# 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, 2018**

**OR**

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

**FOR THE TRANSITION PERIOD FROM TO**

**Commission File Number 001-38096**

# 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.)** |

**79 T.W. Alexander Drive 4501 Research Commons, Suite 100**
**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: Common Stock, Par Value $.0001 Per Share; Common stock traded on 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market on June 30, 2018, was $997,145,067.

The number of shares of Registrant's Common Stock outstanding as of February 25, 2019 was 37,408,234.

**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 12, 2019, are incorporated by reference into Part III of this report.

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**Special note regarding forward-looking statements**

This Annual Report on Form 10-K (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 clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. Our product portfolio is built on a drug discovery platform that targets key cellular pathways with proprietary medicinal chemistry. Our therapies are designed to enable more effective combination treatment strategies and 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 79 T.W. Alexander Drive, 4501 Research Commons, Suite 100, 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" 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.

**Product Pipeline**

Our product pipeline includes three clinical candidates with the potential to significantly improve the treatment of patients with cancer. Two of our three clinical candidates, trilaciclib and lerociclib, are based on our core understanding of cyclin-dependent kinases 4 and 6, collectively referred to as CDK4/6, a pair of proteins that play an important role in the growth and proliferation of all human cells. G1T48, our third product candidate, is the first candidate to advance into clinical trials from our oral selective estrogen receptor degrader (SERD) program. G1T48 is a potential first-in-class oral SERD which we plan to develop as a monotherapy and in combination with other agents, including lerociclib, for the treatment of estrogen receptor-positive (ER+), human epidermal factor receptor 2-negative (HER2-) breast cancer. We own the global rights to all three of our product candidates.

## G1 Therapeutics Product Pipeline

| Candidate | Target | Method Of Action (MOA) | Clinical Status | Global Rights |
|---|---|---|---|---|
| trilaciclib | CDK4/6 | Short-acting intravenous CDK4/6 inhibitor<br>Preserves HSPC and immune system function | Phase 2 | |
| lerociclib | CDK4/6 | Oral CDK4/6 inhibitor<br>Inhibits tumor proliferation and growth | Phase 1/2 | |
| G1T48 | Estrogen Receptor | Oral selective estrogen receptor degrader (SERD)<br>Inhibits estrogen receptor driven tumor proliferation | Phase 1 | |

**Our CDK4/6 Inhibitor Product Candidates**

CDK4/6 are key cell signaling proteins that regulate cell growth and proliferation. The CDK4/6 pathway regulates proliferation and growth of both healthy normal cells and certain tumor cells, representing a validated and promising class of targets for anti-cancer therapeutics. An example of normal cells whose growth and proliferation are regulated by CDK4/6, are hematopoietic stem and progenitor cells, or HSPCs. HSPCs reside in the bone marrow and are the "reservoir" from which all blood and immune system cells are formed. Additionally, CDK4/6 plays an integral role in the growth and proliferation of certain types of tumors.

We have leveraged our deep knowledge of CDK4/6 biology to discover and develop two highly potent and selective CDK4/6 inhibitors that may have broad applicability across multiple cancer indications. We believe we are the only company with two distinct clinical-stage CDK4/6 inhibitors, trilaciclib and lerociclib, each of which has the potential to be the backbone therapy in multiple combination regimens. Our two CDK4/6 inhibitors were rationally designed to treat distinct patient populations with different combination regimens.

Trilaciclib, a short-acting intravenous (IV) therapy, is in development for combinations with chemotherapy and chemotherapy/checkpoint inhibitor regimens. Lerociclib, an oral therapy, is in development for combinations with other targeted therapies.

**Trilaciclib: our novel approach to preserve HSPCs from damage by chemotherapy**

Trilaciclib is a first-in-class, short-acting CDK4/6 inhibitor which we are developing to be administered intravenously prior to chemotherapy. In preclinical studies, administration of trilaciclib prior to chemotherapy has been shown to induce transient cell-cycle arrest of HSPCs, protect HSPCs from chemotherapy-induced damage, preserve bone marrow and immune system function, 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 extensive-stage small cell lung cancer (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, without a single episode 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 of these 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 multi-lineage myelopreservation results were reported in March 2018, with additional data reported at the European Society of Medical Oncology 2018 Congress in October. Enrollment in the second-/third-line SCLC Phase 2 trial was completed in the second quarter of 2018, with positive multi-lineage myelopreservation data reported in the fourth quarter of 2018.

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 multi-lineage myelopreservation data in November 2018 with anti-tumor efficacy data expected to be reported in the second-half of 2019.

All three trials reported that trilaciclib, when added to the standard of care, mitigates clinically significant chemotherapy-induced myelosuppression in patients with SCLC.

Trilaciclib is also being tested outside of SCLC. 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 December 2018 San Antonio Breast Cancer Symposium (SABCS), we presented preliminary trilaciclib data demonstrating improvement in progression-free survival (PFS).

***Market opportunities for trilaciclib***

Cancer is the second leading cause of death in the United States with approximately 1.7 million new cases and 609,000 deaths in 2018, 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 has diminished recently 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 exceeds $7 billion.

Our first trial for trilaciclib is in first-line treatment of extensive-stage SCLC. According to the American Cancer Society, SCLC accounts for approximately 14% of all lung cancers. Approximately 32,000 people are diagnosed annually with SCLC in the United States and approximately 70%, or 22,000, of those have extensive-stage disease. First-line treatment for extensive-stage SCLC in the

United States is typically a chemotherapy regimen of carboplatin and etoposide, each of which has significant myelosuppressive side effects. Going forward, immunotherapy is likely to be added to chemotherapy as part of the standard of care. While these patients often respond to chemotherapy, 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.

We completed preliminary global market research in the fourth quarter of 2018. Many physicians see proactive myelopreservation as a better approach for patients and would incorporate trilaciclib into their SCLC treatment regimen. This market research suggested $500 million to $1 billion peak worldwide net sales potential for trilaciclib in SCLC based on achieving a chemo agnostic, myelopreservation indication.

We are also exploring the use of trilaciclib in metastatic triple negative breast cancer, or mTNBC. 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.

There have been a number of positive registrational studies and approvals evaluating checkpoint inhibitors in combination with chemotherapy and currently there are approximately 300 trials of which we are aware evaluating checkpoint inhibitors in combination with chemotherapy. We believe that administering trilaciclib with chemotherapy/checkpoint inhibitor combinations may increase efficacy. We are collaborating non-exclusively with Genentech to explore the utility in SCLC of trilaciclib and their checkpoint inhibitor Tecentriq combined with chemotherapy.

***Advantages of trilaciclib***

We believe that treating patients with trilaciclib prior to the administration of chemotherapy may have the following benefits and advantages:

- *Potential to minimize chemotherapy-induced myelotoxicity and immunosuppression*. Trilaciclib has been rationally designed and optimized to preserve HSPCs from damage by chemotherapy, thereby minimizing cytopenias across all four blood lineages: red cells, platelets, neutrophils and lymphocytes. 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 for combination with immune checkpoint inhibitors.* We are collaborating non-exclusively with Genentech to explore the utility of trilaciclib and their checkpoint inhibitor Tecentriq combined with chemotherapy in SCLC. We initiated a Phase 2 trial in combination with Tecentriq in the second quarter of 2017, and reported positive multi-lineage myelopreservation data in November 2018.
- *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 reported positive multi-lineage myelopreservation data in 2018 and our market research with payers supports this value proposition of trilaciclib.

***Trilaciclib: preclinical and clinical development***

*Preclinical development*

We have published extensive biochemical, cellular and *in vivo* data on trilaciclib from 2015-2017. Our preclinical data show that trilaciclib can induce transient and reversible cell-cycle arrest of HSPCs; protect HSPCs from damage by chemotherapy; preserve bone marrow and immune system function; improve CBC recovery; 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.

*Ongoing clinical trials*
Trilaciclib (IV CDK4/6 inhibitor):

| **Initial indications** | **Regimen** | **Phase** | **Status and expected milestones** |
|---|---|---|---|
| 1st -line Small Cell Lung Cancer | + etoposide/carboplatin | 1b/2 | Phase 2 enrollment completed in second-quarter 2017<br>Reported positive Phase 2 myelopreservation data in first-quarter 2018 with additional data presented at ESMO 2018 Congress |
| 2nd /3rd –line Small Cell Lung Cancer | + topotecan | 1b/2 | Phase 2 enrollment completed in second-quarter 2018<br>Reported positive myelopreservation data in fourth-quarter 2018 |
| 1st-line Small Cell Lung Cancer | +Tecentriq/carboplatin/ etoposide | 2 | Enrollment completed in first-quarter 2018 (two quarters ahead of schedule); reported positive myelopreservation data in fourth-quarter 2018 and anticipate additional anti-tumor efficacy data in second half of 2019 |
| metastatic Triple Negative Breast Cancer | +gemcitabine/carboplatin | 2 | Enrollment completed in second-quarter 2018<br>Reported preliminary anti-tumor efficacy data at San Antonio Breast Cancer Symposium in fourth-quarter 2018 |

*Ongoing Phase 1b/2 clinical trial in first-line treatment of SCLC*

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, myelopreservation, 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 multi-lineage myelopreservation data from the Phase 2 segment of the trial in March 2018, with additional data from the trial presented at the 2018 European Society of Medical Oncology (ESMO) Congress.

*Ongoing Phase 1b/2 clinical trial in second/third-line treatment of SCLC*

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, myelopreservation, 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 multi-lineage myelopreservation data in the fourth quarter of 2018. We expect to report additional anti-tumor efficacy data in 2019.

*Ongoing Phase 2 clinical trial in first-line treatment of SCLC with a checkpoint inhibitor*

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, overall survival, myelopreservation, 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 multi-lineage myelopreservation data and preliminary progression free survival (PFS) in November 2018. We expect to report additional anti-tumor efficacy data in in the second-half of 2019.

*Ongoing 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, myelopreservation, PK, and anti-tumor activity of trilaciclib in combination with the existing chemotherapy standard of care regimen of gemcitabine and carboplatin. We completed enrollment in the second-quarter of 2018. At the December 2018 San Antonio Breast Cancer Symposium (SABCS), we presented preliminary data demonstrating improvement in progression-free survival (PFS). We expect to report additional anti-tumor efficacy data in the second-half of 2019.

**Lerociclib: Our potential best-in-class CDK4/6 inhibitor for patients with CDK4/6-dependent tumors**

Lerociclib, our second clinical-stage candidate, is a potential best-in-class oral CDK4/6 inhibitor, to be used in combination with other targeted therapies to treat multiple cancers. We rationally designed lerociclib to improve upon and address the shortcomings of the approved CDK4/6 inhibitors Ibrance® (palbociclib), Kisqali® (ribociclib) and Verzenio® (abemaciclib). Our preclinical data and early human clinical data indicate the potential for continuous daily dosing, less dose-limiting neutropenia, and improved tolerability. A Phase 1 trial of lerociclib in 75 healthy volunteers showed a favorable safety profile, and we initiated a Phase 1b/2a trial in ER+, HER2- breast cancer in January 2017. Our plans for lerociclib include combinations in other cancers, such as non-small cell lung cancer, or NSCLC, where we initiated a Phase 1b/2 trial in 2018 in combination with the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, Tagrisso® (osimertinib). We believe that lerociclib has the potential to be the backbone therapy of multiple combination targeted therapy regimens.

***Market opportunity for lerociclib***

The importance of CDK4/6 as a key regulator of tumor cell growth and proliferation in certain tumors has been validated by the FDA's approval of Pfizer's CDK4/6 inhibitor Ibrance for the treatment of ER+, HER2- advanced breast cancer as initial endocrine therapy in combination with an aromatase inhibitor in post-menopausal women and in women with disease progression following endocrine therapy in combination with fulvestrant, the approval in 2017 of Kisqali in combination with an aromatase inhibitor, and the approval in 2017 of Verzenio in combination with fulvestrant. Worldwide sales of Ibrance were $2.1 billion and $3.1 billion in 2016 and 2017, respectively. Wall Street analysts estimate Ibrance peak annual worldwide sales to exceed $7 billion.

***Advantages of lerociclib***

We believe that lerociclib has the potential to be a best-in-class CDK4/6 inhibitor. There are currently three other CDK4/6 inhibitors approved to treat ER+, HER2- breast cancer - Ibrance, Kisqali, and Verzenio. Ibrance and Kisqali have long half-lives that can lead to drug accumulation and neutropenia, requiring a dosing regimen of 21 days on drug and a treatment holiday of at least seven days off drug. Kisqali has also exhibited cardiovascular and liver side effects. Verzenio has demonstrated significant gastrointestinal issues, which can require administration of antidiarrheal therapies. Verzenio has also exhibited liver and blood clotting side effects. We rationally designed lerociclib to improve upon the clinical profiles of currently marketed CDK 4/6 inhibitors.

We believe that lerociclib has the potential to be best-in-class because of the following advantages:

- *Less myelotoxicity*. In preclinical studies, lerociclib has demonstrated less myelotoxicity than Ibrance, but equivalent anti-tumor efficacy. We believe this is due to the inherently different PK properties of lerociclib.
- *Potential for continuous daily dosing.* Patients on Ibrance and Kisqali can only be given the drug on a 21 days-on, followed by 7 days-off, schedule. Even with this dosing holiday, dose-delays and dose reductions due to persistent neutropenia are common. Our preclinical data and clinical data to date with lerociclib support the potential for continuous daily dosing with less dose-limiting neutropenia.
- *Improved cardiovascular and liver safety*. Lerociclib has not shown any of the QT prolongation issues (seen with Kisqali) and liver injury (seen with Kisqali and Verzenio).
- *Improved tolerability profile*. We have designed lerociclib to be selective for CDK4/6, which we believe will have an improved tolerability profile
- *Greater potential for combination therapies.* We believe that lerociclib's safety profile may enable it to be combined more easily with other therapies. Lerociclib, to our knowledge, is the only selective CDK4/6 inhibitor in development that is not currently owned by a large pharmaceutical company. We believe that other pharmaceutical and biotech companies with targeted therapies may want to test a combination of their therapies with lerociclib. Accordingly, we believe we are in a strong position to explore collaborative arrangements with these companies.

