an accumulated deficit of $436.1 million. The Company has reported a net loss in all fiscal periods since inception and expects to incur substantial losses in the future to conduct research and development and pre-commercialization activities.

As of December 31, 2020, the Company had cash and cash equivalents of $207.3 million. The Company expects that its existing cash and cash equivalents will enable it to fund its operating expenses and capital expenditure requirements for greater than 12 months from the date of filing this Annual Report.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The Company has prepared the accompanying financial statements in conformity with generally accepted accounting principles in the United States of America ("U.S. GAAP").

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and the accompanying notes. Actual results could differ from those estimates. These estimates include the Company's common stock valuation, stock compensation, and deferred tax asset valuation allowance.

Revenue Recognition

For elements of those arrangements that we determine should be accounted for under ASC 606, Revenue from Contracts with Customers ("ASC 606"), we assess which activities in our license or collaboration agreements are performance obligations that should be accounted for separately and determine the transaction price of the arrangement, which includes the assessment of the probability of achievement of future milestones and other potential consideration. For arrangements that include multiple performance obligations, such as granting a license or performing manufacturing or research and development activities, we allocate the transaction price based on the relative standalone selling price and recognize revenue that is allocated to the respective performance obligation when (or as) control is transferred to the customer and the performance obligation is satisfied. Accordingly, we develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. These key assumptions may include revenue forecasts, clinical development timelines and costs, discount rates and probabilities of clinical and regulatory success.

Licenses of Intellectual Property

If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue associated with the bundled performance obligation. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of progress and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes developmental and regulatory milestone payments, the Company evaluates whether the achievement of each milestone specifically relates to the Company's efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. The Company evaluates each milestone to determine when and how much of the milestone to include in the transaction price. The Company first estimates the amount of the milestone payment that the Company could receive using either the expected value or the most likely amount approach. The Company primarily uses the most likely amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, the Company considers whether any portion of that estimated amount is subject to the variable consideration constraint (that is, whether it is probable that a significant reversal of cumulative revenue would not occur upon resolution of the uncertainty). The Company updates the estimate of variable consideration included in the transaction price at each reporting date which includes updating the assessment of the likely amount of consideration and the application of the constraint to reflect current facts and circumstances.

Royalties

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

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with an original maturity of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents at December 31, 2020 and 2019 consist of amounts on deposit in banks, including checking accounts, money market accounts and certificates of deposit. Cash deposits are all in financial institutions in the United States. As part of the lease for the new office space, the Company obtained a standby letter of credit in the amount of $0.5 million related to the security deposit. This letter of credit is secured by money market funds at the financial institution. Therefore, these funds are classified as restricted cash on the balance sheet. The letter of credit will be reduced ratably on each anniversary of the commencement of the lease until the end of the lease term.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to credit risk consist of cash and cash equivalents. Deposits with financial institutions are insured, up to certain limits, by the Federal Deposit Insurance Corporation ("FDIC"). The Company's cash deposits often exceed the FDIC insurance limit; however, all deposits are maintained with high credit quality institutions and the Company has not experienced any losses in such accounts. The financial condition of financial institutions is periodically reassessed, and the Company believes the risk of any loss is minimal. The Company believes the risk of any loss on cash due to credit risk is minimal.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation is generally calculated using the straight-line method over the following estimated useful lives:

Computer equipment	5 years
Laboratory equipment	5 years
Furniture and fixtures	7 years
Leasehold improvements	7 years

Costs associated with maintenance and repairs are charged to expense as incurred. Property and equipment held under leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset.

Impairment of Long-lived Assets

The Company evaluates its long-lived assets for indicators of possible impairment by comparison of the carrying amounts to future net undiscounted cash flows expected to be generated by such assets when events or changes in circumstances indicate the carrying amount of an asset may not be recoverable. Should an impairment exist, the impairment loss would be measured based on the excess carrying value of the asset over the asset's fair value based on discounted estimates of future cash flows. For the years ended December 31, 2020, 2019 and 2018, the Company's management evaluated its long-lived assets and determined no impairment charge was needed.

Research and Development

Research and development expenses consist of costs incurred to further the Company's research and development activities and include salaries and related employee benefits, manufacturing of pharmaceutical active ingredients and drug products, costs associated with clinical trials, nonclinical activities, regulatory activities, research-related overhead expenses and fees paid to expert consultants, external service providers and contract research organizations which conduct certain research and development activities on behalf of the Company. Costs incurred in the research and development of products are charged to research and development expense as incurred.

Each reporting period, management estimated and accrued research and development expenses, including external clinical study costs associated with clinical trial activities. The process of estimating and accruing expenses involved reviewing contracts and purchase orders, identifying services that have been provided on the Company's behalf, and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual costs.

Costs for clinical trial activities were estimated based on an evaluation of vendors' progress towards completion of specific tasks, using data such as patient enrollment, clinical site activations or information provided by vendors regarding their actual costs incurred. Payments for these activities are based on the terms of individual contracts and payment timing may differ significantly from the period in which the services were performed. The Company determines accrual estimates through reports from and discussions with applicable personnel and outside service providers as to the progress or state of completion of trials, or the services completed. The estimates of accrued external clinical study costs as of each balance sheet date are based on the facts and circumstances known at the time.

Fair value of Financial Instruments

The Company provides disclosure of financial assets and financial liabilities that are carried at fair value based on the price that would be received upon sale of an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Fair value measurements may be classified based on the amount of subjectivity associated with the inputs to fair valuation of these assets and liabilities using the following three levels:

Level 1 Inputs are unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2 Inputs include quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability and inputs that are derived principally from or corroborated by observable market data by correlation or other means.

Level 3 Unobservable inputs that reflect the Company's estimates of the assumptions that market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available, including its own data.

The carrying amounts of cash, cash equivalents, accounts payable and accrued liabilities approximate fair value because of their short-term nature.

At December 31, 2020 and 2019 these financial instruments and respective fair values have been classified as follows (in thousands):

	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant other unobservable inputs (Level 3)	Balance at December 31, 2020
Assets				
Money market funds	$ 190,180	$ —	$ —	$ 190,180
Certificates of Deposit	15,970	—	—	15,970
Total assets at fair value:	$ 206,150	$ —	$ —	$ 206,150

	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant other unobservable inputs (Level 3)	Balance at December 31, 2019
Assets				
Money market funds	$ 252,563	$ —	$ —	$ 252,563
Certificates of Deposit	15,873	—	—	15,873
Total assets at fair value:	$ 268,436	$ —	$ —	$ 268,436

During the twelve months ended December 31, 2020 and December 31, 2019, there were no changes in valuation methodology.

The Loan Payable (discussed in Note 7), which is classified as a Level 3 liability, has a variable interest rate and the carrying value approximates its fair value. As of December 31, 2020, the carrying value was $19.9 million.

Patent Costs

Costs associated with the submission of patent applications are expensed as incurred given the uncertainty of the future economic benefits of the patents. Patent-related legal expenses included in general and administrative costs were approximately $2,761 thousand, $2,114 thousand, and $1,352 thousand for the years ended December 31, 2020, 2019 and 2018, respectively.

Income Taxes

Income taxes are accounted for using the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to temporary differences between the financial statements carrying amounts of assets and liabilities and their respective tax bases, operating loss carryforwards, and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

In accordance with Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) 740, *Accounting for Income Taxes*, the Company reflects in the financial statements the benefit of positions taken in a previously filed tax return or expected to be taken in a future tax return only when it is considered ‘more-likely-than-not’ that the position taken will be sustained by a taxing authority. As of December 31, 2020 and 2019, the Company had no unrecognized income tax benefits and correspondingly there is no impact on the Company’s effective income tax rate associated with these items. The Company’s policy for recording interest and penalties relating to uncertain income tax positions is to record them as a component of income tax expense in the accompanying statements of operations. As of December 31, 2020 and 2019, the Company had no such accruals.

Stock-Based Compensation

The primary type of stock-based payments utilized by the Company are stock options. The Company accounts for stock-based employee compensation arrangements by measuring the cost of employee services received in exchange for all equity awards granted based on the fair value of the award on the grant date. The fair value of each employee stock option is estimated on the date of grant using an options pricing model. The Company currently uses the Black-Scholes valuation model to estimate the fair value of its share-

based payments. The model requires management to make a number of assumptions including expected volatility, expected life, risk-free interest rate and expected dividends.

The Company accounts for stock-based non-employee compensation arrangements by recording the expense of such services based on the fair value of the equity instrument as estimated using the Black-Scholes pricing model. The fair value of the equity instrument is charged to operating expense over the term of the service agreement. In accordance with the implementation of ASU No. 2018-07 on January 1, 2019, the fair value of non-employee stock options is no longer be re-measured each reporting period.

Segment Information

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. All of the Company's assets are held in the United States.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. There was no difference between net loss and comprehensive loss for each of the periods presented in the accompanying financial statements.

Leases

We determine if an arrangement is a lease at inception. Operating lease assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating leases are included in operating lease assets, other current liabilities, and operating lease liabilities on our balance sheet at December 31, 2020. Operating lease assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at commencement date. As most of our leases do not provide an implicit rate, we use our incremental borrowing rate based on the information available at commencement date to determine the present value of future payments. Our lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

Debt Issuance Costs

Debt issuance costs are amortized to interest expense over the estimated life of the related debt based on the effective interest method. In accordance with ASC 835, Interest, we present debt issuance costs on the condensed balance sheet as a direct deduction from the associated debt.

Coronavirus (COVID-19) Impact on Operations

The Company has implemented business continuity plans to address the COVID-19 pandemic and minimize disruptions to ongoing operations. Enrollment of patients in current and future clinical trials may be impacted by COVID-19. The Company does not anticipate significant supply chain delays or shortages as a result of the COVID-19 pandemic. COVID-19 travel limitations and government-mandated work-from-home or shelter-in-place orders, may reduce the number of in-person meetings with prescribers and fewer patient visits with physicians, potentially resulting in fewer new prescriptions.

The established a COVID-19 response team which continually monitors the impact of COVID-19 on its operations. The COVID-19 response team manages workplace protocols that govern employees use of our office. To mitigate the impact of COVID-19 on its business, the Company put in place the following safety measures for its employees, patients, healthcare professionals, and suppliers to limit exposure: the Company substantially restricted travel, supplied personal protective equipment to employees, limited access to its headquarters and asked most of its staff to work remotely. In addition, the Company transitioned most of its employees to working remotely and added bandwidth and VPN capacity to its infrastructure. The Company will continue to monitor the impact of COVID-19 on its operations and report to the Board regularly on the progress of its response to the COVID-19 outbreak.

Recent Accounting Pronouncements

Adoption of New Accounting Standards

In August 2018, the FASB issued ASU No. 2018-15, Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract ("ASU 2018-15"). The FASB issued ASU 2018-15 to align the requirements for capitalizing implementation costs incurred in a cloud-based hosting

arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software (and hosting arrangements that include an internal-use software license). ASU 2018-15 became effective for annual and interim reporting periods beginning after December 15, 2019. The Company adopted ASU 2018-15 on January 1, 2020 using the prospective method of adoption, and the adoption did not have a material impact to the financial statements.

3. Property and Equipment

Property and equipment consists of the following (in thousands):

	December 31, 2020	December 31, 2019
Computer equipment	$ 327	$ 332
Laboratory equipment	334	871
Furniture and fixtures	866	1,071
Leasehold improvements	1,782	1,941
Accumulated depreciation	(827)	(677)
Property and equipment, net	$ 2,482	$ 3,538

Depreciation expenses relating to property and equipment were $582 thousand, $356 thousand, and $175 thousand for the years ended December 31, 2020, 2019 and 2018, respectively.

