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, 2023

OR

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

FOR THE TRANSITION PERIOD FROM TO

Commission File Number 001-38096

G1 THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

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

700 Park Offices Drive, Suite 200
Research Triangle Park, NC 27709

(Address of principal executive offices including zip code)

Registrant's telephone number, including area code: (919) 213-9835

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

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

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

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

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

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

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

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

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

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

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant as of June 30, 2023, the last business day of the Registrant's most recently completed second fiscal quarter, was $127.5 million based on the closing price of the shares of common stock on The Nasdaq Stock Market on that date.

The number of shares of the Registrant's Common Stock outstanding as of February 26, 2024 was 52,199,394.

Auditor Firm Id:	238	Auditor Name:	PricewaterhouseCoopers LLP	Auditor Location:	New York, NY, United States

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 13, 2024, are incorporated by reference into Part III of this report. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the Registrant's fiscal year ended December 31, 2023.

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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 includes, but are not limited to, statements about:

- developments, projections, and trends relating to us, our competitors, and our industry;
- our plans for our business;
- our ability to attain profitability;
- the implementation of our business strategies, including the timing and our ability to commercialize COSELA, develop and commercialize additional indications for COSELA, including whether our ongoing and potential future clinical trials will achieve clinically relevant results and our plans for future sales and marketing efforts;
- our ability to complete preclinical and clinical testing successfully for new drug or biologic candidates that we may develop;
- our dependence on third parties for the manufacture of our products, supply of our laboratory substances, equipment and other materials, and to conduct clinical trials;
- advancements in technology by us and our competitors and our ability to compete with our competitors and their competing products;
- our reliance on a limited number of suppliers and their ability to adapt to possible disruptions in their operations;
- our ability to grow and diversify our customer base;
- our ability to obtain and maintain coverage and adequate reimbursement for our products;
- the importance of our executive management team;
- our ability to attract, retain and recruit key management and scientific personnel;
- our use of technology and ability to prevent security breaches; unauthorized use or disclosure of health information, personal information, or sensitive personal information; loss of data; and other disruptions;
- our ability to obtain and maintain protection of our trade secrets, licensed intellectual property, patent rights, and other intellectual property rights and to not infringe the rights of others;
- the possibility that a third party may claim we have infringed or misappropriated our intellectual property rights and that we may incur substantial costs and be required to devote substantial time defending against these claims;
- our ability to obtain the benefits we anticipate from partnering, collaboration, or supply agreements that we may enter into;
- developments with respect to U.S. and foreign laws and regulations applicable to our business, and our ability to comply with these regulations;
- how recent and potential future changes in tax policy could negatively impact our business and financial condition;
- our ability to continue to comply with federal and local laws concerning our business and operations and the consequences resulting from our failure to comply with such laws;
- the extent to which global economic and political developments, including the impact of the COVID-19 pandemic and inflation, will affect our business operations, clinical trials, or financial condition;
- our anticipated research and development activities and projected expenditures;
- our anticipated need to raise additional capital to fund our operations, commercialize our products, and expand our operations;
- our projected financial performance and compliance with existing debt covenants;
- our ability to manage the increased expenses and administrative burdens as a public company;
- our ability to effectively respond to any litigation or governmental investigations; and
- the impact of the above factors and other future events on the market price of our common stock.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in the "Risk Factors" section and elsewhere in this Annual Report. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Such forward looking statements speak only as of the date of this Annual Report. Except as may be required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

You should read this Annual Report and the documents that we have filed as exhibits to this Annual Report with the understanding that our actual future results, levels of activity, performance, and events and circumstances may be materially different from what we expect.

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

PART I

Item 1. Business.

Overview

We are a commercial-stage biopharmaceutical company focused on the development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. COSELA® (trilaciclib), our first product approved by the U.S. Food and Drug Administration (“FDA”), is the first and only therapy indicated to proactively help protect bone marrow (myeloprotection) from the damage of chemotherapy and is the first innovation in managing myeloprotection in decades. COSELA (trilaciclib hydrochloride for injection) is also approved by the China National Medical Products Administration ("NMPA") for marketing in mainland China and is commercialized by our partner, Simcere Pharmaceutical Co., Ltd. ("Simcere"), in Greater China (mainland China, Hong Kong, Macau and Taiwan).