***Lerociclib: preclinical and clinical development***

*Preclinical development*

We have published extensive biochemical, cellular and *in vivo* data on lerociclib demonstrating: high potency and selectivity for CDK4/6; equivalent anti-tumor activity to Ibrance when dosed orally once daily for 28-days in a mouse model of ER+, HER2- breast cancer; less myelotoxicity than Ibrance in dog models, suggesting the potential for continuous daily dosing without the need for a treatment holiday; and anti-tumor efficacy in models of certain CDK4/6-dependent tumor types, such as NSCLC and castrate resistant prostate cancer, or CRPC.

*Completed Phase 1 clinical trial*

In the fourth quarter of 2016, we completed a Phase 1 clinical trial of lerociclib in 75 healthy volunteers in the Netherlands. This was a single ascending dose, placebo-controlled trial testing doses of 3 to 600 mg. In addition, lerociclib was dosed at 200 and 300 mg twice a day, 300 mg with and without food, and 300 mg as an oral solution. The goals of the clinical trial were to obtain PK and safety data to inform appropriate starting dose(s) for studies in patients. There were no DLTs, SAEs, or grade 3/4 AEs reported in this study.

*Ongoing clinical trials*

Lerociclib (oral CDK4/6 inhibitor):

| Initial indications | Regimen | Phase | Status and expected milestones |
|---|---|---|---|
| ER+, HER2- Breast Cancer | +Faslodex® | 1b/2a | Phase 1b enrollment completed fourth-quarter 2018; reported positive preliminary Phase 1b data in second-quarter 2018 Phase 2a segment ongoing |
| EGFR mutant Non-small Cell Lung Cancer | + Tagrisso | 1b/2 | Initiated Phase 1b in first-quarter 2018; preliminary Phase 1b data expected in second-half 2019 |

*Ongoing Phase 1b/2a clinical trial in ER+, HER2- breast cancer*

In January 2017, we initiated a Phase 1b/2a trial in ER+, HER2- breast cancer patients in combination with Faslodex (fulvestrant), an FDA-approved SERD. The Phase 1b segment of the trial to enrolled 46 patients in Europe. The goals of the clinical trial are to evaluate the safety, PK, and anti-tumor activity of lerociclib in combination with Faslodex and to determine the dose to be used in future trials. The Phase 1b segment of the trial is open-label and consists of two arms, with lerociclib dosed continuously without a holiday, either once a day or twice a day in combination with Faslodex. The Phase 2a segment of the trial is currently ongoing. All patients in the trial are being administered lerociclib orally continuously without a treatment holiday and intramuscular, or IM, Faslodex per the label.

We reported positive preliminary safety and efficacy Phase 1b data at the 2018 American Society of Clinical Oncology (ASCO) annual meeting. Lerociclib has a shorter half-life and larger volume of distribution than Ibrance and Kisqali and is not expected to show drug accumulation. All of the enrolled patients had a decline in neutrophil counts, which was expected due to a mechanism-based decrease in neutrophil production caused by lerociclib, which also occurs with other CDK4/6 inhibitors such as Ibrance and Kisqali. No cardiovascular or liver side effects have been reported so far and there have been no lerociclib-related SAEs. The incidence of gastrointestinal AEs reported so far are similar to Ibrance and Kisqali and less than Verzenio. These early clinical data indicate the potential for continuous daily dosing of lerociclib incombination with Faslodex without a dose-holiday, and the potential for improved tolerability compared to other marketed CDK4/6 inhibitors.

*Ongoing Phase 1b/2 clinical trial in Non-Small Cell Lung Cancer (NSCLC) in combination with Tagrisso*

In the first quarter of 2018, we initiated a Phase 1b/2 clinical trial in EGFR-mutant NSCLC patients in combination with Tagrisso, and FDA-approved epidermal growth factor receptor tyrosine kinase inhibitor. The goals of the clinical trial are to evaluate the safety, PK, and anti-tumor activity of lerociclib in combination with Tagrisso and to determine the dose to be used in future trials.

**G1T48: Our oral SERD**

G1T48 is a potential best-in-class oral SERD, which we plan to initially develop as a monotherapy and in combination with lerociclib for the treatment of ER+, HER2- breast cancer. We believe we are in a unique position as the only emerging biopharmaceutical company with a wholly owned, proprietary combination of an oral SERD and an oral CDK4/6 inhibitor, a validated regimen in ER+, HER2- breast cancer. Based on compelling preclinical efficacy and safety data, we filed an Investigational New Drug application (IND) with the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2017. We initiated a clinical trial in 2018 and expect to report preliminary Phase 1 data in the second-half of 2019.

***Market opportunity for G1T48***

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, Faslodex, is approved for the treatment of ER+ metastatic breast cancer. Faslodex 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 Faslodex include nausea (9.7%) and bone pain (9.4%).

While there are several oral SERDs in early clinical development, no one candidate has emerged as a clear front runner as an oral alternative to Faslodex based on early results.

***Advantages of G1T48***

We believe that G1T48 has the potential to be first/best-in-class because of the following advantages:

- *Higher potency*. In preclinical models of ER+, HER2- breast cancer, G1T48 is more potent than Faslodex in binding and degrading the ER and inhibiting cell growth.
- *Improved oral efficacy*. G1T48 demonstrated improved activity compared to another oral SERD in development in preclinical models of endocrine resistance mediated by ER mutation. G1T48 also demonstrated better efficacy than other oral SERDs in development in a tamoxifen resistant model of ER+, HER2- breast cancer.
- *Ease of administration*. The only approved SERD, Faslodex, is required to be given via IM injection. We have designed G1T48 to be administered orally.
- *Wholly owned proprietary combination regimen.* To our knowledge, we are the only emerging biopharmaceutical company with both an oral SERD (G1T48) and an oral CDK4/6 inhibitor (lerociclib). We believe that being in the unique position of having this wholly owned proprietary combination of a validated regimen for the treatment of ER+, HER2- breast cancer provides us a strategic and competitive advantage.

***G1T48: Preclinical and clinical development***

We have presented extensive biochemical, cellular and in vivo data on G1T48 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 1/2a clinical trial in 2018 with the goal of evaluating the safety, tolerability, and PK of the drug in breast cancer patients and expect to report preliminary Phase 1 data in the second-half of 2019.

**Our Business Strategy**

Our goal is to be a leader in the discovery and development of CDK4/6 inhibitor-based treatments for cancer. Our strategy includes the following key components:

- ***Develop trilaciclib in combination with chemotherapy across multiple indications.*** We believe that trilaciclib has the potential to be used to treat patients receiving myelosuppressive chemotherapy across multiple oncology indications.
- ***Develop trilaciclib in combination with immune checkpoint inhibitors.*** We believe that using trilaciclib in combination with chemotherapy and checkpoint inhibitors has the potential to significantly enhance efficacy. In December 2016, we entered into a collaboration with Genentech to evaluate trilaciclib in combination with Genentech's checkpoint inhibitor Tecentriq in multiple indications.
- ***Develop lerociclib as a best-in-class treatment across multiple cancer indications.*** We believe that lerociclib has the potential for less dose-limiting neutropenia than Ibrance and Kisqali and an improved safety/tolerability profile versus Kisqali and Verzenio. We plan to develop lerociclib across multiple cancer indications, either alone or with one or more strategic collaborators.
- ***Develop G1T48 as a monotherapy and in combination with lerociclib.*** The use of a selective CDK4/6 inhibitor in combination with a SERD has been validated by the FDA approval and commercial success of Ibrance. With an oral SERD (G1T48) and an oral CDK4/6 inhibitor (lerociclib), we believe we are in a unique position as the only emerging biopharmaceutical company with a wholly owned proprietary combination for this validated anti-cancer regimen.

- ***Pursue global development of combination therapies.*** We believe our expertise in CDK4/6 biology puts us in an advantageous position to develop proprietary best-in-combination or first-in-combination therapies with the potential for improved efficacy and safety. We are developing lerociclib to be used in combination with other targeted therapies such as SERDs. The approval of Ibrance has created significant interest in the use of selective CDK4/6 inhibitors in combination with other targeted therapies for the treatment of cancer. Ibrance, Kisqali and the other selective CDK4/6 inhibitor in clinical development are owned by large pharmaceutical companies. As a result, we believe that we are in a strong position to explore collaborative arrangements with other pharmaceutical and biotechnology companies that are interested in combining their targeted therapies with lerociclib.

**Commercialization**

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 currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture of any drugs that we may commercialize. To date, we have obtained active pharmaceutical ingredients, or API, formulations, and drug products for trilaciclib, lerociclib and G1T48 for our preclinical studies and clinical trials from multiple third-party manufacturers. We obtain our supplies from these manufacturers on a purchase order basis and do not have long-term supply arrangements in place. Redundant suppliers are in place for some of our APIs and drug products. As development proceeds for our product candidates, we will evaluate qualifying additional redundant manufacturers for API and drug product.

**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. If any of our product candidates is approved, they 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.

If trilaciclib is approved, it will be the first approved therapy designed and optimized to preserve 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 when available. In addition, trilaciclib may compete with multiple approved drugs or drugs that may be approved in the future for indications for which we develop trilaciclib.

If lerociclib is approved, it will compete with Pfizer's approved CDK4/6 inhibitor Ibrance; Novartis's approved CDK4/6 inhibitor Kisqali; and Eli Lilly's approved CDK4/6 inhibitor Verzenio.

Lerociclib may compete with multiple approved drugs or drugs that may be approved in the future for indications for which we develop lerociclib.

If G1T48 is approved, it will compete with AstraZeneca's approved IM SERD, Faslodex. G1T48 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; LSZ102, being developed by Novartis; and D-0502, being developed by InventisBio. G1T48 may compete with multiple approved drugs or drugs that may be approved in the future for indications for which we may develop G1T48.

**Intellectual property**

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our CDK4/6 inhibitor molecules, including our CDK4/6 inhibitors in clinical trials and methods of treatment using our CDK4/6 inhibitors, alone and in combination with other therapeutic agents. We also seek protection on processes for the production of our CDK4/6 inhibitors, formulations incorporating our CDK4/6 inhibitors, combinations of our product candidates with other active agents and dosing schedules and regimens related to our CDK4/6 inhibitors. 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 is focused on patenting our CDK4/6 inhibitors, their uses, and methods of manufacturing as well as our licensed-in applications directed to selective estrogen receptor degraders and their uses, manufacture, and combination with our CDK 4/6 inhibitors. We have obtained fourteen 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 five 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 in the United States on SERD compounds that we have exclusively in-licensed from the University of Illinois Chicago. We also seek patent protection on methods of treatment that incorporate our CDK4/6 inhibitors 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 CDK4/6 inhibitors, 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.

Our owned and in-licensed patent estate as of December 31, 2018, on a worldwide basis, includes over 160 granted or pending patent applications spread over more than 25 patent families with 20 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 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 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, exclusive of any patent term extension. Our in-licensed patent covering the composition of matter of our clinical candidate G1T48 will expire in 2036, exclusive of any patent term extension. Our pending applications on additional methods of use of trilaciclib and lerociclib, should they issue, will expire on dates ranging from 2034 to 2039. We plan to file additional applications on aspects of our innovations that may have patent terms that extend beyond these dates.

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 and technology 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 three issued U.S. Patents (U.S. 8,598,186; U.S. 8,598,197; and 9,957,276) and two allowed U.S. application covering the trilaciclib compositions-of-matter and its pharmaceutical composition. We also own four issued U.S. Patents (U.S. 8,598,186; U.S. 8,598,197; U.S. 9,481,691; and 9,957,276) and one allowed U.S. application 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, Korea, and Singapore, pending applications in Brazil, India, and Israel, and an allowed application in Hong Kong. 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 China, Hong Kong, Macau, and Japan, and been allowed in Europe. 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 an international application under the Patent Cooperation Treaty that covers the administration of trilaciclib in combination with a PD-L1 inhibitor such as Tecentriq. 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 lerociclib to treat RB-positive tumors. The family includes two issued U.S. Patents (U.S. 9,527,857 and U.S. 10,076,523) 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, and the '523 patent covers the use of lerociclib to treat Rb-positive breast cancer continuously for 28 days or more. 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 lerociclib as an anti-neoplastic agent against a T or B cell cancer. This patent filing is pending in the United States, Europe, Canada, and China, has issued in Japan. 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 a patent application 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, 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 U.S. patent application and a 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.

***G1T48 Patent Coverage***

We have exclusively licensed from University of Illinois, or the University, two patent families that cover G1T48 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. A U.S. Patent (U.S. 10,119,810) has issued from this family. 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, one international patent application directed to the combination of G1T48 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 2037, 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 G1T48***

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, have made, use, import, sell and offer for sale of certain SERDs, including G1T48, 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 $500,000, 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 may also be required to pay the University milestone payments of up to an aggregate of $2.625 million related to the initiation and execution of clinical trials and first commercial sale of a product in multiple countries. We will also be 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.