4. Patent License Agreement

On November 23, 2016, the Company entered into a license agreement with the Board of Trustees of the University of Illinois (“the University”), which was amended on March 24, 2017. Pursuant to the license agreement, as amended, the University licensed patent rights to the Company, with rights of sublicense, to make, have made, use, import, sell and offer for sale products covered by certain patent rights owned by the University. The rights licensed to the Company are exclusive, worldwide, non-transferable rights, for all fields of use. Under the terms of the agreement the Company paid a one-time only, non-refundable license issue fee in the amount of $0.5 million which was charged to research and development expense in the fourth quarter of 2016.

The Company is also obligated to pay annual maintenance fees to the University. All annual minimum payments are fully creditable against any royalty payments made by the Company. Under the terms of the agreement, the Company must pay the University royalty percentage on all net sales of products and a share of sublicensing revenues. In addition, the University is eligible to receive milestone payments of up to $2.6 million related to the initiation and execution of clinical trials and the first commercial sale of a product in another country. To date, the Company has made milestone payments totaling $0.6 million, of which $0 was incurred during 2020. The Company will be responsible for any future patent prosecution costs that may arise.

The term of the license agreement will continue until the later of (i) the expiration of the last valid claim within the patent rights covering the product in such country, (ii) the expiration of market exclusivity in such country and (iii) the 10th anniversary of the first commercial sale in such country. The University may terminate the agreement in the event (i) the Company fails to pay any amount or make any report when required to be made and fails to cure such failure within thirty (30) days after receipt of notice from the University, (ii) is in breach of any provision of the agreement and fails to remedy within forty-five (45) days after receipt of notice, (iii) makes a report to the University under the agreement that is determined to be materially false, (iv) declares insolvency or bankruptcy or (v) takes an action that causes patent rights or technical information to be subject to lien or encumbrance and fails to remedy any such breach with in forty-five (45) days of receipt of notice from the University. The Company may terminate the agreement at any time on written notice to the University at least ninety (90) days prior to the termination date specified in the notice. Upon expiration or termination of the agreement, all rights revert to the University.

5. Accrued Expenses

Accrued expenses are comprised as follows (in thousands):

	December 31, 2020	December 31, 2019
Accrued external research	$ 3,219	$ 2,737
Accrued professional fees and other	3,920	1,487
Accrued external clinical study costs	5,683	7,996
Accrued compensation expense	3,664	3,183
Accrued expenses	$ 16,486	$ 15,403

6. Leases

We adopted ASC 842 as of January 1, 2019. Prior period amounts have not been adjusted and continue to be reported in accordance with our historic accounting under ASC 840.

Pursuant to a lease agreement dated January 10, 2014 (the “Lease”), on April 1, 2014, the Company leased office and lab space with a free rent period and escalating rent payments; the Lease had an expiration date of July 31, 2017. The Lease was amended on January 27, 2016 to lease new larger office and lab space beginning in August 2016 with a discounted rent period and escalating rent payments and the Lease term was extended to December 31, 2022. The amendment also contained an option for a five-year renewal and a right of first refusal to lease adjacent office space. The Lease was further amended on March 27, 2017 to lease additional office space beginning in August 2017 with a discounted rent period and escalating rent payments. The Lease was amended again in January 2018 to lease additional adjacent office space beginning in August 2018 with a discounted rent period and escalating rent payments. The term of the renewal option contained in the Lease, as amended, was not included in the measurement of the operating lease asset and liability since exercise of the option was uncertain.

On March 20, 2020, the Lease was amended to surrender three of the office spaces previously entered into above, with a termination date of May 31, 2020 and in consideration of a termination fee to be paid. The lease payments and term for the remaining occupied space will remain the same. Due to these changes in lease terms for the three office spaces, in March 2020 the Company modified the operating lease liabilities and operating lease assets of these three office spaces to reflect the new terms.

In November 2018, the Company signed a new lease to secure approximately 60,000 square feet of laboratory and office space at 700 Park Offices Drive in Research Triangle Park, NC (“700 Lease”). The 700 Lease commenced on September 2, 2019 and has an expiration date of September 30, 2027 for the initial term with the Company having the option to renew for an additional 5 years. The term of the renewal option contained in the Lease was not included in the measurement of the operating lease asset and liability since exercise of the option was uncertain. As part of the 700 Lease, the Company obtained a standby letter of credit in the amount of $0.5 million related to the security deposit. This letter of credit is secured by money market funds at the financial institution. Therefore, these funds are classified as restricted cash on the balance sheet. The letter of credit will be reduced ratably on each anniversary of the commencement of the 700 Lease until the end of the lease term.

The tables below reflect the Company's lease position and weighted-average lease terms and discount rates for our operating leases as of December 31, 2020. Operating lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. In determining the present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date.

(in thousands)	Classification on the Balance Sheet	December 31, 2020
Assets		
Operating lease assets	Operating lease assets	$ 8,026
Total lease assets		$ 8,026
Liabilities		
Current		
Operating	Other current liabilities	$ 988
Non-current		
Operating	Operating lease liabilities	7,865
Total lease liabilities		$ 8,853

Lease Term and Discount Rate	December 31, 2020
Weighted-average remaining lease term (years)	
Operating leases	6.6
Weighted-average discount rate	
Operating leases	8.0%

The table below presents information related to the lease costs for operating leases (in thousands):

		Year Ended December 31,		
(in thousands)	Classification	2020	2019	2018
Operating lease costs *(a)*	Research and development	$ 955	$ 609	$ 298
	General and administrative	1,191	368	83
Total operating lease costs		$ 2,146	$ 977	$ 381

(a) Includes variable lease costs which are immaterial.

The table below reconciles the undiscounted cash flow for each of the first five years and total of the remaining years to the operating lease liabilities recorded on the balance sheet as of December 31, 2020 (in thousands):

	Operating leases
Years ending December 31,	
2021	1,657
2022	1,703
2023	1,634
2024	1,679
2025	1,725
Thereafter	3,131
Total future minimum lease payments	$ 11,529
Less: present value adjustment	(2,676)
Total operating lease liabilities	$ 8,853

Cash payments included in the measurement of our operating leases were $1,683 thousand for the twelve months ended December 31, 2020.

7. Loan Payable

On May 29, 2020, the Company entered into a loan and security agreement (the "Loan Agreement") with Hercules Capital, Inc. ("Hercules"), under which Hercules has agreed to lend the Company up to $100.0 million, to be made available in a series of tranches, subject to certain terms and conditions. The first tranche totals $30.0 million, of which the Company received $20.0 million at closing. Upon initiation of the phase 3 trial for metastatic colorectal cancer and upon receiving FDA approval for small cell lung cancer ("the Performance Milestone"), the second tranche of $20.0 million will become available to the Company for drawdown through December 15, 2021. The third tranche of $30.0 million will be available through December 31, 2022. The fourth tranche of $20.0 million will be available at Hercules' approval through December 31, 2022. If the Company achieves the Performance Milestone and does not draw further on the loan, no financial covenants are required. If the Company achieves the Performance Milestone and draws any advance other than the first tranche, financial covenants will apply. As of December 31, 2020, no financial covenants apply as the Company has only drawn down on the first tranche.

Amounts borrowed under the Loan Agreement will bear an interest rate equal to the greater of either (i) (a) the prime rate as reported in The Wall Street Journal, plus (b) 6.40%, and (ii) 9.65%. The Company will make interest only payments through June 1, 2022. The interest only period may be extended through January 1, 2023 upon satisfaction of the Performance Milestone. Following the interest only period, the Company will repay the principal balance and interest of the advances in equal monthly installments through June 1, 2024.

The Company may prepay advances under the Loan Agreement, in whole or in part, at any time subject to a prepayment charge equal to (a) 3.0% of the prepayment amount in the first year; (b) 2.0% of the prepayment amount in the second year; and (c) 1.0% of the prepayment amount in the third year.

Upon prepayment or repayment of all or any of the advances under the Loan Agreement, the Company will pay (in addition to the prepayment charge) an end of term charge of 6.95% of the aggregate funded amount. With respect to the first tranche, the end of term charge of $2.1 million will be payable upon any prepayment or repayment. To the extent that the Company is provided additional advances under the Loan Agreement, the 6.95% end of term charge will be applied to such additional amounts. These amounts will be accrued over the term of the loan using effective-interest method.

The Loan Agreement is secured by substantially all of the Company's assets, including intellectual property, subject to certain exemptions. The Company out-licensed lerociclib as permitted in the Loan Agreement and the Company may out-license rintodestrant upon approval of the licensing terms by Hercules.

The Company incurred financing expenses of $0.4 million related to the Loan Agreement which are recorded as debt issuance costs and as a direct reduction to long-term debt on the Company's balance sheet. Additionally, the Company is treating $0.2 million of the upfront facility fee that related to the initial $20.0 million drawn as a debt discount and treating it in the same way as debt issuance costs. The remainder of the facility fee is related to future undrawn tranches and is accounted for as a deferred financing charge.

Upon issuance, the first tranche was recorded as a liability with an initial carrying value of $19.4 million, net of debt discount and debt issuance costs. The initial carrying value will be accreted to the repayment amount, which includes the outstanding principal plus the end of term charge, through interest expense using the effective-interest method over the term of the debt. During the twelve months ended December 31, 2020, the Company recognized $1.8 million of interest expense related to the Loan Agreement, which is reflected in other income (expense), net on the unaudited condensed statements of operations.

As of December 31, 2020 the future principal payments due under the Loan Agreement, excluding interest, are as follows:

	Amount
2021	—
2022	4,631
2023	9,972
2024	5,397
Total principal outstanding	20,000
End of term charge	395
Unamortized debt issuance costs	(502)
Total	19,893

8. Stockholders' Equity

Common stock

The Company's common stock has a par value of $0.0001 per share and consists of 120,000,000 authorized shares as of December 31, 2020 and 2019, respectively. Holders of common stock are entitled to one vote per share and are entitled to receive dividends, as if and when declared by the Company's Board of Directors.

The Company has reserved authorized shares of common stock for future issuance at December 31, 2020 and December 31, 2019 as follows:

	December 31, 2020	December 31, 2019
Common stock options outstanding	6,644,780	5,744,036
Options available for grant under Equity Incentive Plans	932,051	938,738
	7,576,831	6,682,774

Preferred stock

Upon completion of the IPO, all outstanding preferred stock was automatically converted into 18,933,053 shares of common stock. The Company is also authorized to issue 5,000,000 shares of undesignated preferred stock in one or more series. As December 31, 2020, no shares of preferred stock were issued or outstanding.

9. Stock-Based Compensation

2011 Equity Incentive Plan

In March 2011, the Company adopted the 2011 Equity Incentive Plan (the "Plan"). As amended, 4,400,640 shares of common stock were reserved for issuance under the 2011 Plan. Eligible plan participants included employees, directors, officers, consultants and advisors of the Company. The 2011 plan permitted the granting of incentive stock options, nonqualified stock options and other stock- based awards. In connection with the adoption of the 2017 Plan (as defined below), the 2011 Plan was terminated and no further awards will be made under the 2011 Plan.

2017 Equity Incentive Plan

In May 2017, the Company adopted the 2017 Equity Incentive Plan (the "2017 Plan"). The 2017 Plan provided for the direct award or sale of the Company's common stock and for the grant of up to 1,932,000 stock options to employees, directors, officers, consultants and advisors of the Company. The 2017 Plan provides for the grant of incentive stock options, non-statutory stock options or restricted stock. Effective January 1, 2018, and in accordance with the "evergreen" provision of the 2017 plan, an additional 1,066,692 shares were made available for issuance. Effective January 1, 2019, and in accordance with the "evergreen" provision of the 2017 plan, an additional 1,096,553 shares were made available for issuance. Effective January 1, 2020, and in accordance with the "evergreen" provision of the 2017 plan, an additional 1,096,553 shares were made available for issuance.