Trilaciclib was developed from a technology platform that targets key cellular pathways including transient arrest of the cell cycle at the G1 phase, prior to the beginning of DNA replication. Controlled administration and clean G1 arrest from transient CDK4/6 inhibition may protect bone marrow and the immune system from cytotoxic damage during treatment. Transient CDK4/6 inhibition also may improve survival in combination with leading and emerging treatments by improving long-term immune surveillance. This can be accomplished through protection of the immune system for improved longer-term function and by potentially increasing the generation of memory T cells, which may provide additional benefit after treatment. We are exploring the use of trilaciclib in clinical trials to optimize these potential benefits in combination with leading and emerging treatments for patients. Beyond our initial extensive-stage small cell lung cancer ("ES-SCLC") indication in the United States, we plan to focus our efforts on two core development paths for trilaciclib in order to optimize the opportunity ahead, including: (1) triple negative breast cancer ("TNBC"), where trilaciclib has demonstrated potential benefits across treatment settings in multiple Phase 2 studies, and (2) in antibody-drug conjugate ("ADC") combinations, in TNBC and potentially other additional tumor types.

We believe we have opportunities for significant growth, including (1) optimizing COSELA in our initial ES-SCLC marketed indication in the U.S., (2) commercializing this potentially transformational new treatment option for patients with metastatic TNBC, provided positive Phase 3 results and regulatory approval, (3) advancing development in combination with leading ADC treatments with an opportunity to meaningfully improve their efficacy and safety, and (4) pursuing global expansion through ongoing partnering initiatives.

We use “COSELA” when referring to our FDA approved drug and “trilaciclib” when referring to our development of COSELA for additional indications.

Our Business Strategy

We aspire to improve the lives of those impacted by cancer through the ongoing development and expansion of trilaciclib. Our strategy includes the following key components:

- ***Establish COSELA as the standard of care for ES-SCLC in the United States.***
- ***Maximize long-term value of trilaciclib by executing our development plan across TNBC treatment settings and in ADC Combinations.***
- ***Manage capital efficiently to fully fund operations.***

We believe that, because of the trilaciclib mechanism of action and unique attributes, including rapid onset from IV administration, potent and selective CDK4 and CDK6 inhibition, and short half-life, trilaciclib has the potential to be used to treat patients receiving myelosuppressive cytotoxic therapies and to meaningfully improve anti-tumor efficacy across various TNBC treatment settings and in ADC combinations. Furthermore, we intend to efficiently execute our capital management strategies to ensure our ability to fund our operations, including the commercialization of COSELA in ES-SCLC, and our ongoing and future clinical programs to develop trilaciclib in additional cancer indications.

Commercial Product

On February 12, 2021, FDA approved COSELA (trilaciclib for intravenous injection) to decrease the incidence of chemotherapy-induced myelosuppression in adult patients treated with a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC. COSELA became commercially available in the United States through our specialty distributor network on March 2, 2021.

COSELA is also commercially available in Greater China (i.e., mainland China, Hong Kong, Macau and Taiwan) pursuant to an exclusive license agreement with Simcere in August 2020 to develop and commercialize trilaciclib for any indication in humans through parenteral delivery, including intravenous delivery, in China, Hong Kong, Macau, and Taiwan. See "Business - License Agreements - Exclusive license to Simcere for trilaciclib in Greater China" section of this Annual Report for more details. COSELA (trilaciclib hydrochloride for injection) is indicated in Greater China to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen for ES-SCLC.

Product Portfolio

Our product portfolio consists of three assets: trilaciclib and lerociclib, both of which are CDK4/6 inhibitors, and a CDK2 inhibitor.

Trilaciclib

As a condition of marketing approval in ES-SCLC, we are required to conduct a post marketing trial of trilaciclib in combination with chemotherapy in patients with ES-SCLC to evaluate survival outcomes. To meet this requirement, a trial of trilaciclib or placebo in combination with topotecan in patients with ES-SCLC has been initiated and the first patient was enrolled in October 2023.

Beyond our continued development and commercialization of our initial ES-SCLC indication in the U.S., we are focusing our efforts on two core development paths for trilaciclib, including (1) TNBC, where trilaciclib has demonstrated potential benefits across treatment settings in multiple Phase 2 studies, and (2) ADC combinations, in TNBC and potentially other additional tumor types.