***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 characteristics and potential safety and efficacy of the product. The conduct of the preclinical and other nonclinical tests must comply with certain federal regulations and requirements, including good laboratory practices. 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, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations, including those encompassing good clinical practice, or GCP, requirements that are meant to protect the rights and health of patients 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 involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time 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 patients. The clinical trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, at each site where a clinical trial will be performed for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements or it may impose other conditions.

Clinical trials to support NDAs 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, approvals 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.

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 pharmacology, 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 million for an NDA with clinical information, and the manufacturer and/or sponsor under an approved NDA is also subject to annual product and establishment user fees, currently approximately $100,000 per product and over $500,000 per establishment. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. 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 review may be extended by FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee, 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 inspect the facility or the facilities at which the drug is manufactured. 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 information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. 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 specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe and effective use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory requirements 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 website maintained by the U.S. National Institutes of Health. 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. Sponsors are also obligated to disclose the results of these clinical trials after completion if the product candidate is ultimately approved, and disclosure of the results of these clinical trials will be delayed until such approval. Competitors may use this publicly-available information to gain knowledge regarding the design and progress of our development programs.

***The Hatch-Waxman Act***

*Orange book listing*

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent 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 abbreviated new drug application, or ANDA. The ANDA request to market a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, 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 listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement, certifying that its proposed ANDA label does not contain or carve out any language regarding the patented method-of-use, rather than certify to a listed method-of-use patent.

If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

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

*Exclusivity*

Upon NDA approval of a new chemical entity 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 which the FDA cannot approval an ANDA for a generic drug that includes the change.

An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed on an NCE patent and any time after approval if an ANDA is filed based on a new indication or a new formulation. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

*Patent term extension*

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent 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 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.

***Advertising and promotion***

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or certain manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

***Adverse event reporting and cGMP compliance***

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality-control, drug manufacture, packaging, and labeling procedures, among other things, must continue to conform to cGMP after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMP. Regulatory authorities may impose a range of enforcement actions, including bringing a seizure and injunction in court, withdraw product approvals or request voluntary product recalls if a company fails to comply with cGMP requirements.

***Pediatric information***

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The 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 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 as described above. Conditions for exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric 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.

***Special protocol assessment***

A company may reach an agreement with FDA under the Special Protocol Assessment, or SPA, process as to the required design and size of clinical trials intended to form the primary basis of an efficacy claim. Under the FDC Act and FDA guidance implementing the statutory requirement, an SPA is generally binding upon the FDA except in limited circumstances, such as if the FDA identifies a substantial scientific issue essential to determining safety or efficacy after the clinical trial begins, public health concerns emerge that were unrecognized at the time of the protocol assessment, the sponsor and FDA agree to the change in writing, or if the clinical trial sponsor fails to follow the protocol that was agreed upon with the FDA.

***Expedited review and approval***

The FDA has various programs, including Fast Track, priority review, accelerated approval and breakthrough therapy designation which are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval on the basis of surrogate endpoints. 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 is a process designed to facilitate the development, and expedite the review, of drugs to treat serious diseases and fill an unmet medical need. The 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 as compared to a standard review time of ten months. Although Fast Track 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.

***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 issued Guidance on In-Vitro Companion Diagnostic Devices in August 2014, which is 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 defined 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. 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.

***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 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. 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 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.

The characteristic of the MRP is that the procedure builds on an already existing marketing authorization in a member state of the E.U. that is used as reference in order to obtain marketing authorizations in other E.U. 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.

The MRP is based on the principle of the mutual recognition by European Union member states of their respective national marketing authorizations. Based on a marketing authorization in the reference member state, the applicant may apply for marketing authorizations in other member states. In such case, the reference member state shall update its existing assessment report about the drug in 90 days. After the assessment is completed, 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 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.

***Brexit***

Unless otherwise agreed with the other member states of the European Union, the United Kingdom will leave the European Union in March 2019, or Brexit. As the regulatory framework for pharmaceutical products in the United Kingdom is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. At this time it is unclear whether Brexit will have a material regulatory impact with respect to product candidates and products in the United Kingdom.

***Other Countries***

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

**Employees**

As of December 31, 2018, we had 84 full-time employees, including 63 in research and development and 21 in general and administrative functions. We have no collective bargaining agreements with our employees, and we have not experienced any work stoppages. We consider our relations with our employees to be good.

**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.*

**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 $85.3 million for the year ended December 31, 2018, $60.1 million for the year ended December 31, 2017, and $30.3 million for the year ended December 31, 2016. As of December 31, 2018, we had an accumulated deficit of $214.4 million. Our product candidates span a range from preclinical development to Phase 2 clinical trials, and it may be several years, if ever, before we have a product candidate ready for commercialization. To date, we have financed our operations primarily through sales of our preferred and common stock. 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 if and as we:

- continue development of our product candidates, including initiating additional clinical trials of trilaciclib, lerociclib and G1T48;
- identify and develop new product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any 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;
- 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 planned future 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 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, 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 eventually commercialize a product or 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 and lerociclib. We have not yet demonstrated our ability to successfully complete large-scale, pivotal clinical trials, obtain marketing approvals, 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. 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 increase along with our ongoing activities, particularly as we conduct larger-scale clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant 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, 2018, we had $369.3 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 research and development and other corporate activities. Because the length of time and activities associated with successful research and development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities. In addition, our future capital requirements will depend on many factors, and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of preclinical 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 G1T48, 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, should any of our product candidates receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Conducting preclinical 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, our 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 several years, 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 our 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 one or more of our research or development programs or the commercialization of any product candidate 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 private and public 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.

**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 trilaciclib in four clinical trials: two Phase 1b/2 trials in patients with small cell lung cancer, or SCLC, an additional Phase 2 trial in combination with Tecentriq in SCLC and a Phase 2 trial in patients with metastatic triple-negative breast cancer, or mTNBC. While trilaciclib has shown compelling multi-lineage myelopreservation benefits and favorable tolerability in these trials, we may not see such favorable data in future clinical trials involving trilaciclib. Similarly, favorable results obtained from the early-stage trial of lerociclib may not be replicated in the ongoing Phase 1/2 trial in ER+, HER2- breast cancer and Phase 1b/2 trial in 2018 in combination with the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, Tagrisso for non-small cell lung cancer, or in any future clinical trials. Furthermore, 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.

***Preliminary and interim anti-tumor efficacy data from our clinical studies may change as more patient data become available.***

Preliminary or interim anti-tumor efficacy data from our clinical studies are not necessarily predictive of final results. Preliminary and interim anti-tumor efficacy data are subject to the risk that one or more of the clinical outcomes may materially change, as more patient data become available and we issue our final clinical study report. As a result, preliminary and interim data should be viewed with caution until the final data are available. Material adverse changes in the final data compared to the interim data could significantly harm our business prospects.

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

We currently do not have any products that have gained marketing approval. We have invested substantially all of our efforts and financial resources identifying and developing our CDK4/6 inhibitor product candidates, trilaciclib and lerociclib, and our oral SERD product candidate, G1T48. Our ability to generate product revenues, which may not occur for several years, if ever, will depend on the successful development and eventual commercialization of one or more of our product candidates. We currently generate no revenues

from sales of any drugs, and we may never be able to develop or commercialize a marketable drug. Each of our product candidates will require development, management of development and manufacturing activities, marketing approval in multiple jurisdictions, obtaining manufacturing supply, building of a commercial organization, 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:

- 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;
- build and maintain robust sales, distribution and marketing capabilities, either on our own or in collaboration with strategic partners, if our product candidates are approved;
- gain acceptance for our product candidates, if approved, by patients, the medical community and third-party payors;
- compete effectively with other therapies;
- 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 we elect to enter into, if any;
- 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. If we do not receive marketing approvals for our product candidates, we may not be able to continue our operations.

***Our development of a CDK4/6 to reduce chemotherapy-induced myelosuppression is novel, unproven and rapidly evolving and may never lead to a marketable product.***

Trilaciclib is a short-acting intravenous CDK4/6 inhibitor. The use of a CDK4/6 inhibitor to reduce 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. The scientific evidence to support the feasibility of developing this product candidate is both preliminary and limited. Even though trilaciclib has demonstrated positive results in preclinical studies and early-stage clinical trials, we may not succeed in demonstrating safety and efficacy of trilaciclib in larger-scale clinical trials.

Advancing this novel therapy creates significant challenges for us, including:

- obtaining marketing approval, 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, if approved, into their treatment regimens; and
- establishing sales and marketing capabilities upon obtaining any marketing approval 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 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.

***A Breakthrough Therapy Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.***

We do not currently have Breakthrough Therapy Designation for any of our product candidates but may seek such designation. A Breakthrough Therapy Designation may be granted to a drug that is intended, alone or in combination with one or more other drugs, to

treat a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for development. Drugs designated as Breakthrough Therapies are also eligible for accelerated approval.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe, after completing early clinical trials, that one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to grant such designation. In any event, the receipt of a Breakthrough Therapy designation by itself for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as a Breakthrough Therapy, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

***A Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.***

We do not currently have Fast Track Designation for any of our product candidates but may seek such designation. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain drug approval.

***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.***

If the FDA or a comparable foreign regulatory authority approves any of our product candidates, activities 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 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.

***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.***

Although we do not currently have any drugs on the market, once we begin commercializing our product candidates, we will be 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 will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may 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 will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will 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.

***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.

The current administration supports a repeal of the ACA and an Executive Order has been signed commanding federal agencies to try to waive or delay requirements of the ACA that impose economic or regulatory burdens on states, families, the health-care industry and others. The Executive Order also declares that the administration will seek the "prompt repeal" of the law and that the government should prepare to "afford the States more flexibility and control to create a more free and open healthcare market." At this time, the immediate impact of the Executive Order is not clear. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These new laws may result in additional reductions in Medicare and other healthcare funding.

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.

***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.

***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 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 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.***

We do not currently own or operate, nor do we have any plans to establish in the future, any manufacturing facilities or personnel. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical studies and clinical trials, as well as for the commercial manufacture of our drugs if any of our product candidates receive marketing approval. 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 our product candidates (drug substance and drug product) must be approved by the FDA (and other similar regulatory agencies outside the U.S. 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 cGMPs in connection with the manufacture of our product candidates. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the regulatory requirements of the FDA or others, 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 a 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.

Our 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 or marketing approval. 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 our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.***

In order to conduct large-scale clinical trials of our product candidates, 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 for any of our 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 of our 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 active pharmaceutical ingredients, formulations, 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 active pharmaceutical ingredients, or APIs, 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 APIs and drug products in accordance with cGMP requirements and in sufficient quantities for clinical trials and commercialization. It is possible that our suppliers of API 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 API 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 APIs 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 APIs and drug product for our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain such APIs 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.

***We may seek to establish additional collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.***

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 face significant competition in seeking 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.

**Risks related to the commercialization of our product candidates**

***Even if any of our product candidates receives marketing approval, it 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.***

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our 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 our 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 any 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. If trilaciclib is approved, it would compete 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 trilaciclib. If lerociclib is approved, it would compete with (a) Pfizer's approved CDK4/6 inhibitor, Ibrance, (b) Novartis's approved CDK4/6 inhibitor, Kisqali, (c) Eli Lilly's approved CDK4/6 inhibitor, Verzenio, (d) if approved, other non-selective CDK4/6 inhibitor product candidates in clinical development, including product candidates being developed by FLX Bio and OncoMed Pharmaceuticals, and (e) multiple approved drugs or drugs that may be approved in the future for indications for which we may develop lerociclib. If G1T48 is approved, it would compete with (a) the approved intramuscular SERD, Faslodex, being marketed by AstraZeneca, (b) if approved, other oral SERDs in development by Radius Health, Genentech, AstraZeneca and Novartis; and (c) multiple approved drugs or drugs that may be approved in the future for indications for which we may develop G1T48.

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 any 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 any 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.

**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, trilaciclib 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, future adversarial proceedings or litigation regarding intellectual property rights covering our products and technology, including interference or derivation 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. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and 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 G1T48.***

Our exclusive license with the University of Illinois, or the University, for technology relating to G1T48 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 G1T48, 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 an early-stage clinical development company, and, as of December 31, 2018, had only 84 employees, which includes six executive officers. We are highly dependent on the research and development, clinical and business development expertise of Mark A. Velleca, M.D., Ph.D., our President and Chief Executive Officer, Rajesh Malik, M.D., our Chief Medical Officer and Senior Vice President, R&D, Barclay Phillips, our Chief Financial Officer and Senior Vice President, Corporate Development, Terry Murdock, our Chief Operating Officer, John Demaree, our Chief Commercial Officer and James Stillman Hanson, our General Counsel, 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 expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities 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 development 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 physical 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 development and 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 development and 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.

***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 or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

Earthquakes 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.

***Federal income tax reform could have unforeseen effects on our financial condition and results of operations.***

The Tax Cuts and Jobs Act, or the Tax Act, was enacted on December 22, 2017, and contains many changes to U.S. federal tax laws. The Tax Act requires complex computations that were not previously provided for under U.S. tax law and significantly revised the U.S. tax code by, among other changes, lowering the corporate income tax rate from 35% to 21% and imposing significant additional limitations on the deductibility of interest and net operating loss carryforwards. At December 31, 2018, the Company has completed its accounting for the tax effects of the Tax Act. However, additional guidance may be issued by the Internal Revenue Service, or IRS, the Department of the Treasury, or other governing body that may significantly differ from our interpretation of the law, which may have an adverse effect on our financial condition or results of operations.

**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 trilaciclib, lerociclib and G1T48;
- 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.