Under both the 2011 Plan and the 2017 Plan, options to purchase the Company's common stock may be granted at a price no less than the fair market value of a share of common stock on the date of grant. The fair value shall be the closing sales price for a share as quoted on any established securities exchange for such grant date or the last preceding date for which such quotation exists. Vesting terms of options issued are determined by the Board of Directors or Compensation Committee of the Board. The Company's stock options vest based on terms in the stock option agreements. Stock options have a maximum term of ten years.

As of December 31, 2020, there were a total of 932,051 shares of common stock available for future issuance under the 2017 Plan.

Stock-based Compensation

During the years ended December 31, 2020, 2019 and 2018, the Company recorded employee share-based compensation expense of $18,770, $16,351, and $8,157, respectively. The Company recorded non-employee share-based compensation expense of $0, $98, and $2,068 during the years ended December 31, 2020, 2019 and 2018, respectively. Total share-based compensation expense included in the statements of operations is as follows:

	Year Ended December 31,		
	2020	2019	2018
	in thousands		
Research and development	$ 6,902	$ 6,261	$ 5,218
General and administrative	11,868	10,188	5,007
Total stock-based compensation expense	$ 18,770	$ 16,449	$ 10,225

The fair value of each option grant is estimated on the grant date using the Black-Scholes option-pricing model, using the following weighted average assumptions:

	Year Ended December 31,		
	2020	2019	2018
Expected volatility	74.8 - 81.0%	74.2 - 82.1%	74.9 - 86.5%
Weighted-average risk free rate	0.3-1.7%	1.4 - 2.6%	2.3 - 3.0%
Dividend yield	—%	—%	—%
Expected term (in years)	6.02	6.02	6.04
Weighted-average grant-date fair value per share	$ 12.17	$ 14.94	$ 26.42

The expected term of stock options represents the weighted-average period the stock options are expected to remain outstanding and is based on the option vesting term, contractual terms and industry peers as the Company did not have sufficient historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior.

The expected stock price volatility assumptions for the Company's stock options were determined by examining the historical volatilities for industry peers as the Company does not have sufficient history to estimate volatility using only its common stock. In 2019, the Company began incorporating its historical stock price in conjunction with selected similar publicly traded companies. The Company plans to continue to use the guideline peer group volatility information until the historical volatility of its common stock is sufficient to measure expected volatility for future option grants.

The risk-free interest rate assumption at the date of grant is based on the U.S. Treasury instruments whose term was consistent with the expected term of the Company's stock options.

The expected dividend assumption is based on the Company's history and expectation of dividend payouts.

Stock option activity during 2020 is as follows:

	Options outstanding	Weighted average exercise price	Weighted average Remaining contractual for life (Years)	Aggregate intrinsic value (in thousands)
Balance as of December 31, 2019	5,744,036	$ 16.88	7.5	$ 72,251
Cancelled	(635,797)	$ 30.94		
Granted	2,039,037	$ 18.32		
Exercised	(502,496)	$ 4.59		
Balance as of December 31, 2020	6,644,780	$ 16.91	7.3	$ 35,464
Exercisable at December 31, 2020	3,542,190	$ 12.94	6.0	$ 31,686
Vested at December 31, 2020 and expected to vest	6,644,780	$ 16.91	7.3	$ 35,464

As of December 31, 2020, there was $38,834 of total unrecognized share-based compensation costs, which is expected to be recognized over a weighted-average period of 2.42 years.

Prior to our initial public offering, the fair value of our common shares underlying our stock options was estimated on each grant date by our board of directors. In order to determine the fair value of our common shares underlying granted stock options, our board of directors considered, among other things, timely valuations of our common shares prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

Since the IPO, the board of directors has determined the fair value of each common share underlying share-based awards based on the closing price of the common shares as reported by Nasdaq on the date of grant.

10. License Revenue

ARC License Agreement

On May 22, 2020, the Company entered into an exclusive license agreement with ARC Therapeutics, LLC (“ARC”), a company primarily owned by a related party, whereby the Company granted to ARC an exclusive, worldwide, royalty-bearing license, with the right to sublicense, solely to make, have made, use, sell, offer for sale, import, export, and commercialize products related to its cyclin dependent kinase 2 (“CDK2”) inhibitor compounds. At close, the Company received consideration in the form of an upfront payment of $1.0 million and an equity interest in ARC equal to 10% of its issued and outstanding units valued at $1.1 million. In addition, the Company may receive a future development milestone payment totaling $2.0 million and royalty payments in the mid-single digits based on net sales of the licensed compound after commercialization. The Company has right of first negotiation to re-acquire these assets.

The Company assessed the license agreement in accordance with ASC 606 and identified one performance obligation in the contract, which is the transfer of the license, as ARC can benefit from the license using its own resources. The Company recognized $2.1 million in license revenue consisting of the upfront payment and the 10% equity interest in ARC upon the effective date as the Company determined the license was a right to use the intellectual property and the Company had provided all necessary information to ARC to benefit from the license.

The Company considers the future potential development milestones and sales-based royalties to be variable consideration. The development milestone is excluded from the transaction price because it determined the payment to be fully constrained under ASC 606 due to the inherent uncertainty in the achievement of such milestone due to factors outside of the Company’s control. As sales-based royalties are all related to the license of the intellectual property, the Company will recognize revenue in the period when subsequent sales are made pursuant to the sales-based royalty exception. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Genor License Agreement

On June 15, 2020, the Company entered into an exclusive license agreement with Genor Biopharma Co. Inc. (“Genor”) for the development and commercialization of lerociclib in the Asia-Pacific region, excluding Japan (the “Genor Territory”). Under the license agreement, the Company granted to Genor an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to develop, obtain, hold and maintain regulatory approvals for, and commercialize lerociclib, in the Genor Territory.

Under the license agreement, Genor agreed to pay the Company a non-refundable, upfront cash payment of $6.0 million with the potential to pay an additional $40.0 million upon reaching certain development and commercial milestones. In addition, Genor will pay the Company tiered royalties ranging from high single to low double-digits based on annual net sales of lerociclib in the Genor Territory. The upfront cash payment was received in July 2020. In September 2020, the Company transferred to Genor the related technology and know-how that is necessary to develop, seek regulatory approval for, and commercialize lerociclib in the Genor Territory. Genor will be responsible for the development of the product in the Genor Territory and will be responsible, at its sole cost, for obtaining supply of lerociclib to meet its development, regulatory approval, and commercialization obligations under the agreement.

The Company assessed the license agreement in accordance with ASC 606 and identified the following promises under the contract: (i) to transfer the license, (ii) technology transfer and the transfer of related know-how to occur within 60 days of the effective date of the license agreement, and (iii) the sale and delivery of certain existing inventory specified in the agreement. The Company assessed the promised goods and services to determine if they are distinct. Based on this assessment, the Company determined that Genor cannot benefit from the license separate from the technology transfer and related know-how as they are highly interrelated and therefore not distinct. Accordingly, the transfer of the license and the related technology and know-how represent one combined performance obligation.

In accordance with ASC 606, the Company determined the transaction price at contract inception. The Company considers the future potential development and sales milestones, as well as the sales-based royalties to be variable consideration. The Company excluded the regulatory-based development and sales milestones from the transaction price because it determined such payments to be fully constrained under ASC 606 due to the inherent uncertainty in the achievement of such milestone payments and high susceptibility to factors outside our control. As the sales-based royalties are all related to the license of the intellectual property, the Company will recognize revenue in the period when subsequent sales are made pursuant to the sales-based royalty exception. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. Based on the foregoing, the Company determined that the $6.0 million non-refundable, upfront payment and the $0.6 million owed upon the delivery of existing inventory constituted the entirety of consideration to be included in the transaction price.

The Company then allocated the transaction price to the performance obligations based on the relative stand-alone selling price of each distinct obligation. The Company determined the stand-alone selling prices to equal the amounts paid for each performance obligation. Revenue is recognized for each performance obligation based at a point in time in which control has been transferred. The performance obligation for the transfer of the license and related technology and know-how does not occur until the delivery of the related know-how has been satisfied. This delivery occurred in September 2020 at which point $6.0 million was recognized as revenue. The delivery of existing inventory occurred in the fourth quarter of 2020 at which point $0.6 million was recognized as revenue.

EQRx License Agreement

On July 22, 2020, the Company entered into an exclusive license agreement with EQRx, Inc. (“EQRx”) for the development and commercialization of lerociclib in the U.S., Europe, Japan and all other global markets, excluding the Asia-Pacific region (except Japan) (the “EQRx Territory”). Under the license agreement, the Company granted to EQRx an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to develop, obtain, hold and maintain regulatory approvals for, and commercialize lerociclib in the EQRx Territory.

Under the license agreement, EQRx agreed to pay the Company a non-refundable, upfront cash payment of $20.0 million with the potential to pay an additional $290.0 million upon reaching certain development and commercial milestones. In addition, EQRx will pay the Company tiered royalties ranging from mid-single digits to mid-teens based on annual net sales of lerociclib in the EQRx Territory. The upfront cash payment was received in August 2020. In September 2020, the Company transferred to EQRx the related technology and know-how that is necessary to develop, seek regulatory approval for, and commercialize lerociclib in the EQRx Territory. EQRx will be responsible for the development of the product in the EQRx Territory. The Company will continue until completion, as the clinical trial sponsor, its two primary clinical trials at EQRx’s sole cost and expense. EQRx will reimburse the Company for all of its out-of-pocket costs incurred after the effective date of the license agreement in connection with these clinical trials. The Company will invoice EQRx within 30 days following the end of the quarter, and EQRx will pay within 30 days after its receipt of such invoice.

The Company assessed the license agreement in accordance with ASC 606 and identified the following promises under the contract: (i) to transfer the license, (ii) technology transfer and the transfer of related know-how to occur within 60 days of the effective date of the license agreement, (iii) the Company’s continuation as clinical trial sponsor for two primary clinical trials, and (iv) the sale and delivery of certain existing inventory specified in the agreement. The Company assessed the promised goods and services to determine if they are distinct. Based on this assessment, the Company determined that EQRx cannot benefit from the license separate from the technology transfer and related know-how as they are highly interrelated and therefore not distinct. Accordingly, the transfer of the license and the related technology and know-how represent one combined performance obligation.

In accordance with ASC 606, the Company determined the transaction price at contract inception. The Company considers the future potential development and sales milestones, as well as the sales-based royalties to be variable consideration. The Company excluded the regulatory-based development and sales milestones from the transaction price because it determined such payments to be fully constrained under ASC 606 due to the inherent uncertainty in the achievement of such milestone payments and high susceptibility to factors outside our control. As the sales-based royalties are all related to the license of the intellectual property, the Company will recognize revenue in the period when subsequent sales are made pursuant to the sales-based royalty exception. We concluded that the reimbursement of costs incurred for the two primary clinical trials qualifies for the practical expedient under ASC 606, which allows the Company to recognize revenue in the amount for which we have a right to invoice if our right to consideration is an amount that corresponds directly to the value of performance completed to date. We, therefore, will not allocate that transaction price to the performance obligations. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. Based on the foregoing, the Company determined that the $20.0 million non-refundable, upfront payment and the $0.7 million owed upon delivery of existing inventory constituted the entirety of consideration to be included in the transaction price.

The Company then allocated the transaction price to the performance obligations based on the relative stand-alone selling price of each distinct obligation. The Company determined the stand-alone selling prices to equal the amounts paid for each performance obligation. Revenue is recognized for the transfer of the license and the related technology and know-how and delivery of existing

inventory performance obligations based at a point in time in which control has been transferred. The performance obligation for the transfer of the license and the related technology and know-how does not occur until the delivery of the related technology and know-how has been satisfied. This delivery occurred in September 2020 at which point $20.0 million was recognized as revenue. Revenue is recognized for the reimbursement of costs associated with the two primary clinical trials based on the amount to be invoiced to EQRx for work completed from the effective date of the license agreement through December 31, 2020. During the twelve-months ended December 31, 2020, the Company recognized revenue of $1.3 million associated with this performance obligation, of which we have invoiced and received payment for $0.2 million. As of December 31, 2020, the remaining $1.1 million has not been invoiced and a contract asset for this amount was recognized on the balance sheet. The delivery of existing inventory occurred in the fourth quarter of 2020 at which point $0.7 million was recognized as revenue.

Simcere License Agreement

On August 3, 2020, the Company entered into an exclusive license agreement with Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd ("Simcere") for the development and commercialization of trilaciclib in all indications in Greater China (mainland China, Hong Kong, Macau, and Taiwan) (the "Simcere Territory"). Under the license agreement, the Company granted to Simcere an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to develop, obtain, hold and maintain regulatory approvals for, and commercialize trilaciclib in the Simcere Territory.

Under the license agreement, Simcere agreed to pay the Company a non-refundable, upfront cash payment of $14.0 million with the potential to pay an additional $156.0 million upon reaching certain development and commercial milestones. In addition, Simcere will pay the Company tiered low double-digit royalties on annual net sales of trilaciclib in the Simcere Territory. The upfront cash payment of $14.0 million (less applicable withholding taxes of $1.4 million) was received in September 2020. In return, the Company will furnish to Simcere the related technology and know-how that is necessary to develop, seek regulatory approval for, and commercialize trilaciclib in the Simcere Territory. Simcere will be responsible for all development and commercialization costs in its territory and may be able to participate in global clinical trials as agreed upon by the companies. No plans have currently been established for any combined participation in global clinical trials, however, each company will be responsible for the associated costs in their respective territories. The license agreement also provides for the companies to enter into a separate supply agreement which shall be entered into by the companies following the effective date of the license agreement. The supply agreement was executed in January 2021.

The Company assessed the license agreement in accordance with ASC 606 and identified the following promises under the contract: (i) to transfer the license, (ii) technology transfer and the transfer of related know-how to occur promptly following the effective date of the license agreement, (iii) participation in the joint steering committee ("JSC"), and (iv) participation in the joint development committee ("JDC"). The Company determined that Simcere cannot benefit from the license separate from the technology transfer and related technology and know-how as they are highly interrelated and therefore not distinct. Accordingly, the transfer of the license and the related technology and know-how were combined as a single performance obligation. The Company assessed the participation on the JSC and the JDC and concluded that the promises are immaterial in the context of the license agreement and therefore are excluded as performance obligations.

The Company assessed the supply agreement to determine whether it is a distinct performance obligation. The license agreement provides for the companies to enter into a supply agreement following the effective date of the license agreement. Simcere may notify the Company of its desire to manufacture, or have manufactured using a third-party CMO, supply of trilaciclib at which point the related manufacturing know-how will be transferred to Simcere at its sole cost and expense. Based on the foregoing, the supply agreement is considered an option and was assessed to determine whether a material right exists. The Company determined that the negotiated price for performing services under a supply agreement are at standalone selling prices, and as such these services would not be provided at a significant or incremental discount and is not considered a material right.

In accordance with ASC 606, the Company determined the transaction price at contract inception. The Company considers the future potential development and sales milestones, as well as the sales-based royalties to be variable consideration. The Company excluded the regulatory-based development and sales milestones from the transaction price because it determined such payments to be fully constrained under ASC 606 due to the inherent uncertainty in the achievement of such milestone payments and high susceptibility to factors outside our control. As the sales-based royalties are all related to the license of the intellectual property, the Company will recognize revenue in the period when subsequent sales are made pursuant to the sales-based royalty exception. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. Based on the foregoing, the Company determined that the $14.0 million non-refundable, upfront payment constituted the entirety of consideration to be included in the transaction price.

As there is one combined performance obligation, the Company allocated the entirety of the transaction price to the one performance obligation. Revenue is recognized based at a point in time in which control has been transferred. The performance obligation for the transfer of the license and related technology and know-how does not occur until the delivery of the related technology and know-how has been satisfied. This delivery occurred in December 2020 at which point $14.0 million was recognized as revenue.

11. Net Loss per Common Share

Basic net loss per common share is computed using the weighted average number of common shares outstanding during the period including nominal issuances of common stock warrants. Diluted net loss per common share is computed using the sum of the weighted average number of common shares outstanding during the period and, if dilutive, the weighted average number of potential shares of common stock, including the assumed exercise of stock options, stock warrants and unvested restricted common stock. For the years ended December 31, 2020, 2019 and 2018, the following potentially dilutive securities have been excluded from the computations of diluted weighted-average shares outstanding because the effect would be anti-dilutive:

	Year Ended December 31,		
	2020	2019	2018
Stock options issued and outstanding	6,576,688	5,443,730	4,318,731
	6,576,688	5,443,730	4,318,731

Amounts in the table above reflect the common stock equivalents of the noted instruments.

12. Income Taxes

Income taxes are accounted for using the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to temporary differences between the financial statements carrying amounts of assets and liabilities and their respective tax bases, operating loss carryforwards, and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

In accordance with FASB ASC 740, *Accounting for Income Taxes*, the Company reflects in the financial statements the benefit of positions taken in a previously filed tax return or expected to be taken in a future tax return only when it is considered ‘more-likely-than-not’ that the position taken will be sustained by a taxing authority. As of December 31, 2020 and 2019, the Company had no unrecognized income tax benefits and correspondingly there is no impact on the Company’s effective income tax rate associated with these items. The Company’s policy for recording interest and penalties relating to uncertain income tax positions is to record them as a component of income tax expense in the accompanying statements of operations. As of December 31, 2020 and 2019, the Company had no such accruals.

The components of income tax expense (benefit) attributable to continuing operations are as follows:

	Year ended December 31,		
	2020	2019	2018
Current Expense:			
Federal	$ —	$ —	$ —
State	—	—	—
Foreign	1,410	—	—
	1,410	—	—
Deferred Expense:			
Federal	—	—	—
State			
Foreign	—	—	—
	$ 1,410	$ —	$ —

The differences between the company's income tax expense attributable to continuing operations and the expense computed at the 21% U.S. statutory income tax rate were as follows (in thousands):

	Year ended December 31,		
	2020	2019	2018
Federal income tax benefit at statutory rate:	$ (20,547)	$ (25,714)	$ (17,910)
Increase (reduction) in income tax resulting from:			
State Income Taxes	(1,779)	(2,369)	(1,518)
Increase in Valuation Allowance	23,782	29,499	26,614
Write off Sec. 382 Limited Carryforwards	—	1,858	—
Stock Compensation	1,341	461	(3,011)
Research and Development Credit	(3,091)	(3,529)	(4,187)
Foreign Withholding Tax	1,410	—	—
Other	294	(206)	12
	$ 1,410	$ —	$ —

The tax effects of temporary differences and operating loss carryforwards that gave rise to significant portions of the deferred tax assets and deferred tax liabilities were as follows at December 31, 2020 and 2019 (in thousands):

	Year ended December 31,	
	2020	2019
Deferred tax assets		
Accrued expenses	$ 2,863	$ 2,205
Operating lease liabilities	2,034	2,348
Stock compensation	7,147	4,865
Capitalized patents and licenses	-	2,156
R&D credits	13,965	10,874
Net operating loss carryforwards	85,842	65,869
Other	20	6
Deferred tax assets	111,871	88,323
Deferred tax liabilities		
Operating lease assets	(1,844)	(2,263)
Other	(245)	(60)
Deferred tax liabilities	(2,089)	(2,323)
Valuation allowance	(109,782)	(86,000)
Net deferred tax assets	$ —	$ —

At December 31, 2020 and December 31, 2019, the Company evaluated all significant available positive and negative evidence, including the existence of losses in recent years and management's forecast of future taxable income, and, as a result, determined it was more likely than not that federal and state deferred tax assets, including benefits related to net operating loss carryforwards, would not be realized. The valuation allowance was increased from $86.0 million at December 31, 2019 to $109.8 million at December 31, 2020. The increase in valuation allowance was due primarily to the increase in net operating loss carryforwards and income tax credits.

The table below summarizes changes in the deferred tax valuation allowance (in thousands):

	2020	2019	2018
Balance at beginning of year	$ 86,000	$ 56,501	$ 29,887
Charges to costs and expenses	25,170	31,357	26,614
Write-offs	(1,388)	(1,858)	—
Balance at end of year	109,782	86,000	56,501

At December 31, 2020, the Company has federal net operating loss carryforwards ("NOLs") of approximately $373.1 million, which are available to offset future taxable income. Of the $373.1 million available, $95.4 million will begin to expire in 2029. The remaining $277.6 million has an indefinite carryforward period. Under the Tax Cuts and Jobs Act ("Tax Act"), federal NOLs arising

after December 31, 2017 may be carried forward indefinitely. However, for NOLs arising after December 31, 2017, NOL carryforwards will be limited to 80% of taxable income. The Company's NOLs generated in 2017 and in prior years will not be subject to the 80% limitation under the Tax Act. In addition, the Company has state net operating loss carryforwards totaling approximately $379.8 million, which are available to offset future state taxable income. State net operating losses begin to expire in 2024. Because the Company has incurred cumulative net operating losses since inception, all tax years remain open to examination by U.S. federal and state income tax authorities. As of December 31, 2020, the Company also had federal research and development (R&D) credit carryforwards of approximately $14.0 million available to offset future income tax which begin to expire in 2035.

In accordance with FASB ASC 740, *Accounting for Income Taxes*, the Company reflects in the financial statements the benefit of positions taken in a previously filed tax return or expected to be taken in a future tax return only when it is considered 'more-likely-than-not' that the position taken will be sustained by a taxing authority. As of December 31, 2020 and 2019, the Company had no unrecognized income tax benefits and correspondingly there is no impact on the Company's effective income tax rate associated with these items. The Company's policy for recording interest and penalties relating to uncertain income tax positions is to record them as a component of income tax expense in the accompanying statements of income. As of December 31, 2020 and 2019, the Company had no such accruals.

Section 382 Limitation

The Company's ability to utilize its net operating loss and research and development credit carryforwards may be substantially limited due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the Code), as well as similar state provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change," as defined by Section 382 of the Code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percent of the outstanding stock of a company by certain stockholders or public groups.

In April 2019, the Company completed an evaluation study as to whether an "ownership change" had occurred and determined that the limitation would be approximately $8.0 million on federal net operating loss carryforwards, $1.2 million on state net operating loss carryforwards, and $0.1 million on R&D tax credit carryforwards. The carryforward amounts reported above have already been reduced for these limitations. The Company continues to maintain a valuation allowance on the remaining NOLs as it believes that it is more likely than not that all of the deferred tax asset associated with the NOLs will not be realized regardless of whether an "ownership change" has occurred.

13. Related Party Transactions

The Company paid approximately $6 thousand to a member of the Board of Directors for scientific advisory services outside of his role on the board of directors for each of the years ended December 31, 2020, 2019 and 2018.

The Company granted an exclusive, worldwide, royalty-bearing license of its CDK2 inhibitor compounds to ARC Therapeutics, LLC ("ARC"), a company primarily owned by a related party, in exchange for cash and equity in ARC with a total value of approximately $2.1 million, which resulted in the recognition of related party revenue as discussed in Note 10.

The Company entered into a senior advisor agreement with John E. (Jack) Bailey, Jr., a member of the Board of Directors, effective October 1, 2020. Pursuant to the terms of the agreement, Mr. Bailey received $60,000 per month for his services through December 31, 2020. Mr. Bailey became the Company's President and Chief Executive Officer effective January 1, 2021.