***Our executive officers, directors and principal stockholders and their affiliates, if they choose to act together, will continue to have the ability to exercise significant influence over all matters submitted to stockholders for approval.***

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock, in the aggregate, beneficially own shares representing a majority of our outstanding capital stock. As a result, if these stockholders were to choose to act together, they would be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. This concentration of ownership control may adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change in control;
- entrenching our management and the board of directors;
- impeding a merger, consolidation, takeover or other business combination involving us that other stockholders may desire; and/or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

***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.

***If securities or industry analysts do not publish research or reports about our business, or if they publish negative evaluations of our stock or negative reports about our business, our stock price and trading volume could decline.***

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, there can be no assurance that analysts will cover us or provide favorable coverage. If one or more of the analysts who covers us downgrades our stock or changes his or her opinion of our stock, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our stock price or trading volume to decline.

***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, and particularly now that we are no longer an emerging growth company as of December 31,2018, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. 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 will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are first required to furnish a report by our management on our internal control over financial reporting for the year ending December 31, 2018. In addition, since we are no longer an emerging growth company as of December 31, 2018, we are also required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we have engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. Further, if we identify one or more material weaknesses in our internal control over financial reporting in the future, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***Our ability to use our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be limited.***

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change," is subject to limitations on its ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes. For these purposes, an ownership change generally occurs where the equity ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's

stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a three-year period. We may have experienced such ownership changes in the past, and we may experience shifts in our stock ownership, some of which are outside the Company's control. These ownership changes may subject our existing NOLs or credits to substantial limitations under Sections 382 and 383. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. As of December 31, 2018, we had federal NOLs of approximately $191.5 million. Limitations on our ability to utilize those NOLs to offset U.S. federal taxable income could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

***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 20,500 square feet of laboratory and office space. This lease on our corporate headquarters expires on December 31, 2022. In November 2018, we signed a new lease to secure 60,000 square feet of laboratory and office space near our current location in Research Triangle Park, North Carolina. We expect this space to be available in the third quarter of 2019. The new lease expires in the second half of 2027. None of our leases are material to our business operations. We believe our facilities are 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.

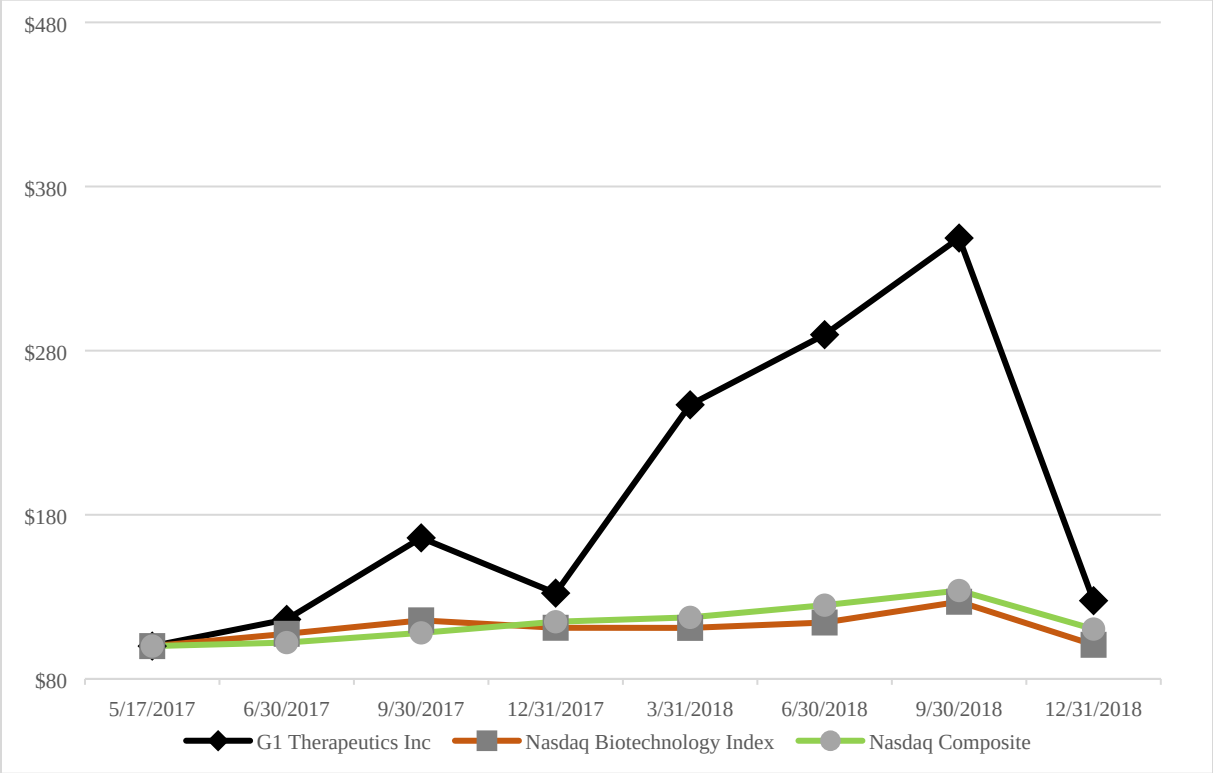
***Holders***

As of February 25, 2019, there were approximately 11 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 and 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, 2018. 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 fourth quarter of 2018.

**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, 2018, 2017 and 2016 and the balance sheet data as of and December 31, 2018 and 2017 from our audited financial statements included elsewhere in this Annual Report. The statement of operations data for the year ended December 31, 2015 and the balance sheet data as of December 31, 2016 and 2015 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, | | | |
|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 |
| | (in thousands except share and per share amounts) | | | |
| Statements of Operations Data: | | | | |
| Grant revenue | $ — | $ — | $ — | $ 522 |
| Operating expenses: | | | | |
| Research and development | 70,683 | 53,881 | 25,161 | 12,730 |
| General and administrative | 18,603 | 7,087 | 5,230 | 3,216 |
| Total operating expenses | 89,286 | 60,968 | 30,391 | 15,946 |
| Operating loss | (89,286) | (60,968) | (30,391) | (15,424) |
| Other income (expenses): | | | | |
| Other income | 3,998 | 888 | 182 | 18 |
| Change in fair value of warrant liability | — | (41) | (82) | (85) |
| Change in fair value of Series B purchase option liability | — | — | — | (4,772) |
| Total other income (expense), net | 3,998 | 847 | 100 | (4,839) |
| Net loss and comprehensive loss | (85,288) | (60,121) | (30,291) | (20,263) |
| Accretion of redeemable convertible preferred stock(1) | — | (4,757) | (4,405) | (1,427) |
| Net loss attributable to common stockholders | (85,288) | (64,878) | (34,696) | (21,690) |
| Basic and diluted net loss per share(2) | $ (2.56) | $ (3.57) | $ (23.33) | $ (16.13) |
| Weighted average shares outstanding, basic and diluted(2) | 33,316,719 | 18,197,970 | 1,486,986 | 1,344,584 |

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 |
| | (in thousands) | | | |
| Balance Sheet Data: | | | | |
| Cash, cash equivalents and short-term investments | $ 369,290 | $ 103,812 | $ 47,305 | $ 22,938 |
| Working capital(3) | 357,771 | 92,957 | 42,276 | 21,582 |
| Total assets | 371,270 | 105,171 | 48,212 | 23,897 |
| Redeemable convertible preferred stock | — | — | 107,580 | 53,424 |
| Total stockholders' equity/(deficit) | 358,820 | 93,388 | (64,993) | (31,695) |

(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 9 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 clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. Our product portfolio is built on a drug discovery platform that targets key cellular pathways with proprietary medicinal chemistry. Our therapies are designed to enable more effective combination treatment strategies and improve outcomes for patients across multiple oncology indications.

**Product Pipeline**

Our product pipeline includes three clinical product candidates with the potential to significantly improve the treatment of patients with cancer. Two of our three clinical candidates, trilaciclib and lerociclib, are based on our core understanding of cyclin-dependent kinases 4 and 6, or CDK4/6, a pair of proteins that play an important role in the growth and proliferation of all human cells. G1T48, our third product candidate, is the first candidate to advance into clinical trials from our oral selective estrogen receptor degrader (SERD) program. G1T48 is a potential first-in-class oral SERD which we plan to develop as a monotherapy and in combination with other agents, including lerociclib, for the treatment of estrogen receptor-positive (ER+), human epidermal growth factor receptor-negative (HER2-) breast cancer. We own the global rights to all three of our product candidates.

## G1 Therapeutics Product Pipeline

| Candidate | Target | Method of Action (MOA) | Clinical Status | Global Rights |
|---|---|---|---|---|
| trilaciclib | CDK4/6 | Short-acting intravenous CDK4/6 inhibitor<br>Preserves HSPC and immune system function | Phase 2 | |
| lerociclib | CDK4/6 | Oral CDK4/6 inhibitor<br>Inhibits tumor proliferation and growth | Phase 1/2 | |
| G1T48 | Estrogen Receptor | Oral selective estrogen receptor degrader (SERD)<br>Inhibits estrogen receptor driven tumor proliferation | Phase 1 | |

**Trilaciclib: our novel approach to preserve HSPCs from damage by chemotherapy**

Trilaciclib is a first-in-class, short-acting CDK4/6 inhibitor which we are developing to be administered intravenously prior to chemotherapy. In preclinical studies, administration of trilaciclib prior to chemotherapy has been shown to induce transient cell-cycle arrest of HSPCs, protect HSPCs from chemotherapy-induced damage, preserve bone marrow and immune system function, 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.

*Ongoing Phase 1b/2 clinical trial in first-line treatment of SCLC*

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, myelopreservation, 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 the 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 multi-lineage myelopreservation data from the Phase 2 segment of the trial in March 2018, with additional data from the trial presented at the 2018 European Society of Medical Oncology (ESMO) Congress.

*Ongoing Phase 1b/2 clinical trial in second/third-line treatment of SCLC*

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, myelopreservation, 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 multi-lineage myelopreservation data in the fourth quarter of 2018. We expect to report additional anti-tumor efficacy data in 2019.

*Ongoing Phase 2 clinical trial in first-line treatment of SCLC with a checkpoint inhibitor*

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, overall survival, myelopreservation, PK, and anti-tumor activity of trilaciclib in combination with a checkpoint inhibitor Tecentriq and chemotherapy. We completed enrollment in the first quarter of 2018. We reported positive multi-lineage myelopreservation data and preliminary progression free survival (PFS) in November 2018. We expect to report mature additional anti-tumor efficacy data in the second-half of 2019.

*Ongoing 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, myelopreservation, PK, and anti-tumor activity of trilaciclib in combination with the existing chemotherapy standard of care regimen of gemcitabine and carboplatin. We completed enrollment in the second-quarter of 2018. At the December 2018 San Antonio Breast Cancer Symposium (SABCS), we presented preliminary data demonstrating improvement in progression-free survival (PFS). We expect to report mature additional anti-tumor efficacy data in the second-half of 2019.

**Lerociclib: Our potential best-in-class CDK4/6 inhibitor for patients with CDK4/6-dependent tumors**

Lerociclib, our second clinical-stage candidate, is a potential best-in-class oral CDK4/6 inhibitor, to be used in combination with other targeted therapies to treat multiple cancers. We rationally designed lerociclib to improve upon and address the shortcomings of the approved CDK4/6 inhibitors Ibrance, Kisqali and Verzenio. Our preclinical data and early human clinical data indicate the potential for continuous daily dosing, less dose-limiting neutropenia, and improved tolerability. A Phase 1 trial of lerociclib in 75 healthy volunteers showed a favorable safety profile, and we initiated a Phase 1b/2a trial in ER+, HER2- breast cancer in January 2017. Our

plans for lerociclib include combinations in other cancers, such as non-small cell lung cancer, or NSCLC, where we initiated a Phase 1b/2 trial in 2018 in combination with the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, Tagrisso. We believe that lerociclib has the potential to be the backbone therapy of multiple combination targeted therapy regimens.

*Completed Phase 1 clinical trial*

In the fourth quarter of 2016, we completed a Phase 1 clinical trial of lerociclib in 75 healthy volunteers in the Netherlands. This was a single ascending dose, placebo-controlled trial testing doses of 3 to 600 mg. In addition, lerociclib was dosed at 200 and 300 mg twice a day, 300 mg with and without food, and 300 mg as an oral solution. The goals of the clinical trial were to obtain PK and safety data to inform appropriate starting dose(s) for studies in patients. There were no DLTs, SAEs, or grade 3/4 AEs reported in this study.

*Ongoing Phase 1b/2a clinical trial in ER+, HER2- breast cancer*

In January 2017, we initiated a Phase 1b/2a trial in ER+, HER2- breast cancer patients in combination with Faslodex, an FDA-approved SERD. The Phase 1b segment of the trial enrolled 46 patients in Europe. The goals of the clinical trial are to evaluate the safety, PK, and anti-tumor activity of lerociclib in combination with Faslodex and to determine the dose to be used in future trials. The Phase 1b segment of the trial is open-label and consists of two arms, with lerociclib dosed continuously without a holiday, either once a day or twice a day in combination with Faslodex. The Phase 2a segment of the trial is currently ongoing. All patients in the trial are being administered lerociclib orally continuously without a treatment holiday and IM Faslodex per the label.