The Company entered into a senior advisor agreement on September 29, 2020 with Mark A. Velleca, M.D., Ph.D., a member of the Board of Directors, with an effective date of January 1, 2021. Pursuant to the terms of the agreement, Dr. Velleca will receive $200,000 annually, paid in equal quarterly installments, for his services. The senior advisory agreement will expire on December 31, 2023.

14. Subsequent Events (Unaudited)

From January 14, 2021 through February 9, 2021, the Company utilized a Sales Agreement for "at the market offerings" with Cowen to sell 3,513,027 shares of common stock, resulting in $86.4 million in net proceeds. As of February 9, 2021, there is no remaining availability under the sales agreement with Cowen.

On February 23, 2021, the Board of Directors adopted the G1 Therapeutics, Inc. Inducement Equity Incentive Plan (the "Inducement Plan"), to be effective immediately, pursuant to which we reserved 500,000 shares of our common stock to be used exclusively for grants of awards (as defined below) to individuals who were not previously employees or directors of G1, or who are returning to employment following a *bona fide* period of non-employment with G1, in each case as an inducement material to the individual's entry into employment with G1 within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. In accordance with Rule 5635(c)(4), we did not seek approval of the Inducement Plan by our shareholders. An "award" is any right to receive shares of our

common stock or other property pursuant to the Inducement Plan, including non-statutory stock options and restricted stock unit awards. In addition, the Compensation Committee adopted forms of agreements for use with the Inducement Plan.

Complete copies of the Inducement Plan, along with the form of Stock Option Agreement under the Inducement Plan, and the form of Restricted Stock Unit Agreement under the Inducement Plan, is filed herewith as Exhibit [10.7], and is incorporated herein by reference. The above summary of the terms of the Inducement Plan and the forms of agreement does not purport to be complete and is qualified in its entirety by reference to such exhibits.

15. Quarterly Results of Operations (Unaudited)

The following table contains quarterly financial information for 2020 and 2019. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Three Months Ended (unaudited) (in thousands, except share and per share amounts)			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
License Revenue	$ -	$ 2,140	$ 26,599	$ 16,546
Total operating expenses	31,821	32,962	36,344	40,634
Loss from operations	(31,821)	(30,822)	(9,745)	(24,088)
Total other income (expense), net	798	(388)	(998)	(780)
Loss before income taxes	(31,023)	(31,210)	(10,743)	(24,868)
Income tax expense	—	—	931	479
Net loss	$ (31,023)	$ (31,210)	$ (11,674)	$ (25,347)
Net loss per share, basic and diluted	$ (0.82)	$ (0.83)	$ (0.31)	$ (0.67)
Weighted average common shares outstanding, basic and diluted	37,659,722	37,786,208	38,009,204	38,053,609

	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
License Revenue	$ -	$ -	$ -	$ -
Total operating expenses	25,881	32,583	34,024	36,553
Loss from operations	(25,881)	(32,583)	(34,024)	(36,553)
Total other income (expense), net	1,929	1,893	1,660	1,112
Loss before income taxes	(23,952)	(30,690)	(32,364)	(35,441)
Income tax expense	—	—	—	—
Net loss	$ (23,952)	$ (30,690)	$ (32,364)	$ (35,441)
Net loss per share, basic and diluted	$ (0.64)	$ (0.82)	$ (0.86)	$ (0.94)
Weighted average common shares outstanding, basic and diluted	37,396,980	37,470,926	37,540,380	37,586,218

Exhibit 4.2

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

General

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated by-laws are summaries of material terms and provisions and are qualified by reference to our amended and restated certificate of incorporation and amended and restated by-laws, copies of which have been filed with the SEC as exhibits to the registration statement of which this prospectus is a part.

Our authorized capital stock consists of 120,000,000 shares of common stock, par value $0.0001 per share, and 5,000,000 shares of preferred stock, par value $0.0001 per share, all of which are undesignated. Only share of our common stock are and no shares of preferred stock outstanding.

Common stock

We are authorized to issue one class of common stock. Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described under the "—Anti-Takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-Laws" section below, a majority vote of the holders of common stock is generally required to take action under our amended and restated certificate of incorporation and amended and restated by-laws.

Preferred stock

Our board of directors is authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. Our board of directors can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of restricting dividends on our common stock, diluting the voting power of our common stock, impairing the liquidation rights of our common stock, or delaying, deferring or preventing a

change in control of our company, which might harm the market price of our common stock. See also the "—Anti-Takeover Effects of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated By-Laws" section below.

Our board of directors will make any determination to issue such shares based on its judgment as to our company's best interests and the best interests of our stockholders. We have no shares of preferred stock outstanding.

Warrants

There are no warrants outstanding.

Anti-takeover effects of Delaware law, our amended and restated certificate of incorporation and our amended and restated by-laws

Our amended and restated certificate of incorporation and amended and restated by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies

In accordance with our amended and restated certificate of incorporation, our board of directors is divided into three classes serving three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board of directors, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

No written consent of stockholders

Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of stockholders

Our amended and restated by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements

Our amended and restated by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the amended and restated by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Amendment to by-laws and certificate of incorporation

As required by the Delaware General Corporation Law, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our amended and restated certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our amended and restated by-laws and amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated by-laws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares

entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Blank check preferred stock

Our amended and restated certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its amended and restated certificate of incorporation or by-laws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Exclusive jurisdiction of certain actions

Our amended and restated certificate of incorporation requires, to the fullest extent permitted by law, that derivative actions brought in our name, actions against our directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

Nasdaq Global Select Market Listing

Our common stock is listed on The Nasdaq Global Select Market under the trading symbol "GTHX."

G1 THERAPEUTICS, INC.

2021 INDUCEMENT EQUITY INCENTIVE PLAN

1. DEFINITIONS.

Unless otherwise specified or unless the context otherwise requires, the following terms, as used in this G1 Therapeutics, Inc. 2021 Inducement Equity Incentive Plan, have the following meanings:

Administrator means the Board of Directors, unless it has delegated power to act on its behalf to the Committee, in which case the term "Administrator" means the Committee.

Affiliate means a corporation which, for purposes of Section 424 of the Code, is a parent or subsidiary of the Company, direct or indirect.

Agreement means an agreement between the Company and a Participant pertaining to a Stock Right delivered pursuant to the Plan in such form as the Administrator shall approve.

Board of Directors means the Board of Directors of the Company.

Cause means, with respect to a Participant (a) dishonesty with respect to the Company or any Affiliate, (b) insubordination, substantial malfeasance or non-feasance of duty, (c) unauthorized disclosure of confidential information, (d) breach by a Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or similar agreement between the Participant and the Company or any Affiliate, and (e) conduct substantially prejudicial to the business of the Company or any Affiliate; provided, however, that any provision in an agreement between a Participant and the Company or an Affiliate, which contains a conflicting definition of Cause for termination and which is in effect at the time of such termination, shall supersede this definition with respect to that Participant. The determination of the Administrator as to the existence of Cause will be conclusive on the Participant and the Company.

Code means the United States Internal Revenue Code of 1986, as amended including any successor statute, regulation and guidance thereto.

Committee means the committee of the Board of Directors, if any, to which the Board of Directors has delegated power to act under or pursuant to the provisions of the Plan, the composition of which shall at all times satisfy the provisions of Section 162(m) of the Code.

Common Stock means shares of the Company's common stock, $0.0001 par value per share.

Company means G1 Therapeutics, Inc., a Delaware corporation.

Director means any member of the Board of Directors.

Disability or Disabled means permanent and total disability as defined in Section 22(e)(3) of the Code.

Employee means any employee of the Company or of an Affiliate (including, without limitation, an employee who is also serving as an officer or director of the Company or of an Affiliate), designated by the Administrator to be eligible to be granted one or more Stock Rights under the Plan.

Exchange Act means the United States Securities Exchange Act of 1934, as amended.

Fair Market Value of a Share of Common Stock means:

(1) If the Common Stock is listed on a national securities exchange or traded in the over-the-counter market and sales prices are regularly reported for the Common Stock, the closing or, if not applicable, the last price of the Common Stock on the composite tape or other comparable reporting system for the trading day on the applicable date and if such applicable date is not a trading day, the last market trading day prior to such date;

(2) If the Common Stock is not traded on a national securities exchange but is traded on the over-the-counter market, if sales prices are not regularly reported for the Common Stock for the trading day referred to in clause (1), and if bid and asked prices for the Common Stock are regularly reported, the mean between the bid and the asked price for the Common Stock at the close of trading in the over-the-counter market for the trading day on which Common Stock was traded on the applicable date and if such applicable date is not a trading day, the last market trading day prior to such date; and

(3) If the Common Stock is neither listed on a national securities exchange nor traded in the over-the-counter market, such value as the Administrator, in good faith, shall determine in compliance with applicable laws.

Non-Qualified Option means an option which is not intended to qualify as an incentive stock option under Section 422 of the Code.

Option means a Non-Qualified Option granted under the Plan.

Participant means an Employee or a Director to whom one or more Stock Rights are granted under the Plan. As used herein, “Participant” shall include the Participant’s “Survivors” where the context requires.

Plan means this G1 Therapeutics, Inc. 2021 Inducement Equity Incentive Plan.

Securities Act means the United States Securities Act of 1933, as amended.

Shares means shares of the Common Stock as to which Stock Rights have been or may be granted under the Plan or any shares of capital stock into which the Shares are changed or for which they are exchanged within the provisions of Paragraph 3 of the Plan. The Shares issued under the Plan may be authorized and unissued shares or shares held by the Company in its treasury, or both.

Stock-Based Award means a grant by the Company under the Plan of an equity award or an equity based award which is not an Option or a Stock Grant.

Stock Grant means a grant by the Company of Shares under the Plan.

Stock Right means a right to Shares or the value of Shares of the Company granted pursuant to the Plan, in the form of a Non-Qualified Option, a Stock Grant or a Stock-Based Award.

Survivor means a deceased Participant's legal representatives and/or any person or persons who acquired the Participant's rights to a Stock Right by will or by the laws of descent and distribution.

2. PURPOSES OF THE PLAN.

The Plan is intended to encourage ownership of Shares by Employees and Directors of the Company in order to attract and retain such people, to induce them to work for the benefit of the Company or of an Affiliate and to provide additional incentive for them to promote the success of the Company or of an Affiliate. The Company intends that the Plan be reserved for persons to whom the Company may issue securities without stockholder approval as an inducement pursuant to Listing Rule 5635(c)(4) of the corporate governance rules of the Nasdaq Stock Market. The Plan provides for the granting and awarding of Non-Qualified Options, Stock Grants and Stock-Based Awards.

3. SHARES SUBJECT TO THE PLAN.

(a) The number of Shares which may be issued from time to time pursuant to this Plan shall be Five Hundred Thousand (500,000) or the equivalent of such number of Shares after the Administrator, in its sole discretion, has interpreted the effect of any stock split, stock dividend, combination, recapitalization or similar transaction in accordance with Paragraph 24 of this Plan.

(b) If an Option ceases to be "outstanding," in whole or in part (other than by exercise), or if the Company shall reacquire (at not more than its original issuance price) any Shares issued pursuant to a Stock Grant or Stock-Based Award, or if any Stock Right expires or is forfeited, cancelled, or otherwise terminated or results in any Shares not being issued, the unissued or reacquired Shares which were subject to such Stock Right shall again be available for issuance from time to time pursuant to this Plan. Notwithstanding the foregoing, if a Stock Right is exercised, in whole or in part, by tender of Shares or if the Company or an Affiliate's tax withholding obligation is satisfied by withholding Shares, the number of Shares deemed to have

been issued under the Plan for purposes of the limitation set forth in Paragraph 3(a) above shall be the number of Shares that were subject to the Stock Right or portion thereof, and not the net number of Shares actually issued.

4. ADMINISTRATION OF THE PLAN.

The Administrator of the Plan will be the Board of Directors, except to the extent the Board of Directors delegates its authority to the Committee, in which case the Committee shall be the Administrator. Subject to the provisions of the Plan, the Administrator is authorized to:

(a) Interpret the provisions of the Plan and all Stock Rights and to make all rules and determinations which it deems necessary or advisable for the administration of the Plan;

(b) Determine which Employees and Directors shall be granted Stock Rights;

(c) Determine the number of Shares for which a Stock Right or Stock Rights shall be granted;

(d) Specify the terms and conditions upon which a Stock Right or Stock Rights may be granted;

(e) Amend any term or condition of any outstanding Stock Right, other than reducing the exercise price or purchase price or extending the expiration date of an Option, provided that (i) such term or condition as amended is not prohibited by the Plan; (ii) any such amendment shall not impair the rights of a Participant under any Stock Right previously granted without such Participant's consent or in the event of death of the Participant the Participant's Survivors; and (iii) any such amendment shall be made only after the Administrator determines whether such amendment would cause any adverse tax consequences to the Participant, including, but not limited to, pursuant to Section 409A of the Code;

(f) Buy out for a payment in cash or Shares, a Stock Right previously granted, awarded and/or cancel any such Stock Right and grant in substitution therefor other Stock Rights, covering the same or a different number of Shares and having an exercise price or purchase price per share which may be lower or higher than the exercise price or purchase price of the cancelled Stock Right, based on such terms and conditions as the Administrator shall establish and the Participant shall accept; and

(g) Adopt any sub-plans applicable to residents of any specified jurisdiction as it deems necessary or appropriate in order to comply with or take advantage of any tax or other laws applicable to the Company, any Affiliate or to Participants or to otherwise facilitate the administration of the Plan, which sub-plans may include additional restrictions or conditions applicable to Stock Rights or Shares issuable pursuant to a Stock Right;

provided, however, that all such interpretations, rules, determinations, terms and conditions shall be made and prescribed in the context of not causing any adverse tax consequences under Section 409A of the Code. Subject to the foregoing, the interpretation and construction by the Administrator of any provisions of the Plan or of any Stock Right granted under it shall be final, unless otherwise determined by the Board of Directors, if the Administrator is the Committee. In

addition, if the Administrator is the Committee, the Board of Directors may take any action under the Plan that would otherwise be the responsibility of the Committee.

To the extent permitted under applicable law, the Board of Directors or the Committee may allocate all or any portion of its responsibilities and powers to any one or more of its members and may delegate all or any portion of its responsibilities and powers to any other person selected by it. The Board of Directors or the Committee may revoke any such allocation or delegation at any time. Notwithstanding the foregoing, only the Board of Directors or the Committee shall be authorized to grant a Stock Right to any Director or to any "officer" of the Company as defined by Rule 16a-1 under the Exchange Act.

5. ELIGIBILITY FOR PARTICIPATION.

The Administrator will, in its sole discretion, name the Participants in the Plan; provided, however, that each Participant must be an Employee or a Director at the time a Stock Right is granted and a person to whom the Company may issue securities without stockholder approval as an inducement pursuant to Listing Rule 5635(c)(4) of the corporate governance rules of the Nasdaq Stock Market. Notwithstanding the foregoing, the Administrator may authorize the grant of a Stock Right to a person not then an Employee or a Director; provided, however, that the actual grant of such Stock Right shall be conditioned upon such person becoming eligible to become a Participant at or prior to the time of the execution of the Agreement evidencing such Stock Right. Non-Qualified Options, Stock Grants and Stock-Based Awards may be granted to any Employee or any Director. The granting of any Stock Right to any individual shall neither entitle that individual to, nor disqualify him or her from, participation in any other grant of Stock Rights or any grant under any other benefit plan established by the Company or any Affiliate for Employees or Directors.

6. TERMS AND CONDITIONS OF OPTIONS.

Each Option shall be set forth in writing in an Option Agreement, duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Administrator may provide that Options be granted subject to such terms and conditions, consistent with the terms and conditions specifically required under this Plan, as the Administrator may deem appropriate. The Option Agreements shall be subject to at least the following terms and conditions:

(a) Each Non-Qualified Option shall be subject to the terms and conditions which the Administrator determines to be appropriate and in the best interest of the Company, subject to the following minimum standards for any such Non-Qualified Option:

(i) Exercise Price: Each Option Agreement shall state the exercise price (per share) of the Shares covered by each Option, which exercise price shall be determined by the Administrator and shall be at least equal to the Fair Market Value per share of Common Stock on the date of grant of the Option.

(ii) Number of Shares: Each Option Agreement shall state the number of Shares to which it pertains.

(iii) Vesting: Each Option Agreement shall state the date or dates on which it first is exercisable and the date after which it may no longer be exercised, and may provide that the Option rights accrue or become exercisable in installments over a period of months or years, or upon the occurrence of certain performance conditions or the attainment of stated goals or events.

(iv) Additional Conditions: Exercise of any Option may be conditioned upon the Participant's execution of a Share purchase agreement in a form satisfactory to the Administrator providing for certain protections for the Company and its other shareholders, including requirements that:

A. The Participant's or the Participant's Survivors' right to sell or transfer the Shares may be restricted; and

B. The Participant or the Participant's Survivors may be required to execute letters of investment intent and must also acknowledge that the Shares will bear legends noting any applicable restrictions.

(v) Term of Option: Each Option shall terminate not more than ten years from the date of the grant or at such earlier time as the Option Agreement may provide.

7. TERMS AND CONDITIONS OF STOCK GRANTS.

Each Stock Grant to a Participant shall state the principal terms in an Agreement duly executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Agreement shall be in a form approved by the Administrator and shall contain terms and conditions which the Administrator determines to be appropriate and in the best interest of the Company, subject to the following minimum standards:

(a) Each Agreement shall state the purchase price per share, if any, of the Shares covered by each Stock Grant, which purchase price shall be determined by the Administrator but shall not be less than the minimum consideration required by the Delaware General Corporation Law, if any, on the date of the grant of the Stock Grant;

(b) Each Agreement shall state the number of Shares to which the Stock Grant pertains; and

(c) Each Agreement shall include the terms of any right of the Company to restrict or reacquire the Shares subject to the Stock Grant.

8. TERMS AND CONDITIONS OF OTHER STOCK-BASED AWARDS.

The Administrator shall have the right to grant other Stock-Based Awards based upon the Common Stock having such terms and conditions as the Administrator may determine, including, without limitation, the grant of Shares based upon certain conditions, the grant of securities convertible into Shares and the grant of stock appreciation rights, phantom stock awards or stock units. The principal terms of each Stock-Based Award shall be set forth in an Agreement, duly

executed by the Company and, to the extent required by law or requested by the Company, by the Participant. The Agreement shall be in a form approved by the Administrator and shall contain terms and conditions which the Administrator determines to be appropriate and in the best interest of the Company. Each Agreement shall include the terms of any right of the Company including the right to terminate the Stock-Based Award without the issuance of Shares, the terms of any vesting conditions or events upon which Shares shall be issued. Under no circumstances may the Agreement covering stock appreciation rights (a) have an exercise price (per share) that is less than the Fair Market Value per share of Common Stock on the date of grant or (b) expire more than ten years following the date of grant.

The Company intends that the Plan and any Stock-Based Awards granted hereunder be exempt from the application of Section 409A of the Code or meet the requirements of paragraphs (2), (3) and (4) of subsection (a) of Section 409A of the Code, to the extent applicable, and be operated in accordance with Section 409A so that any compensation deferred under any Stock-Based Award (and applicable investment earnings) shall not be included in income under Section 409A of the Code. Any ambiguities in the Plan shall be construed to effect the intent as described in this Paragraph 8.

9. EXERCISE OF OPTIONS AND ISSUE OF SHARES.

An Option (or any part or installment thereof) shall be exercised by giving written notice to the Company or its designee (in a form acceptable to the Administrator, which may include electronic notice), together with provision for payment of the aggregate exercise price in accordance with this Paragraph for the Shares as to which the Option is being exercised, and upon compliance with any other condition(s) set forth in the Option Agreement. Such notice shall be signed by the person exercising the Option (which signature may be provided electronically in a form acceptable to the Administrator), shall state the number of Shares with respect to which the Option is being exercised and shall contain any representation required by the Plan or the Option Agreement. Payment of the exercise price for the Shares as to which such Option is being exercised shall be made (a) in United States dollars in cash or by check; or (b) at the discretion of the Administrator, through delivery of shares of Common Stock held for at least six months (if required to avoid negative accounting treatment) having a Fair Market Value equal as of the date of the exercise to the aggregate cash exercise price for the number of Shares as to which the Option is being exercised; or (c) at the discretion of the Administrator, by having the Company retain from the Shares otherwise issuable upon exercise of the Option, a number of Shares having a Fair Market Value equal as of the date of exercise to the aggregate exercise price for the number of Shares as to which the Option is being exercised; or (d) at the discretion of the Administrator, in accordance with a cashless exercise program established with a securities brokerage firm, and approved by the Administrator; or (e) at the discretion of the Administrator, by any combination of (a), (b), (c) and (d) above; or (f) at the discretion of the Administrator, by payment of such other lawful consideration as the Administrator may determine.

The Company shall then reasonably promptly deliver the Shares as to which such Option was exercised to the Participant (or to the Participant's Survivors, as the case may be). In determining what constitutes "reasonably promptly," it is expressly understood that the issuance and delivery of the Shares may be delayed by the Company in order to comply with any law or regulation (including, without limitation, state securities or "blue sky" laws) which requires the

Company to take any action with respect to the Shares prior to their issuance. The Shares shall, upon delivery, be fully paid, non-assessable Shares.

10. PAYMENT IN CONNECTION WITH THE ISSUANCE OF STOCK GRANTS AND STOCK-BASED AWARDS AND ISSUE OF SHARES.

Any Stock Grant or Stock-Based Award requiring payment of a purchase price for the Shares as to which such Stock Grant or Stock-Based Award is being granted shall be made (a) in United States dollars in cash or by check; or (b) at the discretion of the Administrator, through delivery of shares of Common Stock held for at least six months (if required to avoid negative accounting treatment) and having a Fair Market Value equal as of the date of payment to the purchase price of the Stock Grant or Stock-Based Award; or (c) at the discretion of the Administrator, by any combination of (a) and (b) above; or (d) at the discretion of the Administrator, by payment of such other lawful consideration as the Administrator may determine.

The Company shall, when required by the applicable Agreement, reasonably promptly deliver the Shares as to which such Stock Grant or Stock-Based Award was made to the Participant (or to the Participant's Survivors, as the case may be), subject to any escrow provision set forth in the applicable Agreement. In determining what constitutes "reasonably promptly," it is expressly understood that the issuance and delivery of the Shares may be delayed by the Company in order to comply with any law or regulation (including, without limitation, state securities or "blue sky" laws) which requires the Company to take any action with respect to the Shares prior to their issuance.

11. RIGHTS AS A SHAREHOLDER.

No Participant to whom a Stock Right has been granted shall have rights as a shareholder with respect to any Shares covered by such Stock Right except after due exercise of an Option or issuance of Shares as set forth in any Agreement, tender of the aggregate exercise or purchase price, if any, for the Shares being purchased and registration of the Shares in the Company's share register in the name of the Participant.