We reported positive preliminary safety and efficacy Phase 1b data at the 2018 ASCO annual meeting. Lerociclib has a shorter half-life and larger volume of distribution than Ibrance and Kisqali and is not expected to show drug accumulation. All of the enrolled patients had a decline in neutrophil counts, which was expected due to a mechanism-based decrease in neutrophil production caused by lerociclib, which also occurs with other CDK4/6 inhibitors such as Ibrance. No cardiovascular or liver side effects have been reported so far and there have been no lerociclib-related SAEs. The incidence of gastrointestinal AEs reported so far are similar to Ibrance and Kisqali and less than Verzenio. These early clinical data indicate the potential for continuous daily dosing of lerociclib in combination with Faslodex without a dose-holiday, and the potential for improved tolerability compared to other marketed CDK4/6 inhibitors.

*Ongoing Phase 1b/2 clinical trial in Non-Small Cell Lung Cancer (NSCLC) in combination with Tagrisso*

In the first quarter of 2018, we initiated a Phase 1b/2 clinical trial in EGFR-mutant NSCLC patients in combination with Tagrisso, and FDA-approved epidermal growth factor receptor tyrosine kinase inhibitor. The goals of the clinical trial are to evaluate the safety, PK, and anti-tumor activity of lerociclib in combination with Tagrisso and to determine the dose to be used in future trials.

**G1T48: Our oral SERD**

G1T48 is a potential first/best in-class oral SERD, which we plan to initially develop as a monotherapy and in combination with lerociclib for the treatment of ER+, HER2- breast cancer. We believe we are in a unique position as the only emerging biopharmaceutical company with a wholly owned, proprietary combination of an oral SERD and an oral CDK4/6 inhibitor, a validated regimen in ER+, HER2- breast cancer. Based on compelling preclinical efficacy and safety data, we filed an Investigational New Drug application (IND) with the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2017. We initiated a clinical trial in 2018 and expect to report preliminary Phase 1 data in the second-half of 2019.

**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. We do not have any products approved for sale and have not generated any revenues from product sales. We recorded $0 million of revenue for the years ended December 31, 2018, 2017 and 2016, respectively. We do not expect to generate revenue in the foreseeable future. To date, we have financed our operations primarily through public offerings of equity securities and private placements of convertible debt and equity securities. From inception through December 31, 2018, we raised an aggregate of $574.8 million to fund our operations.

As of December 31, 2018, we had cash and cash equivalents of $369.3 million. Since inception, we have incurred net losses. Our net losses were $85.3 million, $60.1 million and $30.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of $214.4 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative expenses associated with our

operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We expect our expenses will increase substantially in connection with our ongoing activities as we:

- continue development of our product candidates, including initiating additional clinical trials of trilaciclib, lerociclib and G1T48;
- identify and develop new product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any 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
- incur increased costs as a result of operating as a public company.

**License agreement with the University of Illinois**

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 G1T48, 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 $125 thousand, of which $75 thousand was incurred during 2018 with the initial dosing of the first patient in the Phase 1 trial for G1T48. We will also be responsible for any future patent prosecution costs that may arise. See “Business—Intellectual Property—Exclusive License for G1T48.”

**Financial operations overview**

***Revenues***

To date, we have not generated any revenues from the commercial sale of approved products or out-licensing of our product candidates, and we do not expect to generate substantial revenue from the commercial sale of our products for the foreseeable future, if ever. In the future, we will seek to generate revenue primarily from product sales and, potentially, regional or global collaborations with strategic partners. We have received all of our revenues to date from government grants related to our research.

***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 2016, we had two clinical-stage product candidates, trilaciclib and lerociclib. In 2017, we had ongoing clinical trials for two of our product candidates, trilaciclib and lerociclib, and began incurring costs related to our G1T48 product candidate as we prepared to initiate a clinical trial in 2018. In 2018, we had three clinical-stage product candidates, trilaciclib, lerociclib and G1T48.

***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 potential commercialization of our product candidates.

We expect to continue to incur additional general and administrative expenses in 2019 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 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 the change in fair value of warrant liabilities and other liabilities.

***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.

**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.

***Accrued research and development expenses***

As part of the process of preparing our financial statements, we are required to estimate and accrue expenses, the largest of which is related to accrued research and development expenses. This process for estimating and accruing expenses involves reviewing contracts and purchase orders, identifying services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual costs.

Costs for preclinical study and 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 expenses 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.

***Warrant liability***

Warrants to purchase our preferred stock have been classified as liabilities and recorded at their estimated fair value. In each reporting period, any change in fair value of the warrants has been recorded as expense in the case of an increase in fair value and income in the case of a decrease in fair value. We used significant assumptions in estimating the fair value of our warrant liability including the estimated volatility, risk free interest rate, estimated fair value of our redeemable convertible preferred shares and the estimated life of the warrant. These assumptions were used in our option pricing method and the probability weighted expected return method, a blend of which were considered in establishing fair value. Following the initial public offering in May 2017, the warrant liabilities no longer exist and are therefore no longer reflected on the balance sheets presented herein.

***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 recognize compensation costs related to stock options granted to non-employees based on the estimated fair value of the awards on the date of grant in the same manner as we do options for employees; however, the fair value of the stock options granted to non-employees is re-measured each reporting period until the service is complete, and the resulting increase or decrease in value, if any, is recognized as expense or income, respectively, during the period the related services are rendered. Beginning in 2019, the fair value of non-employee stock options will no longer be re-measured each reporting period in accordance with the implementation of ASU No. 2018-07.

We recorded non-cash stock-based compensation expense for employee and non-employee stock option grants of $10.2 million, $3.4 million and $1.4 million for the years ended December 31, 2018, 2017 and 2016, 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; 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 8 – Stock Option Plan" 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, 2018, 2017 and 2016.

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.

As of December 31, 2018, we had federal and state operating loss carryforwards of approximately $191.5 million available to reduce future taxable income that will begin to expire in 2024. As of December 31, 2018, we also had research and development (R&D) tax credit carryforwards of approximately $7.5 million for federal purposes available to offset future income tax.

Utilization of the net operating loss carryforwards may be subject to a substantial annual limitation due to the ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization. An analysis to determine the limitation of the net operating loss carryforwards has not been performed.

On December 22, 2017, the Tax Cuts and Jobs Act ("Tax Act") was signed into law. As of December 31, 2018, the Company has completed its accounting for all tax effects related to the enactment of the Tax Act. As of December 31, 2017, the Company estimated the remeasurement of its net deferred tax asset based on the 21% federal corporate income tax rate. The remeasurement is no longer provisional and during the year ended December 31, 2018, there was no change from the previously recorded provisional amount.

**Results of operations**

***Comparison of the year ended December 31, 2018 and December 31, 2017***

| | Year Ended December 31, | | Change |
|---|---|---|---|
| | 2018 | 2017 | $ |
| | | (in thousands) | |
| Revenue | $ — | $ — | $ — |
| Operating Expenses: | | | |
| Research and Development | 70,683 | 53,881 | 16,802 |
| General and Administrative | 18,603 | 7,087 | 11,516 |
| Total Operating Expenses | 89,286 | 60,968 | 28,318 |
| Loss from Operations | (89,286) | (60,968) | (28,318) |
| Other Income | 3,998 | 847 | 3,151 |
| Net Loss | $ (85,288) | $ (60,121) | $ (25,167) |

*Revenue*

Revenue was $0 for the years ended December 31, 2018 and December 31, 2017.

*Research and development*

Research and development expenses were $70.7 million for the year ended December 31, 2018 as compared to $53.9 million for the year ended December 31, 2017. The increase of $16.8 million, or 31%, was primarily due to an increase of $14.2 million in our clinical program costs which reflects increased costs in our ongoing clinical trials, as well as increased headcount-related expenses to support these trials. The increase in research and development expenses was also due to an increase in costs for manufacturing of pharmaceutical active ingredient and drug product to support our clinical trials, offset by a decrease in external costs related to preclinical development. The following table summarizes our research and development expenses allocated to trilaciclib, lerociclib and G1T48, and unallocated research and development expenses for the periods indicated:

| | Year Ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| | (in thousands) | |
| Clinical Expenses—trilaciclib | $ 35,116 | $ 26,801 |
| Clinical Expenses—lerociclib | 8,383 | 4,336 |
| Clinical Expenses—G1T48 | 2,251 | 366 |
| Chemical Manufacturing and Development | 17,323 | 13,142 |
| Discovery and Pre-clinical Expenses | 7,610 | 9,236 |
| Total Research and Development Expenses | $ 70,683 | $ 53,881 |

*General and administrative*

General and administrative expenses were $18.6 million for the year ended December 31, 2018 as compared to $7.1 million for the year ended December 31, 2017. The increase of $11.5 million, or 162%, was due to an increase of $7.6 million in personnel related costs due to increased headcount and non-cash stock option expense charges, and an increase of $3.9 million in professional services, insurance, and other administrative costs necessary to support our operations as a public company.

*Total other income (expense), net*

Total other income, net was $4.0 million for the year ended December 31, 2018 as compared to $0.8 million for the year ended December 31, 2017. The increase in income of $3.2 million was due to additional interest income earned on a higher balance of cash and cash equivalents during the year ended December 31, 2018 as compared to the year ended December 31, 2017.

***Comparison of the year ended December 31, 2017 and December 31, 2016***

| | Year Ended December 31, | | Change |
|---|---|---|---|
| | 2017 | 2016 | $ |
| | | (in thousands) | |
| Revenue | $ — | $ — | $ — |
| Operating Expenses: | | | |
| Research and Development | 53,881 | 25,161 | 28,720 |
| General and Administrative | 7,087 | 5,230 | 1,857 |
| Total Operating Expenses | 60,968 | 30,391 | 30,577 |
| Loss from Operations | (60,968) | (30,391) | (30,577) |
| Other Income | 847 | 100 | 747 |
| Net Loss | $ (60,121) | $ (30,291) | $ (29,830) |

*Revenue*

Revenue was $0 for the years ended December 31, 2017 and December 31, 2016.

*Research and development*

Research and development expenses were $53.9 million for the year ended December 31, 2017 as compared to $25.2 million for the year ended December 31, 2016. The increase of $28.7 million, or 114%, was primarily due to an increase of $16.3 million in our clinical program costs which reflects increased costs in our ongoing clinical trials and initiation of our trial in SCLC with Tecentriq, as well as increased headcount-related expenses to support these trials. The increase in research and development expenses was also due to an increase in costs for manufacturing of pharmaceutical active ingredient and drug product to support our clinical trials and an increase in external costs related to preclinical development. The following table summarizes our research and development expenses allocated to trilaciclib, lerociclib and G1T48, and unallocated research and development expenses for the periods indicated:

| | Year Ended December 31, | |
|---|---|---|
| | 2017 | 2016 |
| | (in thousands) | |
| Clinical Expenses—trilaciclib | $ 26,801 | $ 11,693 |
| Clinical Expenses—G1T38 | 4,336 | 3,504 |
| Clinical Expenses—G1T48 | 366 | — |
| Chemical Manufacturing and Development | 13,142 | 4,967 |
| Discovery and Pre-clinical Expenses | 9,236 | 4,997 |
| Total Research and Development Expenses | $ 53,881 | $ 25,161 |

*General and administrative*

General and administrative expenses were $7.1 million for the year ended December 31, 2017 as compared to $5.2 million for the year ended December 31, 2016. The increase of $1.9 million, or 36%, was due to an increase of $1.4 million in personnel related costs as a result of headcount-related costs, an increase of $1.5 million in professional services, insurance, board compensation and other

administrative costs necessary to support our operations as a public company and offset by a decrease of $1.0 million in transaction related costs from our deferred public offering.

*Total other income (expense), net*

Total other income, net was $0.8 million for the year ended December 31, 2017 as compared to $0.1 million for the year ended December 31, 2016. The increase in income of $0.7 million was due to additional interest income earned on a higher balance of cash and cash equivalents during the year ended December 31, 2017 as compared to the year ended December 31, 2016.

**Liquidity and Capital Resources**

We have incurred significant operating losses since our inception. We incurred net losses of $85.3 million for the year ended December 31, 2018, $60.1 million for the year ended December 31, 2017, and $30.3 million for the year ended December 31, 2016. As of December 31, 2018, we had an accumulated deficit of $214.4 million. Our product candidates span a range from preclinical development to Phase 2 clinical trials, and it may be several years, if ever, before we have a product candidate ready for commercialization. To date, we have financed our operations primarily through sales of our preferred and common stock. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future.

*Initial public offering*

On May 22, 2017, we closed our IPO of 7,781,564 shares of common stock at a public offering price of $15 per share, including 781,564 shares of common stock issued upon exercise by the underwriters of their option to purchase additional shares. The gross proceeds from the IPO were $116.7 million and net proceeds were $107.1 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

*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. As of December 31, 2018 we have remaining authorization to sell up to $88.2 million under this 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.

As of December 31, 2018, we had cash, cash equivalents and short-term investments of $369.3 million. 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. In order to complete the process of obtaining regulatory approval for our product candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding.

***Cash flows***

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

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | | (in thousands) | |
| Net cash used in operating activities | $ (74,307) | $ (50,519) | $ (25,141) |
| Net cash used in investing activities | (709) | (294) | (250) |
| Net cash provided by financing activities | 340,494 | 107,320 | 49,758 |
| Net increase in cash and cash equivalents | $ 265,478 | $ 56,507 | $ 24,367 |

*Net cash used in operating activities*

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.

During the year ended December 31, 2017, net cash used in operating activities was $50.5 million, which consisted of a net loss of $60.1 million, partially offset by non-cash stock compensation of $3.4 million, working capital adjustments of $6.1 million and $0.1 million of depreciation expense.

During the year ended December 31, 2016, net cash used in operating activities was $25.1 million, which consisted of a net loss of $30.3 million, partially offset by non-cash stock compensation expense of $1.4 million, working capital adjustments of $3.7 million and $0.1 million of depreciation expense.

*Net cash used in investing activities*

Net cash used in investing activities was $0.7 million, $0.3 million and $0.3 million for the years ended December 31, 2018, 2017 and 2016, 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, 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.

During the year ended December 31, 2017, net cash provided by financing activities was $107.3 million, consisting of $107.1 million of net proceeds from our IPO and $0.2 million of proceeds from the exercise of stock options and warrants.

During the year ended December 31, 2016, net cash provided by financing activities was $49.8 million, consisting of $50.0 million in proceeds from the issuance of Series C preferred stock, offset by $0.2 million of issuance costs.

***Operating capital requirements and plan of operations***

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. 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 any approved products. 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. In order to complete the process of obtaining regulatory approval for our product

candidates and to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding.

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 G1T48, 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, should any of our product candidates receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

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. 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 and operating lease commitments. The following table summarizes these contractual obligations as of December 31, 2018:

| | 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) | $ 13,814 | $ 680 | $ 3,387 | $ 3,592 | $ 6,155 |
| Total contractual obligations(2) | $ 13,814 | $ 680 | $ 3,387 | $ 3,592 | $ 6,155 |

(1) Represents future minimum lease payments under the non-cancelable lease for our headquarters in Research Triangle Park, NC and our estimated future minimum lease payments for the new office space. The lease for the new office space was signed in November 2018 for 60,000 square feet of laboratory space and office space in Research Triangle Park, NC. The term of the

lease agreement will be 8 years from the commencement date for the initial term, currently estimated to begin in the third quarter of 2019, with the Company having the option to renew for an additional 5 years. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) 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, 2018, 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 G1T48 with the University of Illinois that are based on the progress of G1T48, as these payments are not determinable.

**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.

**JOBS Act: emerging growth company status**

As of the year ended December 31, 2018, we ceased to be an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, since the market value of our common stock held by non-affiliates exceeded $700 million as of June 30, 2018. As a result, beginning with this Annual Report on Form 10-K for the year ended December 31, 2018, we are subject to Section 404(b) of the Sarbanes-Oxley Act, which requires that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting, included herein.

**Recent Accounting Pronouncements**

See Note 2 to our consolidated financial statements included elsewhere in this report regarding the impact of certain recent accounting pronouncements on our consolidated financial statements.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We had cash and cash equivalents of $369.3 million as of December 31, 2018, 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 had no outstanding debt as December 31, 2018.

**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, 2018, 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, 2018, our disclosure controls and procedures were effective at the reasonable assurance level.

**Changes in Internal Controls Over Financial Reporting**

There have been no changes in our internal control over financial reporting during the quarter ended December 31, 2018 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, 2018.

The effectiveness of our internal control over financial reporting as of December 31, 2018, 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 2019 Annual Meeting of Stockholders, which will be filed with the SEC within 120 days after the end of our 2018 fiscal year pursuant to Regulation 14A for our 2019 Annual Meeting of Stockholders (the "Proxy Statement"), under the captions "Management and Corporate Governance," "Code of Conduct and Ethics," and "Section 16(a) Beneficial Ownership Reporting Compliance."

**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*.

**INDEX TO FINANCIAL STATEMENTS**



(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 | 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* | 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. |
| 10.4* | 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. |

| | |
|---|---|
| 10.5* | 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. |
| 10.6* | 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. |
| 10.7* | Director Agreement, by and between the Registrant and Seth A. Rudnick, M.D., dated July 15, 2016, filed as Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference. |
| 10.8* | Advisory Board Members Agreement, by and between the Registrant and Seth A. Rudnick, M.D., dated July 15, 2016, filed as Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference. |
| 10.9* | Advisory Board Members Agreement, by and between the Registrant and Seth A. Rudnick, M.D., dated July 27, 2018, filed as Exhibit 10.5 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. |
| 10.10* | 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. |
| 10.11* | Employment Agreement by and between the Registrant and John Demaree, dated as of July 3, 2018, filed as Exhibit 10.3 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. |
| 10.12* | 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. |
| 10.13* | 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. |
| 10.14* | 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), and incorporated herein by reference. |
| 10.15* | Employment Agreement by and between the Registrant and Barclay A. Phillips, dated as of November 13, 2017, filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on November 13, 2017 (File No. 001-38096), and incorporated herein by reference. |
| 10.16* | Non-Qualified Stock Option Agreement by and between the Registrant and Barclay A. Phillips, dated December 6, 2017, filed as Exhibit 10.18 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2017 filed on February 21, 2018 (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 | XBRL Instance Document |
| 101.SCH | XBRL Taxonomy Extension Schema Document |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document |

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* 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 28, 2019

By: /s/ Mark A. Velleca
**Mark A. Velleca, M.D., Ph.D.**
**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/ Mark A. Velleca<br>**Mark A. Velleca, M.D., Ph.D.** | President, Chief Executive Officer and Director<br>(Principal Executive Officer) | February 28, 2019 |
| /s/ Barclay A. Phillips<br>**Barclay A. Phillips** | Chief Financial Officer and Senior Vice President of Corporate Development<br>(Principal Financial Officer) | February 28, 2019 |
| /s/ Jennifer K. Moses<br>**Jennifer K. Moses** | Vice President of Finance and Accounting<br>(Principal Accounting Officer) | February 28, 2019 |
| /s/ Fredric N. Eshelman<br>**Fredric N. Eshelman, Pharm.D.** | Director | February 28, 2019 |
| /s/ Willie A. Deese<br>**Willie A. Deese** | Director | February 28, 2019 |
| /s/ Glenn P. Muir<br>**Glenn P. Muir** | Director | February 28, 2019 |
| /s/ Garry A. Nicholson<br>**Garry A. Nicholson** | Director | February 28, 2019 |
| /s/ Seth A. Rudnick<br>**Seth A. Rudnick, Ph.D.** | Director | February 28, 2019 |
| **/s/** Cynthia L. Schwalm<br>**Cynthia L. Schwalm** | Director | February 28, 2019 |
| /s/ Andrew P. Witty<br>**Sir Andrew P. Witty** | Director | February 28, 2019 |

## 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, 2018 and 2017, 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, 2018, 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, 2018, 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, 2018 and 2017**,** and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

***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.

/s/ PricewaterhouseCoopers LLP
Raleigh, North Carolina
February 28, 2019

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, 2018 | December 31, 2017 |
|---|---|---|
| **Assets** | | |
| Current assets | | |
| Cash and cash equivalents | $ 369,290 | $ 103,812 |
| Prepaid expenses and other current assets | 843 | 849 |
| Total current assets | 370,133 | 104,661 |
| Property and equipment, net | 1,137 | 510 |
| Total assets | $ 371,270 | $ 105,171 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities | | |
| Accounts payable | $ 3,377 | $ 4,184 |
| Accrued expenses | 8,985 | 7,520 |
| Total current liabilities | 12,362 | 11,704 |
| Other non-current liabilities | 88 | 79 |
| Total liabilities | 12,450 | 11,783 |
| Commitments and contingencies | | |
| Stockholders' equity (deficit) | | |
| Common stock, $0.0001 par value, 120,000,000 shares authorized as of December 31, 2018 and December 31, 2017, respectively; 37,268,792 and 28,420,511 shares issued as of December 31, 2018 and December 31, 2017, respectively; 37,242,126 and 28,393,845 shares outstanding as of December 31, 2018 and December 31, 2017, respectively | 4 | 3 |
| Treasury stock, 26,666 shares | (8) | (8) |
| Additional paid-in capital | 573,230 | 222,511 |
| Accumulated deficit | (214,406) | (129,118) |
| Total stockholders' equity | 358,820 | 93,388 |
| Total liabilities and equity | $ 371,270 | $ 105,171 |

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, | | |
|---|---|---|---|
| | **2018** | **2017** | **2016** |
| Grant revenue | $ — | $ — | $ — |
| Operating expenses | | | |
| Research and development | 70,683 | 53,881 | 25,161 |
| General and administrative | 18,603 | 7,087 | 5,230 |
| Total operating expenses | 89,286 | 60,968 | 30,391 |
| Operating loss | (89,286) | (60,968) | (30,391) |
| Other income (expense) | | | |
| Other income | 3,998 | 888 | 182 |
| Change in fair value in warrant liability and other liabilities | — | (41) | (82) |
| Total other income, net | 3,998 | 847 | 100 |
| Net loss | $ (85,288) | $ (60,121) | $ (30,291) |
| Accretion of redeemable convertible preferred stock | — | (4,757) | (4,405) |
| Net loss attributable to common stockholders | $ (85,288) | $ (64,878) | $ (34,696) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (2.56) | $ (3.57) | $ (23.33) |
| Weighted average common shares outstanding, basic and diluted | 33,316,719 | 18,197,970 | 1,486,986 |

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)**

| | Preferred stock series C | | Preferred stock series B | | Preferred stock series A | | Preferred stock series 1 | | Common stock | | Treasury stock | | Additional paid-in capital | Accumulated deficit | Total stock-holders' equity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | Shares | Amount | Shares | Amount | Shares | Amount | Shares | Amount | | | |
| **Balance at December 31, 2015** | **—** | **$ —** | **7,642,734** | **$ 38,692** | **4,998,895** | **$ 13,801** | **682,026** | **$ 931** | **1,487,219** | **$ —** | **(26,666)** | **$ (8)** | **$ —** | **$ (31,686)** | **$ (31,694)** |
| Issuance of Series C redeemable convertible preferred stock | 5,609,398 | 50,000 | — | — | — | — | — | — | — | — | — | — | — | — | — |
| Accretion of redeemable, convertible preferred stock | — | 1,673 | — | 1,663 | — | 630 | — | 439 | — | — | — | — | (1,397) | (3,008) | (4,405) |
| Exercise of common stock options | — | — | — | — | — | — | — | — | 17,728 | — | — | — | 6 | — | 6 |
| Stock-based compensation | — | — | — | — | — | — | — | — | — | — | — | — | 1,391 | — | 1,391 |
| Stock financing costs | — | (249) | — | — | — | — | — | — | — | — | — | — | — | — | — |
| Net loss during year | — | — | — | — | — | — | — | — | — | — | — | — | — | (30,291) | (30,291) |
| **Balance at December 31, 2016** | **5,609,398** | **$ 51,424** | **7,642,734** | **$ 40,355** | **4,998,895** | **$ 14,431** | **682,026** | **$ 1,370** | **1,504,947** | **$ —** | **(26,666)** | **$ (8)** | **$ —** | **$ (64,985)** | **$ (64,993)** |
| Accretion of redeemable, convertible preferred stock | — | 3,732 | — | 620 | — | 235 | — | 171 | — | — | — | — | (745) | (4,012) | (4,757) |
| Initial public offering | — | — | — | — | — | — | — | — | 7,781,564 | 1 | — | — | 108,502 | — | 108,503 |
| Automatic conversion of preferred stock | (5,609,398) | (55,156) | (7,642,734) | (40,975) | (4,998,895) | (14,666) | (682,026) | (1,541) | 18,933,053 | 2 | — | — | 112,335 | — | 112,337 |
| Automatic conversion of preferred warrants | — | — | — | — | — | — | — | — | — | — | — | — | 208 | — | 208 |
| Exercise of common stock options | — | — | — | — | — | — | — | — | 160,579 | — | — | — | 214 | — | 214 |
| Exercise of common stock warrants | — | — | — | — | — | — | — | — | 40,368 | — | — | — | 1 | — | 1 |
| Stock-based compensation | — | — | — | — | — | — | — | — | — | — | — | — | 3,394 | — | 3,394 |
| IPO financing costs | — | — | — | — | — | — | — | — | — | — | — | — | (1,398) | — | (1,398) |
| Net loss during year | — | — | — | — | — | — | — | — | — | — | — | — | — | (60,121) | (60,121) |
| **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** |

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, | | |
|---|---|---|---|
| | **2018** | **2017** | **2016** |
| **Cash flows from operating activities** | | | |
| Net loss | $ (85,288) | $ (60,121) | $ (30,291) |
| Adjustments to reconcile net loss to net cash used in operating activities | | | |
| Depreciation and amortization | 175 | 89 | 67 |
| Stock-based compensation | 10,225 | 3,394 | 1,391 |
| Gain/loss on disposal of property and equipment | 8 | 6 | 18 |
| Increase in fair value of warrant activity | — | 41 | 82 |
| Change in operating assets and liabilities | | | |
| Prepaid expenses and other assets | 113 | (253) | 216 |
| Accounts payable | (1,002) | 1,578 | 1,477 |
| Accrued Expenses | 1,446 | 4,709 | 1,871 |
| Deferred Rent | 16 | 38 | 28 |
| Net cash used in operating activities | (74,307) | (50,519) | (25,141) |
| **Cash flows from investing activities** | | | |
| Purchases of property and equipment | (709) | (294) | (250) |
| Net cash used in investing activities | (709) | (294) | (250) |
| **Cash flows from financing activities** | | | |
| Proceeds from stock options and warrants exercised | 1,797 | 215 | 7 |
| Proceeds from Series C preferred stock | — | — | 50,000 |
| Issuance costs for preferred share financings | — | — | (249) |
| Proceeds from public offering, net of underwriting fees and commissions | 339,589 | 108,503 | — |
| Payment of public offering costs | (892) | (1,398) | — |
| Net cash provided by financing activities | 340,494 | 107,320 | 49,758 |
| Net change in cash and cash equivalents | 265,478 | 56,507 | 24,367 |
| **Cash and cash equivalents** | | | |
| Beginning of period | 103,812 | 47,305 | 22,938 |
| End of period | $ 369,290 | $ 103,812 | $ 47,305 |
| **Non-cash investing and financing activities** | | | |
| Accretion of redeemable convertible preferred stock | $ — | $ 4,757 | $ 4,405 |
| Conversion of preferred stock and preferred warrants to common stock and common warrants | $ — | $ 112,545 | $ — |
| Purchases of equipment in accounts payable and accrued expenses | $ 100 | $ — | $ — |
| Prepaid project costs in accounts payable and accrued expenses | $ 107 | $ — | $ — |

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

## 1. Description of business

G1 Therapeutics, Inc. (the "Company") is a clinical-stage biopharmaceutical company based in Research Triangle Park, North Carolina focused on the discovery, development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. The Company was incorporated on May 19, 2008 in the state of Delaware.