12. ASSIGNABILITY AND TRANSFERABILITY OF STOCK RIGHTS.

By its terms, a Stock Right granted to a Participant shall not be transferable by the Participant other than (i) by will or by the laws of descent and distribution, or (ii) as approved by the Administrator in its discretion and set forth in the applicable Agreement provided that no Stock Right may be transferred by a Participant for value. The designation of a beneficiary of a Stock Right by a Participant, with the prior approval of the Administrator and in such form as the Administrator shall prescribe, shall not be deemed a transfer prohibited by this Paragraph. Except as provided above during the Participant's lifetime a Stock Right shall only be exercisable by or issued to such Participant (or his or her legal representative) and shall not be assigned, pledged or hypothecated in any way (whether by operation of law or otherwise) and shall not be subject to execution, attachment or similar process. Any attempted transfer, assignment, pledge, hypothecation or other disposition of any Stock Right or of any rights granted thereunder contrary to the provisions of this Plan, or the levy of any attachment or similar process upon a Stock Right, shall be null and void.

13. EFFECT ON OPTIONS OF TERMINATION OF SERVICE OTHER THAN FOR CAUSE OR DEATH OR DISABILITY.

Except as otherwise provided in a Participant's Option Agreement, in the event of a termination of service (whether as an Employee or Director) with the Company or an Affiliate before the Participant has exercised an Option, the following rules apply:

(a) A Participant who ceases to be an Employee or a Director (for any reason other than termination for Cause, Disability, or death for which events there are special rules in Paragraphs 14, 15 and 16, respectively), may exercise any Option granted to him or her to the extent that the Option is exercisable on the date of such termination of service, but only within such term as the Administrator has designated in a Participant's Option Agreement.

(b) The provisions of this Paragraph, and not the provisions of Paragraph 15 or 16, shall apply to a Participant who subsequently becomes Disabled or dies after the termination of employment or director status; provided, however, in the case of a Participant's Disability or death within three months after the termination of employment or director status, the Participant or the Participant's Survivors may exercise the Option within one year after the date of the Participant's termination of service, but in no event after the date of expiration of the term of the Option.

(c) Notwithstanding anything herein to the contrary, if subsequent to a Participant's termination, but prior to the exercise of an Option, the Administrator determines that, either prior or subsequent to the Participant's termination, the Participant engaged in conduct which would constitute Cause, then such Participant shall forthwith cease to have any right to exercise any Option.

(d) A Participant to whom an Option has been granted under the Plan who is absent from the Company or an Affiliate because of temporary disability (any disability other than a Disability as defined in Paragraph 1 hereof), or who is on leave of absence for any purpose, shall not, during the period of any such absence, be deemed, by virtue of such absence alone, to have terminated such Participant's employment or director status with the Company or with an Affiliate, except as the Administrator may otherwise expressly provide.

(e) Except as required by law or as set forth in a Participant's Option Agreement, Options granted under the Plan shall not be affected by any change of a Participant's status within or among the Company and any Affiliates, so long as the Participant continues to be an Employee or Director.

14. EFFECT ON OPTIONS OF TERMINATION OF SERVICE FOR CAUSE.

Except as otherwise provided in a Participant's Option Agreement, the following rules apply if the Participant's service (whether as an Employee or Director) with the Company or an Affiliate is terminated for Cause prior to the time that all his or her outstanding Options have been exercised:

(a) All outstanding and unexercised Options as of the time the Participant is notified his or her service is terminated for Cause will immediately be forfeited.

(b) Cause is not limited to events which have occurred prior to a Participant's termination of service, nor is it necessary that the Administrator's finding of Cause occur prior to termination. If the Administrator determines, subsequent to a Participant's termination of service but prior to the exercise of an Option, that either prior or subsequent to the Participant's termination the Participant engaged in conduct which would constitute Cause, then the right to exercise any Option is forfeited.

15. EFFECT ON OPTIONS OF TERMINATION OF SERVICE FOR DISABILITY.

Except as otherwise provided in a Participant's Option Agreement:

(a) A Participant who ceases to be an Employee or Director by reason of Disability may exercise any Option granted to such Participant to the extent that the Option has become exercisable but has not been exercised on the date of the Participant's termination of service due to Disability;

(b) In the event rights to exercise the Option accrue periodically, a Disabled Participant may exercise any Option granted to such Participant to the extent of a pro rata portion through the date of the Participant's termination of service due to Disability of any additional vesting rights that would have accrued on the next vesting date had the Participant not become Disabled. The proration shall be based upon the number of days accrued in the current vesting period prior to the date of the Participant's termination of service due to Disability;

(c) A Disabled Participant may exercise the Option only within the period ending one year after the date of the Participant's termination of service due to Disability, notwithstanding that the Participant might have been able to exercise the Option as to some or all of the Shares on a later date if the Participant had not been terminated due to Disability and had continued to be an Employee, Director or, if earlier, within the originally prescribed term of the Option; and

(d) The Administrator shall make the determination both of whether Disability has occurred and the date of its occurrence (unless a procedure for such determination is set forth in another agreement between the Company and such Participant, in which case such procedure shall be used for such determination). If requested, the Participant shall be examined by a physician selected or approved by the Administrator, the cost of which examination shall be paid for by the Company.

16. EFFECT ON OPTIONS OF DEATH WHILE AN EMPLOYEE OR DIRECTOR.

Except as otherwise provided in a Participant's Option Agreement:

(a) In the event of the death of a Participant while the Participant is an Employee or Director, such Option may be exercised by the Participant's Survivors to the extent that the Option has become exercisable but has not been exercised on the date of death;

(b) In the event rights to exercise the Option accrue periodically, a deceased Participant's Survivors may exercise any Option granted to such Participant to the extent of a pro rata portion through the date of death of any additional vesting rights that would have accrued on the next vesting date had the Participant not died. The proration shall be based upon the number of days accrued in the current vesting period prior to the Participant's date of death; and

(c) If the Participant's Survivors wish to exercise the Option, they must take all necessary steps to exercise the Option within one year after the date of death of such Participant, notwithstanding that the decedent might have been able to exercise the Option as to some or all of the Shares on a later date if he or she had not died and had continued to be an Employee or Director or, if earlier, within the originally prescribed term of the Option.

17. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF TERMINATION OF SERVICE.

In the event of a termination of service (whether as an Employee or Director) with the Company or an Affiliate for any reason before the Participant has accepted a Stock Grant or a Stock-Based Award and paid the purchase price, if required, such grant shall terminate.

For purposes of this Paragraph 17 and Paragraph 18 below, a Participant to whom a Stock Grant or a Stock-Based Award has been issued under the Plan who is absent from work with the Company or with an Affiliate because of temporary disability (any disability other than a Disability as defined in Paragraph 1 hereof), or who is on leave of absence for any purpose, shall not, during the period of any such absence, be deemed, by virtue of such absence alone, to have terminated such Participant's employment or director status with the Company or with an Affiliate, except as the Administrator may otherwise expressly provide.

In addition, for purposes of this Paragraph 17 and Paragraph 18 below, any change of employment or other service within or among the Company and any Affiliates shall not be treated as a termination of employment or director status so long as the Participant continues to be an Employee or Director.

18. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF TERMINATION OF SERVICE OTHER THAN FOR CAUSE, DEATH OR DISABILITY.

Except as otherwise provided in a Participant's Agreement, in the event of a termination of service for any reason (whether as an Employee or Director), other than termination for Cause, death or Disability for which there are special rules in Paragraphs 19, 20 and 21 below, before all forfeiture provisions or Company rights of repurchase shall have lapsed, then the Company shall

have the right to cancel or repurchase that number of Shares subject to a Stock Grant or Stock-Based Award as to which the Company's forfeiture or repurchase rights have not lapsed.

19. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF TERMINATION OF SERVICE FOR CAUSE.

Except as otherwise provided in a Participant's Agreement, the following rules apply if the Participant's service (whether as an Employee or Director) with the Company or an Affiliate is terminated for Cause:

(a) All Shares subject to any Stock Grant or Stock-Based Award that remain subject to forfeiture provisions or as to which the Company shall have a repurchase right shall be immediately forfeited to the Company as of the time the Participant is notified his or her service is terminated for Cause.

(b) Cause is not limited to events which have occurred prior to a Participant's termination of service, nor is it necessary that the Administrator's finding of Cause occur prior to termination. If the Administrator determines, subsequent to a Participant's termination of service, that either prior or subsequent to the Participant's termination the Participant engaged in conduct which would constitute Cause, then all Shares subject to any Stock Grant or Stock-Based Award that remained subject to forfeiture provisions or as to which the Company had a repurchase right on the date of termination shall be immediately forfeited to the Company.

20. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF TERMINATION OF SERVICE FOR DISABILITY.

Except as otherwise provided in a Participant's Agreement, the following rules apply if a Participant ceases to be an Employee or Director by reason of Disability: to the extent the forfeiture provisions or the Company's rights of repurchase have not lapsed on the date of Disability, they shall be exercisable; provided, however, that in the event such forfeiture provisions or rights of repurchase lapse periodically, such provisions or rights shall lapse to the extent of a pro rata portion of the Shares subject to such Stock Grant or Stock-Based Award through the date of Disability as would have lapsed had the Participant not become Disabled. The proration shall be based upon the number of days accrued prior to the date of Disability.

The Administrator shall make the determination both as to whether Disability has occurred and the date of its occurrence (unless a procedure for such determination is set forth in another agreement between the Company and such Participant, in which case such procedure shall be used for such determination). If requested, the Participant shall be examined by a physician selected or approved by the Administrator, the cost of which examination shall be paid for by the Company.

21. EFFECT ON STOCK GRANTS AND STOCK-BASED AWARDS OF DEATH WHILE AN EMPLOYEE OR DIRECTOR.

Except as otherwise provided in a Participant's Agreement, the following rules apply in the event of the death of a Participant while the Participant is an Employee or Director: to the extent the forfeiture provisions or the Company's rights of repurchase have not lapsed on the date of death, they shall be exercisable; provided, however, that in the event such forfeiture provisions

or rights of repurchase lapse periodically, such provisions or rights shall lapse to the extent of a pro rata portion of the Shares subject to such Stock Grant or Stock-Based Award through the date of death as would have lapsed had the Participant not died. The proration shall be based upon the number of days accrued prior to the Participant's date of death.

22. PURCHASE FOR INVESTMENT.

Unless the offering and sale of the Shares shall have been effectively registered under the Securities Act, the Company shall be under no obligation to issue Shares under the Plan unless and until the following conditions have been fulfilled:

(a) The person who receives a Stock Right shall warrant to the Company, prior to the receipt of Shares, that such person is acquiring such Shares for his or her own account, for investment, and not with a view to, or for sale in connection with, the distribution of any such Shares, in which event the person acquiring such Shares shall be bound by the provisions of the following legend (or a legend in substantially similar form) which shall be endorsed upon the certificate evidencing the Shares issued pursuant to such exercise or such grant:

> "The shares represented by this certificate have been taken for investment and they may not be sold or otherwise transferred by any person, including a pledgee, unless (1) either (a) a Registration Statement with respect to such shares shall be effective under the Securities Act of 1933, as amended, or (b) the Company shall have received an opinion of counsel satisfactory to it that an exemption from registration under such Act is then available, and (2) there shall have been compliance with all applicable state securities laws."

(b) At the discretion of the Administrator, the Company shall have received an opinion of its counsel that the Shares may be issued in compliance with the Securities Act without registration thereunder.

23. DISSOLUTION OR LIQUIDATION OF THE COMPANY.

Upon the dissolution or liquidation of the Company, all Options granted under this Plan which as of such date shall not have been exercised and all Stock Grants and Stock-Based Awards which have not been accepted, to the extent required under the applicable Agreement, will terminate and become null and void; provided, however, that if the rights of a Participant or a Participant's Survivors have not otherwise terminated and expired, the Participant or the Participant's Survivors will have the right immediately prior to such dissolution or liquidation to exercise or accept any Stock Right to the extent that the Stock Right is exercisable or subject to acceptance as of the date immediately prior to such dissolution or liquidation. Upon the dissolution or liquidation of the Company, any outstanding Stock-Based Awards shall immediately terminate unless otherwise determined by the Administrator or specifically provided in the applicable Agreement.