The Company's product pipeline includes three clinical candidates with the potential to significantly improve the treatment of patients with cancer. Two of the three clinical candidates, trilaciclib and lerociclib, are based on the Company's core understanding of cyclin-dependent kinases 4 and 6, or CDK4/6, a pair of proteins that play an important role in the growth and proliferation of all human cells. G1T48, the Company's third product candidate, is the first candidate to advance into clinical trials from their oral selective estrogen receptor degrader discovery (SERD) program. G1T48 is a potential first-in-class oral SERD, which the Company plans to develop as a monotherapy and in combination with other agents, including lerociclib for the treatment of estrogen receptor-positive, human epidermal growth factor receptor-negative breast cancer, or ER+, HER2- breast cancer. The Company owns the global rights to all of their product candidates.

Trilaciclib, the Company's most advanced clinical-stage candidate, is a first-in-class, short-acting CDK4/6 inhibitor designed to preserve hematopoietic stem cell and progenitor cells andimmune system function during chemotherapy. Based on compelling response rates and favorable tolerability shown in early-stage trials, trilaciclib is currently being evaluated in four randomized Phase 1b/2 trials: two in patients with small cell lung cancer, or SCLC, an additional Phase 2 trial in combination with Tecentriq in SCLC and a Phase 2 in patients with metastatic triple-negative breast cancer, or mTNBC.

Lerociclib, the Company's second clinical-stage candidate, is a potential best-in-class oral CDK4/6 inhibitor, to be used in combination with other targeted therapies to treat multiple cancers. A Phase 1 trial of lerociclib in 75 healthy volunteers showed a favorable safety profile, and the Company initiated a Phase 1/2 trial in ER+, HER2- breast cancer in January 2017. The Company's plans for lerociclib include future combinations in other cancers, such as non-small cell lung cancer, or NSCLC, where we initiated a Phase 1b/2 trial in 2018 in combination with the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, Tagrisso. We believe that lerociclib has the potential to be the backbone therapy of multiple combination targeted therapy regimens.

As part of the Company's strategy to develop wholly-owned proprietary combinations, the Company has exclusively in-licensed G1T48, a potential best-in-class oral selective estrogen receptor degrader, or SERD. The Company expects to initially develop G1T48 as a monotherapy and in combination with lerociclib for the treatment of ER+, HER2- breast cancer. The Company initiated a clinical trial in 2018 and expects to report preliminary Phase 1 data in 2019.

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, 2018, the Company had an accumulated deficit of $214.4 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, 2018, the Company had cash and cash equivalents of $369.3 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. 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").

### Reclassifications

The Company has reclassified certain prior period amounts in its statements of cash flows to conform to the current period presentation. The reclassification relates to separately presenting accounts payable, accrued expenses, and deferred rent, which were previously included in the change in accounts payable and accrued expenses caption. For the year ended December 31, 2017, the Company reclassified $1.6 million into changes in accounts payable caption, $4.7 million into changes in the accrued expenses

caption, and $38 thousand into the changes in deferred rent caption. For the year ended December 31, 2016, the Company reclassified $1.5 million into changes in accounts payable caption, $1.9 million into changes in the accrued expenses caption, and $28 thousand into the changes in deferred rent caption.

**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, warrant valuation and deferred tax asset valuation allowance.

**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, 2018 and 2017 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.

**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, 2018, 2017 and 2016, the Company's management evaluated its long-lived assets and determined no impairment charge was needed.

**Warrant liability**

Warrants to purchase the Company's redeemable convertible preferred stock were classified as liabilities and recorded at their estimated fair value. In each reporting period, any change in fair value of the warrants has been recorded as expense in the case of an increase in fair value and income in the case of a decrease in fair value.

**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, the Company estimates and accrues expenses, the largest of which is related to accrued research and development expenses. This process involves reviewing contracts and purchase orders, identifying services that have been performed 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 preclinical studies and clinical trial activities are recognized 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 expenses 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, 2018 and 2017 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, 2018 |
|---|---|---|---|---|
| **Assets** | | | | |
| Money market funds | $ 352,934 | $ — | $ — | $ 352,934 |
| Certificates of Deposit | 15,501 | — | — | 15,501 |
| **Total assets at fair value:** | $ 368,435 | $ — | $ — | $ 368,435 |

| | 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, 2017 |
|---|---|---|---|---|
| **Assets** | | | | |
| Money market funds | $ 87,694 | $ — | $ — | $ 87,694 |
| Certificates of Deposit | 15,203 | — | — | 15,203 |
| **Total assets at fair value:** | $ 102,897 | $ — | $ — | $ 102,897 |

The change in the fair value measurement using significant inputs (Level 3) is summarized below (in thousands):

| | |
|---|---|
| **Balance at December 31, 2016** | $ 167 |
| Change in fair value in warrant liability | 41 |
| Conversion of warrant to common stock warrant | (208) |
| **Balance at December 31, 2017** | $ — |
| Change in fair value in warrant liability | $ — |
| **Balance at December 31, 2018** | $ — |

**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 $1,352 thousand, $997 thousand, and $1,034 thousand for the years ended December 31, 2018, 2017 and 2016, 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, 2018 and 2017, 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, 2018 and 2017, 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.

**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.

**Redeemable convertible preferred stock**

The Company classifies its redeemable convertible preferred stock, for which the Company does not control the redemption, outside of permanent equity. The Company records redeemable convertible preferred stock at fair value upon issuance, net of any offering costs, and the carrying value is adjusted to the redemption value at the end of each reporting period. These adjustments are effected through charges against additional paid-in capital and accumulated deficit.

**Recent Accounting Pronouncements**

*Adoption of New Accounting Standards*

In May 2014, the FASB and the International Accounting Standards Board jointly issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"), which supersedes the revenue recognition requirements in ASC 605 and most industry-specific guidance. The new standard requires that an entity recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods and services. The update also requires additional disclosures about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, along with any significant judgements and assets recognized from costs incurred to obtain or fulfill a contract. ASU 2014-09 is effective for public entities for annual and interim periods within those annual periods beginning after December 15, 2017. The Company adopted this ASU on January 1, 2018. The Company's future revenue contracts and arrangements, if any, will be recognized under ASU 2014-09.

In March 2016, the FASB issued ASU 2016-09, *Compensation - Stock Compensation (Topic 718): Improvements to Employee Shared-Based Payment Accounting* ("ASU 2016-09"), which provides guidance related to how companies account for certain aspects of share-based payment awards to employees, including the accounting for income taxes, forfeitures, and statutory tax withholding requirements, as well as classification in the statement of cash flows. This ASU is effective for annual and interim periods beginning after December 15, 2016. The Company adopted ASU 2016-09 effective January 1, 2017. The adoption of this standard did not have a material impact on the Company's financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"). The FASB issued ASU 2016-15 to improve U.S. GAAP by providing guidance on the cash flow statement classification of eight specific areas where there is existing diversity in practice. The FASB expects that the guidance in this ASU will reduce the current and potential future diversity in practice in such areas. This ASU is effective for annual and interim periods beginning after December 15, 2017, with early adoption permitted. The Company adopted ASU 2016-15 on January 1, 2018. The adoption of this standard did not have a material impact on the Company's financial statements.

In May 2017, the FASB issued ASU 2017-09, *Compensation—Stock Compensation (Topic 718)*: Scope of Modification Accounting ("ASU 2017-09"). This guidance is intended to provide clarity and reduce diversity in practice as to when changes to the terms or conditions of share-based payments are accounted for as modifications. Under this new guidance, entities will apply modification accounting if the fair value, vesting conditions or classification of the award changes. This guidance will be effective for annual reporting periods beginning after December 15, 2017, including interim periods within those annual reporting periods, and early adoption is permitted. The guidance per ASU 2017-09 is to be adopted prospectively to an award modified on or after the adoption date. The Company adopted ASU 2017-09 on January 1, 2018. The adoption of this standard did not have a material impact on the Company's financial statements.

*Recently Issued Accounting Standards*

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* ("ASU 2016-02"). This guidance revises the accounting related to leases by requiring lessees to recognize a lease liability and a right-of-use asset for all leases. The new lease guidance also simplifies the accounting for sale and leaseback transactions. This ASU is effective for annual reporting periods beginning after December 15, 2018 and early adoption is permitted. In July of 2018, the FASB issued ASU No. 2018-10, *Codification Improvements to Topic 842, Leases* ("ASU 2018-10") and ASU No. 2018-11, *Leases (Topic 842): Targeted Improvements* ("ASU 2018-11") which amended certain aspects of ASU 2016-02. ASU 2018-10 amends narrow aspects of the guidance issued in the amendments in ASU 2016-02 based on comments and questions raised by stakeholders during the assessment and implementation of ASU 2016-02. ASU 2018-11 provides for another transition method in addition to the modified retrospective approach required by ASU 2016-02. This option allows entities to initially apply the new leases standard at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. We plan to adopt the ASU effective January 1, 2019 using the modified retrospective transition method and will not adjust comparative period financial information or make the new required lease disclosures for periods before the effective date. The Company is currently evaluating the impact of the adoption of these related lease standards on the Company's financial statements but will be recognizing a right-of-use asset and lease liability on our balance sheet for leases classified as operating lease. We do not anticipate an impact to our statement of operations.

In June 2018, the FASB issued ASU No. 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"). ASU 2018-07 expands the scope of Topic 718, Compensation – Stock Compensation, to include share-based payments issued to non-employees for goods or services. Consequently, non-employees and employees will be substantially aligned. ASU 2018-07 supersedes Subtopic 505-50, Equity – Equity-Based Payments to Non-Employees. The amendments are effective for fiscal years beginning after December 15, 2018. Early adoption is permitted, but not earlier than the adoption of Topic 606, Revenue from Contracts with Customers. The Company does not anticipate a material impact to the Company's financial statements as a result of the adoption of this guidance.

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. ASU 2018-15 is effective for annual and interim reporting periods beginning after December 15, 2019, and early adoption is permitted. The amendments under ASU 2018-15 may be applied either retrospectively or prospectively to all implementation costs incurred after adoption. The Company is evaluating the impact of ASU 2018-15 on its financial statements and the timing of adoption.

**3. Property and equipment**

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

| | December 31, 2018 | December 31, 2017 |
|---|---|---|
| Computer equipment | $ 246 | $ 112 |
| Laboratory equipment | 611 | 283 |
| Furniture and fixtures | 293 | 174 |
| Leasehold improvements | 238 | 121 |
| Construction in progress | 71 | 1 |
| Accumulated depreciation | (322) | (181) |
| Property and equipment, net | $ 1,137 | $ 510 |

Depreciation expenses relating to property and equipment were $175 thousand, $89 thousand, and $67 thousand for the years ended December 31, 2018, 2017 and 2016, 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 $500 thousand 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 $2,625 thousand 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 $125 thousand, of which $75 thousand was incurred and accrued during 2018 with the enrollment and dosing of the first patient in the Phase 1 trial for G1T48. 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, 2018 | December 31, 2017 |
|---|---|---|
| Accrued external research and professional fees | $ 1,591 | $ 1,402 |
| Accrued external clinical study costs | 4,692 | 4,788 |
| Accrued compensation expense | 2,693 | 1,328 |
| Deferred rent, current portion | 9 | 2 |
| Accrued expenses | $ 8,985 | $ 7,520 |

**6. Lease obligations**

**Operating lease commitments**

Pursuant to a lease dated January 10, 2014, on April 1, 2014, the Company leased office and lab space under a lease agreement with a free rent period and escalating rent payments; the lease was set to expire on July 31, 2017.

On January 27, 2016, the Company signed an amendment to the Company's existing lease to move to a larger office and lab space beginning in August 2016 with a discounted rent period and escalating rent payments; the lease 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.

On March 27, 2017, the Company signed an amendment to the Company's existing lease to lease additional, adjacent office space. Beginning August 2017, the combined space was leased with a discounted rent period and escalating rent payments. The lease is set to expire on December 31, 2022. The Company has maintained an option for a five year renewal on the combined space.

In January 2018, we signed an amendment to our current lease to secure an additional office space in our existing building. In August 2018, we began making lease payments for the combined space with a discounted rent period and escalating rent payments. The lease is set to expire on December 31, 2022. The lease maintained an option for a five year renewal on the combined space.

Rent expense amounted to $381 thousand, $252 thousand and $126 thousand for the years ended December 31, 2018, 2017 and 2016, respectively.

The following is a schedule by years of minimum future rental payments on noncancelable operating leases as of December 31, 2018 (in thousands):

| | |
|---|---|
| 2019 | $ 680 |
| 2020 | 1,427 |
| 2021 | 1,960 |
| 2022 | 2,015 |
| 2023 | 1,577 |
| Thereafter | 6,155 |
| | $ 13,814 |

In November 2018, the Company signed a new lease to secure 60,000 square feet of laboratory and office space in Research Triangle Park, NC. The term of the lease will be 8 years from the commencement date for the initial term, currently estimated to be in the third quarter of 2019, with the Company having with the option to renew for an additional 5 years. As such, the minimum future rental payments above include the estimated payments under this new lease.

## 7. Stockholders' Equity

### Redeemable convertible preferred stock

The Company has determined that the Series C, Series B, Series A and Series 1 redeemable convertible preferred stock were redeemable, after a stated period of time, based on voting thresholds that vary by stockholder class, as outlined in the Company's certificate of incorporation. The Company classified its redeemable convertible preferred stock outside of permanent equity and into mezzanine equity.

The Company recorded its redeemable convertible preferred stock at fair value upon issuance, net of any issuance costs or discounts, and the carrying value is increased by periodic accretion to its redemption value until the earliest possible date of redemption. These increases were recorded as charges against additional paid-in-capital until the additional paid-in-capital balance is reduced to zero. At that time, additional accretion adjustments were recorded as additions to accumulated deficit.

In April 2016, the Company's Board of Directors and stockholders approved the Fifth Amended and Restated Certification of Incorporation which increased the authorized number of shares of its redeemable convertible preferred stock to 57,108,717, of which 2,112,025 were be designated as Series 1 redeemable convertible preferred stock, 14,996,692 as Series A redeemable convertible preferred stock, 23,000,000 as Series B redeemable convertible preferred stock and 17,000,000 as Series C redeemable convertible preferred stock. In the second quarter of 2016, the Company authorized 16,828,217 shares of its Series C redeemable convertible preferred stock and issued 5,609,398 shares of its Series C redeemable convertible preferred stock for cash consideration at a price of $8.91 per share. Total additional proceeds amounted to $50.0 million.

Prior to the IPO, the holders of the Company's convertible preferred stock had certain voting and dividend rights, as well as liquidation preferences and conversion privileges. All rights, preferences and privileges associated with the convertible preferred stock were terminated at the time of the Company's IPO in conjunction with the conversion of all outstanding shares of convertible preferred stock into shares of common stock.

On May 22, 2017, the Company closed its IPO of 7,781,564 shares of the Company's common stock at a public offering price of $15.00 per share, including 781,564 shares of common stock issued upon exercise by the underwriters of their option to purchase additional shares. The gross proceeds from the IPO were $116.7 million and net proceeds were $107.1 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

Upon closing of the IPO, all outstanding shares of the Company's preferred stock were automatically converted into 18,933,053 shares of common stock. In connection with the IPO, the Board of Directors and the stockholders of the Company approved a one-for-three reverse stock split of the Company's common stock. The reverse stock split became effective on May 11, 2017. All share and per share amounts in the financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to accumulated deficit.

### 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 5.0 million shares of undesignated preferred stock in one or more series. As December 31, 2018, no shares of preferred stock were issued or outstanding.

### 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, 2018 and 2017, 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, 2018 and December 31, 2017 as follows:

| | December 31, 2018 | December 31, 2017 |
|---|---|---|
| Common stock options outstanding | 4,502,133 | 4,116,333 |
| Options available for grant under Equity Incentive Plans | 1,547,306 | 1,602,687 |
| | 6,049,439 | 5,719,020 |

**8. Stock option plan**

**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.

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, 2018, there were a total of 1,547,306 shares of common stock available for future issuance under the 2017 Plan.

**Stock-based Compensation**

During the years ended December 31, 2018, 2017 and 2016, the Company recorded employee share-based compensation expense of $8,157, $1,772, and $907, respectively. The Company recorded non-employee share-based compensation expense of $2,068, $1,622, and $484 during the years ended December 31, 2018, 2017 and 2016, respectively. Total share-based compensation expense included in the statements of operations is as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | | in thousands | |
| Research and development | $ 5,218 | $ 2,531 | $ 911 |
| General and administrative | 5,007 | 863 | 480 |
| Total stock-based compensation expense | $ 10,225 | $ 3,394 | $ 1,391 |

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, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Expected volatility | 74.9 - 86.5% | 74.2 - 79.3% | 74.8 - 83.9% |
| Weighted-average risk free rate | 2.3 - 3.0% | 1.9 - 2.2% | 1.2 - 2.1% |
| Dividend yield | —% | —% | —% |
| Expected term (in years) | 6.04 | 6.01 | 6.40 |
| Weighted-average grant-date fair value per share | $ 26.42 | $ 10.71 | $ 3.24 |

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.

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 2018 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, 2017** | 4,116,333 | $ 4.41 | 7.8 | $ 63,577 |
| Cancelled | (149,877) | $ 7.75 | | |
| Granted | 1,271,950 | 38.07 | | |
| Exercised | (736,273) | 2.44 | | |
| **Balance as of December 31, 2018** | 4,502,133 | $ 14.13 | 7.6 | $ 46,575 |
| Exercisable at December 31, 2018 | 2,361,694 | 3.07 | 6.5 | $ 38,285 |
| Vested at December 31, 2018 and expected to vest | 4,502,133 | 14.13 | 7.6 | $ 46,575 |

As of December 31, 2018, there was $33,984 of total unrecognized share-based compensation costs, which is expected to be recognized over a weighted-average period of 3.11 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.

**9. 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, 2018, 2017 and 2016, 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, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Stock options issued and outstanding | 4,318,731 | 3,838,358 | 3,224,682 |
| Stock warrants | — | 11,385 | 25,444 |
| | 4,318,731 | 3,849,743 | 3,250,126 |

Amounts in the table above reflect the common stock equivalents of the noted instruments.

**10. 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, 2018 and 2017, 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, 2018 and 2017, the Company had no such accruals.

The components of income tax expense (benefit) attributable to continuing operations are as follows:

| | Year ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| **Current Expense:** | | | |
| Federal | $ — | $ — | $ — |
| State | — | — | — |
| | — | — | — |
| **Deferred Expense:** | | | |
| Federal | — | — | — |
| State | — | — | — |
| | $ — | $ — | $ — |

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, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Federal income tax benefit at statutory rate: | $ (17,910) | $ (20,441) | $ (10,299) |
| Increase (reduction) in income tax resulting from: | | | |
| State Income Taxes | (1,518) | (1,623) | (397) |
| Increase in Valuation Allowance | 26,614 | 8,977 | 10,936 |
| Increase in fair value of Series B purchase option liability | — | — | — |
| Equity Financing Expenses | — | 39 | 371 |
| Stock Compensation | (3,011) | 152 | 200 |
| Research and Development Credit | (4,187) | (1,882) | (803) |
| Effect on Tax Cuts & Job Acts Rate Reduction | — | 14,770 | — |
| Other | 12 | 8 | (8) |
| | $ — | $ — | $ — |

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, 2018 and 2017 (in thousands):

| | Year ended December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Deferred tax assets | | |
| Accrued expenses | $ 1,413 | $ 1,412 |
| Deferred rent | 23 | 20 |
| Stock compensation | 2,038 | 360 |
| Charitable contributions | 2 | 2 |
| Capitalized patents and licenses | 1,544 | 1,225 |
| R&D credits | 7,521 | 3,333 |
| Net operating loss carryforwards | 43,997 | 23,556 |
| Deferred tax assets | 56,538 | 29,908 |
| Deferred tax liabilities | | |
| Property, plant and equipment, primarily due to differences in depreciation | (37) | (21) |
| Deferred tax liabilities | (37) | (21) |
| Valuation allowance | (56,501) | (29,887) |
| Net deferred tax assets | $ — | $ — |

At December 31, 2018 and December 31, 2017, 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 $29,887 at December 31, 2017 to $56,501 at December 31, 2018. 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):

| | 2018 | 2017 | 2016 |
|---|---|---|---|
| Balance at beginning of year | $ 29,887 | $ 20,910 | $ 9,974 |
| Charges to costs and expenses | 26,614 | 8,977 | 10,936 |
| Write-offs | — | — | — |
| Balance at end of year | 56,501 | 29,887 | 20,910 |

At December 31, 2018, the Company has federal net operating loss carryforwards (NOLs) of approximately $191.5 million, which are available to offset future taxable income. Of the $191.5 million available, $100.7 million will begin to expire in 2029. The remaining $90.8 million has an indefinite carryforward period. Under the 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 limitations under the Tax Act. In addition, the Company has state net operating loss carryforwards totaling approximately $191.5 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, 2018, the Company also had federal research and development (R&D) credit carryforwards of approximately $7.5 million available to offset future income tax which begin to expire in 2034.

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, 2018 and 2017, 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, 2018 and 2017, the Company had no such accruals.

On December 22, 2017, the Tax Cuts and Jobs Act ("Tax Act") was signed into law. As of December 31, 2018, the Company has completed its accounting for all tax effects related to the enactment of the Tax Act. As of December 31, 2017, the Company estimated

the remeasurement of its net deferred tax asset based on the 21% federal corporate income tax rate. The remeasurement is no longer provisional and during the year ended December 31, 2018, there was no change from the previously recorded provisional amount.

**Potential 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.

The Company has not completed a study to assess whether one or more ownership changes have occurred since the Company became a loss corporation under the definition of Section 382. If the Company has experienced an ownership change, utilization of the NOL or R&D credit carryforwards would be subject to an annual limitation, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term, tax-exempt rate, and then could be subject to additional adjustments, as required. Any such limitation may result in the expiration of a portion of the NOL or R&D credit carryforwards before utilization. Until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit under ASC-740. Any carryforwards that expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance. Due to the existence of the valuation allowance, it is not expected that any possible limitation will have an impact on the results of operations of the Company.

**11. Related party transactions**

The Company paid approximately $6 thousand, $11 thousand, $14 thousand to the Chairman of the Board of Directors for scientific advisory services outside of his role on the board of directors during the years ended December 31, 2018, 2017 and 2016, respectively.

**12. Quarterly Results of Operations (Unaudited)**

The following table contains quarterly financial information for 2018 and 2017. 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, 2018 | June 30, 2018 | September 30, 2018 | December 31, 2018 |
| Total operating expenses | $ 20,725 | $ 21,653 | $ 20,822 | $ 26,086 |
| Operating loss | (20,725) | (21,653) | (20,822) | (26,086) |
| Total other income (expense), net | 315 | 785 | 904 | 1,994 |
| Net loss | $ (20,410) | $ (20,868) | $ (19,918) | $ (24,092) |
| Net loss attributable to common stockholders | $ (20,410) | $ (20,868) | $ (19,918) | $ (24,092) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (0.70) | $ (0.64) | $ (0.59) | $ (0.65) |
| Weighted average common shares outstanding, basic and diluted | 29,360,470 | 32,781,921 | 33,829,437 | 37,203,233 |

| | March 31, 2017 | June 30, 2017 | September 30, 2017 | December 31, 2017 |
|---|---|---|---|---|
| Total operating expenses | $ 12,378 | $ 15,379 | $ 15,929 | $ 17,282 |
| Operating loss | (12,378) | (15,379) | (15,929) | (17,282) |
| Total other income (expense), net | 33 | 185 | 328 | 301 |
| Net loss and comprehensive loss | $ (12,345) | $ (15,194) | $ (15,601) | $ (16,981) |
| Accretion of redeemable convertible preferred stock | (4,468) | (289) | — | — |
| Net loss attributable to common stockholders | $ (16,813) | $ (15,483) | $ (15,601) | $ (16,981) |
| Net loss per share attributable to common stockholders, basic and diluted | $ (11.24) | $ (1.09) | $ (0.55) | $ (0.60) |
| Weighted average common shares outstanding, basic and diluted | 1,496,336 | 14,208,115 | 28,318,656 | 28,362,323 |

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

# FORM 10-K/A

**(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, 2018**

**OR**

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

**FOR THE TRANSITION PERIOD FROM TO**

**Commission File Number 001-38096**

# 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.)** |

**79 T.W. Alexander Drive 4501 Research Commons, Suite 100**
**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: Common Stock, Par Value $.0001 Per Share; Common stock traded on The Nasdaq Stock Market (trading symbol: GTHX)

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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market on June 30, 2018, was $997,145,067.

The number of shares of Registrant's Common Stock outstanding as of February 25, 2019 was 37,408,234.

**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 12, 2019, are incorporated by reference into Part III of this report.

**Explanatory Note**

G1 Therapeutics, Inc. is filing this Amendment No. 1 ("Amendment No. 1") to its Annual Report on Form 10-K for the fiscal year ended December 31, 2018 as filed with the Securities and Exchange Commission on February 28, 2019 (the "Original Form 10-K") solely to replace Exhibits 31.1 and 31.2 (the "Section 302 Certifications") included in the Original Form 10-K with corrected Section 302 Certifications. Due to an administrative error, the Section 302 Certifications in the Original Form 10-K incorrectly omitted Section 4.b). New Section 302 Certifications with Section 4.b). are filed as Exhibits 31.1 and 31.2 attached hereto.

Except as otherwise expressly noted herein, this Amendment No. 1 does not modify or update in any way the financial position, results of operations, cash flows, or other disclosure in, or exhibits to, the Original Form 10-K, nor does it reflect events occurring after the filing of the Original Form 10-K. Accordingly, this Amendment No. 1 should be read in conjunction with the Original Form 10-K.

**PART IV**

**Item 15. Exhibits, Financial Statement Schedules.**

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

(c) Exhibits.

| Exhibit Number | Description |
|---|---|
| 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. |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

G1 THERAPEUTICS, INC.

Date: April 26, 2019

By: */s/ James Stillman Hanson*

Name: James Stillman Hanson
Title: General Counsel