24. ADJUSTMENTS.

Upon the occurrence of any of the following events, a Participant's rights with respect to any Stock Right granted to him or her hereunder shall be adjusted as hereinafter provided, unless otherwise specifically provided in a Participant's Agreement:

(a) Stock Dividends and Stock Splits. If (i) the shares of Common Stock shall be subdivided or combined into a greater or smaller number of shares or if the Company shall issue any shares of Common Stock as a stock dividend on its outstanding Common Stock, or (ii) additional shares or new or different shares or other securities of the Company or other non-cash assets are distributed with respect to such shares of Common Stock, each Stock Right and the number of shares of Common Stock deliverable thereunder shall be appropriately increased or decreased proportionately, and appropriate adjustments shall be made including, in the exercise or purchase price per share, to reflect such events. The number of Shares subject to the limitations in Paragraphs 3(a) shall also be proportionately adjusted upon the occurrence of such events.

(b) Corporate Transactions. If the Company is to be consolidated with or acquired by another entity in a merger, consolidation, sale of all or substantially all of the Company's assets or the acquisition of all of the outstanding voting stock of the Company in a single transaction or a series of related transactions by a single entity other than a transaction to merely change the state of incorporation (a "Corporate Transaction"), the Administrator or the board of directors of any entity assuming the obligations of the Company hereunder (the "Successor Board"), shall, as to outstanding Options, either (i) make appropriate provision for the continuation of such Options by substituting on an equitable basis for the Shares then subject to such Options either the consideration payable with respect to the outstanding shares of Common Stock in connection with the Corporate Transaction or securities of any successor or acquiring entity; or (ii) upon written notice to the Participants, provide that such Options must be exercised (either (A) to the extent then exercisable or, (B) at the discretion of the Administrator, any such Options being made partially or fully exercisable for purposes of this Subparagraph), within a specified number of days of the date of such notice, at the end of which period such Options which have not been exercised shall terminate; or (iii) terminate such Options in exchange for payment of an amount equal to the consideration payable upon consummation of such Corporate Transaction to a holder of the number of shares of Common Stock into which such Option would have been exercisable (either (A) to the extent then exercisable or, (B) at the discretion of the Administrator, any such Options being made partially or fully exercisable for purposes of this Subparagraph) less the aggregate exercise price thereof. For purposes of determining the payments to be made pursuant to subsection (iii) above, in the case of a Corporate Transaction the consideration for which, in whole or in part, is other than cash, the consideration other than cash shall be valued at the fair value thereof as determined in good faith by the Board of Directors.

With respect to outstanding Stock Grants, the Administrator or the Successor Board, shall make appropriate provision for the continuation of such Stock Grants on the same terms and conditions by substituting on an equitable basis for the Shares then subject to such Stock Grants either the consideration payable with respect to the outstanding Shares of Common Stock in connection with the Corporate Transaction or securities of any successor or acquiring entity. In lieu of the foregoing, in connection with any Corporate Transaction, the Administrator may provide that, upon consummation of the Corporate Transaction, each outstanding Stock Grant shall

be terminated in exchange for payment of an amount equal to the consideration payable upon consummation of such Corporate Transaction to a holder of the number of shares of Common Stock comprising such Stock Grant (to the extent such Stock Grant is no longer subject to any forfeiture or repurchase rights then in effect or, at the discretion of the Administrator, all forfeiture and repurchase rights being waived upon such Corporate Transaction).

In taking any of the actions permitted under this Paragraph 24(b), the Administrator shall not be obligated by the Plan to treat all Stock Rights, all Stock Rights held by a Participant, or all Stock Rights of the same type, identically.

(c) Recapitalization or Reorganization. In the event of a recapitalization or reorganization of the Company other than a Corporate Transaction pursuant to which securities of the Company or of another corporation are issued with respect to the outstanding shares of Common Stock, a Participant upon exercising an Option or accepting a Stock Grant after the recapitalization or reorganization shall be entitled to receive for the price paid upon such exercise or acceptance if any, the number of replacement securities which would have been received if such Option had been exercised or Stock Grant accepted prior to such recapitalization or reorganization.

(d) Adjustments to Stock-Based Awards. Upon the happening of any of the events described in Subparagraphs (a), (b) or (c) above, any outstanding Stock-Based Award shall be appropriately adjusted to reflect the events described in such Subparagraphs. The Administrator or the Successor Board shall determine the specific adjustments to be made under this Paragraph 24, including, but not limited to the effect of any Corporate Transaction and, subject to Paragraph 4, its determination shall be conclusive.

(e) Modification of Options. Notwithstanding the foregoing, any adjustments made pursuant to Subparagraph (a), (b) or (c) above with respect to Options shall be made only after the Administrator determines whether such adjustments would cause any adverse tax consequences for the holders of Options, including, but not limited to, pursuant to Section 409A of the Code. If the Administrator determines that such adjustments made with respect to Options would constitute a modification or other adverse tax consequence, it may refrain from making such adjustments, unless the holder of an Option specifically agrees in writing that such adjustment be made and such writing indicates that the holder has full knowledge of the consequences of such "modification" on his or her income tax treatment with respect to the Option.

25. ISSUANCES OF SECURITIES.

Except as expressly provided herein, no issuance by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number or price of shares subject to Stock Rights. Except as expressly provided herein, no adjustments shall be made for dividends paid in cash or in property (including without limitation, securities) of the Company prior to any issuance of Shares pursuant to a Stock Right.

26. FRACTIONAL SHARES.

No fractional shares shall be issued under the Plan and the person exercising a Stock Right shall receive from the Company cash in lieu of such fractional shares equal to the Fair Market Value thereof.

27. WITHHOLDING.

In the event that any federal, state, or local income taxes, employment taxes, Federal Insurance Contributions Act ("F.I.C.A.") withholdings or other amounts are required by applicable law or governmental regulation to be withheld from the Participant's salary, wages or other remuneration in connection with the issuance of a Stock Right or Shares under the Plan or for any other reason required by law, the Company may withhold from the Participant's compensation, if any, or may require that the Participant advance in cash to the Company, or to any Affiliate of the Company which employs or employed the Participant, the statutory minimum amount of such withholdings unless a different withholding arrangement, including the use of shares of the Company's Common Stock or a promissory note, is authorized by the Administrator (and permitted by law). For purposes hereof, the fair market value of the shares withheld for purposes of payroll withholding shall be determined in the manner set forth under the definition of Fair Market Value provided in Paragraph 1 above, as of the most recent practicable date prior to the date of exercise. If the Fair Market Value of the shares withheld is less than the amount of payroll withholdings required, the Participant may be required to advance the difference in cash to the Company or the Affiliate employer. The Administrator in its discretion may condition the exercise of an Option for less than the then Fair Market Value on the Participant's payment of such additional withholding.

28. TERMINATION OF THE PLAN.

The Plan will terminate on February 23, 2031. The Plan may be terminated at an earlier date by vote of the shareholders or the Board of Directors of the Company; provided, however, that any such earlier termination shall not affect any Agreements executed prior to the effective date of such termination. Termination of the Plan shall not affect any Stock Rights theretofore granted.

29. AMENDMENT OF THE PLAN AND AGREEMENTS.

The Plan may be amended by the Administrator. Any modification or amendment of the Plan shall not, without the consent of a Participant, adversely affect his or her rights under a Stock Right previously granted to him or her. With the consent of the Participant affected, the Administrator may amend outstanding Agreements in a manner which may be adverse to the Participant but which is not inconsistent with the Plan. In the discretion of the Administrator, outstanding Agreements may be amended by the Administrator in a manner which is not adverse to the Participant. Nothing in this Paragraph 29 shall limit the Administrator's authority to take any action permitted pursuant to Paragraph 24.

30. EMPLOYMENT OR OTHER RELATIONSHIP.

Nothing in this Plan or any Agreement shall be deemed to prevent the Company or an Affiliate from terminating the employment or director status of a Participant, nor to prevent a Participant from terminating his or her own employment or director status or to give any Participant a right to be retained in employment or other service by the Company or any Affiliate for any period of time.

31. SECTION 409A.

If a Participant is a "specified employee" as defined in Section 409A of the Code (and as applied according to procedures of the Company and its Affiliates) as of his separation from service, to the extent any payment under this Plan or pursuant to the grant of a Stock-Based Award constitutes deferred compensation (after taking into account any applicable exemptions from Section 409A of the Code), and to the extent required by Section 409A of the Code, no payments due under this Plan or pursuant to a Stock-Based Award may be made until the earlier of: (i) the first day of the seventh month following the Participant's separation from service, or (ii) the Participant's date of death; provided, however, that any payments delayed during this six-month period shall be paid in the aggregate in a lump sum, without interest, on the first day of the seventh month following the Participant's separation from service.

The Administrator shall administer the Plan with a view toward ensuring that Stock Rights under the Plan that are subject to Section 409A of the Code comply with the requirements thereof and that Options under the Plan be exempt from the requirements of Section 409A of the Code, but neither the Administrator nor any member of the Board, nor the Company nor any of its Affiliates, nor any other person acting hereunder on behalf of the Company, the Administrator or the Board shall be liable to a Participant or any Survivor by reason of the acceleration of any income, or the imposition of any additional tax or penalty, with respect to a Stock Right, whether by reason of a failure to satisfy the requirements of Section 409A of the Code or otherwise.

32. INDEMNITY.

Neither the Board nor the Administrator, nor any members of either, nor any employees of the Company or any parent, subsidiary, or other Affiliate, shall be liable for any act, omission, interpretation, construction or determination made in good faith in connection with their responsibilities with respect to this Plan, and the Company hereby agrees to indemnify the members of the Board, the members of the Committee, and the employees of the Company and its parent or subsidiaries in respect of any claim, loss, damage, or expense (including reasonable counsel fees) arising from any such act, omission, interpretation, construction or determination to the full extent permitted by law.

33. CLAWBACK.

Notwithstanding anything to the contrary contained in this Plan, the Company may recover from a Participant any compensation received from any Stock Right (whether or not settled) or cause a Participant to forfeit any Stock Right (whether or not vested) in the event that the Company's Clawback Policy then in effect is triggered.

34. GOVERNING LAW.

This Plan shall be construed and enforced in accordance with the law of the State of Delaware.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (Nos. 333-236229, 333-232106, 333-226701, and 333-218468) and Form S-3 (No. 333-225678) of G1 Therapeutics, Inc. of our report dated February 24, 2021 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
February 24, 2021

Exhibit 31.1

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

I, John E. Bailey, Jr., certify that:

1. I have reviewed this Annual Report on Form 10-K of G1 Therapeutics, Inc.;

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

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

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

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

   (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: February 24, 2021

By: /s/ John E. Bailey, Jr.
John E. Bailey, Jr.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

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

I, Jennifer K. Moses, certify that:

1. I have reviewed this Annual Report on Form 10-K of G1 Therapeutics, Inc.;

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

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

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

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

   (b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Date: February 24, 2021

By: /s/ Jennifer K. Moses

Jennifer K. Moses
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), the undersigned officer of G1 Therapeutics, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2020 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 24, 2021

/s/ John E. Bailey, Jr.
John E. Bailey, Jr.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION UNDER SECTION 906

Pursuant to section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), the undersigned officer of G1 Therapeutics, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report for the year ended December 31, 2020 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 24, 2021

/s/ Jennifer K. Moses
Jennifer K. Moses
Chief Financial Officer
(Principal Financial and Accounting Officer)