Trilaciclib is a novel therapy designed to transiently arrest cells that are dependent on CDK4/6 for proliferation, including hematopoietic stem and progenitor cells ("HSPCs"), in the G1 phase. The unique product attributes of trilaciclib include: (1) rapid onset from IV administration, (2) potent and selective CDK4 and CDK6 inhibition, and (3) a short half-life. These attributes enable a controlled administration of trilaciclib intended to achieve a precisely timed effect, a robust clean G1-phase arrest, and an optimal environment for T-cells to proliferate.

Trilaciclib has demonstrated an ability to protect the bone marrow and immune system from damage during cytotoxic treatment. This may lead to reduced hematologic adverse events ("AEs"), which can mitigate the need for rescue interventions and hospitalizations and potentially increase the ability of patients to receive longer durations of treatment. Trilaciclib may also improve survival in combination with leading and emerging treatments through its potential to improve long term immune surveillance in patients following treatment. This may occur through protection of immune system function, as well as the potential for trilaciclib to increase the generation of memory T cells. These potential effects may provide additional longer-term benefit for cancer patients after initial trilaciclib treatment.

Development Pipeline for trilaciclib

Candidate	Indication	Phase / Status	Milestone	Endpoints	Development & Commercialization Rights (all indications)
trilaciclib	1L metastatic triple negative breast cancer (mTNBC)	Registrational Phase 3 trial (enrollment complete)	Final OS analysis expected in 3Q 2024	Primary: OS Secondary: PRO, myeloprotection, PFS/ORR	G1 Therapeutics owns all global development and commercial rights across all indications, with the exception of Greater China (Simcere)
	Antibody-drug conjugate (ADC) combination trial in mTNBC	Phase 2 trial (enrollment complete)	Initial OS endpoint presented in 1Q 2024; additional survival results expected mid-2024	Primary: PFS Secondary: ORR, OS, safety, myeloprotection, others	
	Neoadjuvant TNBC - Mechanism of action (MOA) trial	Phase 2 trial (trial complete)	Results presented at ASCO 2023	Primary: Immune-based MOA Secondary: pCR, immune response, others	
	1L Bladder cancer (mUC)	Phase 2 trial (trial complete)	Results to be presented at a future medical meeting	Primary: PFS Secondary: ORR, OS, safety and efficacy, others	

PFS=progression-free survival; OS=overall survival; PRO=patient reported outcome; ORR=overall response rate; pCR=pathological complete response; MOA=mechanism of action; mUC=metastatic urothelial carcinoma.

In addition to the above-described ongoing clinical trials, we are supporting multiple investigator sponsored studies ("ISS") and conducting a post-marketing trial. See "Business - Preclinical and Clinical Development - Ongoing Clinical Trials" section of this Annual Report for more details.

Market opportunities for trilaciclib

Cancer is the second leading cause of death in the United States with an estimated 2.0 million new cases and 611,000 deaths expected to occur in 2024, according to the American Cancer Society. Cytotoxic therapies (chemotherapies, antibody-drug conjugates, others) are the standard of care treatment for many of these cancers.

Cytotoxic therapies have significant clinical utility and continue to be the most effective treatment for many cancers. However, cytotoxic therapies also damage HSPCs (myelosuppression) and the immune system (immunosuppression), leading to severe adverse effects and potentially limiting anti-tumor activity. 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 only current treatments for chemotherapy-induced myelosuppression are rescue interventions like growth factors and/or transfusions given after myelosuppression occurs. COSELA is the only product approved to proactively prevent chemotherapy-induced myelosuppression and we continue to evaluate the utility of trilaciclib to prevent myelosuppression in clinical trials with existing and newer cytotoxic therapies.

Additionally, significant unmet medical need continues to exist for products that can meaningfully improve the anti-tumor efficacy of existing and emerging standard of care therapies. Despite continued advancements of new treatment modalities, additional novel therapies are needed to further improve anti-tumor efficacy, including in combination with newer agents. Trilaciclib is a novel compound with the potential to meaningfully improve anti-tumor efficacy across tumor types when administered in treatment combinations. We are studying trilaciclib in Phase 2 and Phase 3 clinical trials to evaluate its potential to improve anti-tumor efficacy and reduce adverse events that are commonly associated with cytotoxic therapies:

- *Extensive-stage small cell lung cancer (ES-SCLC).* According to the American Cancer Society, small cell lung cancer ("SCLC") accounts for approximately 10-15% of all lung cancers. Approximately 27,000 people are treated annually in the United States for ES-SCLC in first and second line. First-line treatment of ES-SCLC in the United States is typically a chemotherapy regimen of carboplatin and etoposide, which has significant myelosuppressive side effects. Combination treatment with chemotherapy and immunotherapy has emerged as the standard of care in the United States. While these patients often respond to first-line therapy, approximately 90% progress within one year and die within two years. Five-year survival rates are less than 5% for patients with ES-SCLC. Topotecan, approved for SCLC in 2007, is a standard treatment used in the second/third line setting and is highly myelosuppressive. Based on market research we have completed to date, many physicians see proactive myeloprotection as a better approach for patients and would incorporate trilaciclib into their treatment regimen. We believe the total addressable market of the trilaciclib opportunity for all eligible ES-SCLC patients in the U.S. exceeds $700 million.
- *Breast cancer*. We are evaluating the use of trilaciclib in a variety of TNBC treatment settings, including metastatic and early stage TNBC. According to the World Health Organization, an estimated 2.3 million cases of breast cancer are diagnosed annually worldwide. In 2023, it is estimated that 43,700 women and 530 men died of breast cancer. TNBC makes up approximately 15-20% of such diagnosed breast cancers. Because TNBC cells lack key growth-signaling receptors, patients do not respond well to medications that block estrogen, progesterone, or HER2 receptors. Instead, treating TNBC typically involves cytotoxic therapy, radiation, and surgery. In general, survival rates tend to be lower with TNBC compared to other forms of breast cancer, and TNBC is also more likely to return after it has been treated, especially in the first few years after treatment. We believe the total addressable market in metastatic TNBC exceeds $1 billion in the U.S.

Advantages of trilaciclib

Trilaciclib is a novel transient IV CDK4/6 inhibitor with unique attributes including rapid onset from IV administration, potent and selective CDK4 and CDK6 inhibition and a short half-life. We believe that treating patients with trilaciclib prior to the administration of cytotoxic therapy or immunotherapy regimens may have the following benefits and advantages:

- *Potential to decrease the incidence of chemotherapy-induced myelosuppression*. Trilaciclib has been rationally designed and optimized to preserve HSPCs from damage by cytotoxic therapy, thereby minimizing cytopenias across neutrophils, red cells, and platelets. Trilaciclib has the potential to decrease the clinically relevant consequences of these cytopenias and improve patient outcomes.
- *Potential to reduce cytotoxic therapy 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 the potential to enable maintenance of the indicated and planned chemotherapeutic dose and schedule.
- *Potential to improve anti-tumor efficacy and prolong overall survival in treatment combinations.* Trilaciclib has demonstrated the ability to improve anti-tumor efficacy and increase overall survival in our Phase 2 mTNBC study. Trilaciclib may increase patients' ability to receive more cytotoxic therapy, protect their immune systems from damage, and improve their long-term immune surveillance.

- *Potential for use with cytotoxic therapy / antibody-drug conjugate combinations.* ADCs including TROP2 ADCs are among the fastest growing class of anti-cancer therapy. We have demonstrated that trilaciclib can be combined with ADCs to provide significant reductions in on-target adverse events compared to historical ADC monotherapy data, and may improve overall survival compared to that of ADCs alone.
- *Potential for use with cytotoxic therapy / immune checkpoint inhibitors combinations.* Immune checkpoint inhibitors are often combined with cytotoxic therapy. We have demonstrated that trilaciclib mitigates myelosuppression in ES-SCLC patients treated with chemotherapy in combination with the immune checkpoint inhibitor Tecentriq. Additionally, our preclinical data suggests there may be potential synergistic benefits in terms of anti-tumor efficacy when combining trilaciclib with checkpoint inhibitors in the appropriate treatment settings.
- *Potential to reduce the cost of rescue interventions.* Chemotherapy-induced myelosuppression leads to severe adverse side effects, which often require costly rescue interventions such as hospitalizations, transfusions, antibiotic usage and/or treatment with growth factor support. Because trilaciclib is expected to reduce myelosuppression, we believe it has the potential to reduce these costs. The positive proactive multilineage myeloprotection data we have reported to date and our market research with payers supports the value proposition of trilaciclib to reduce these costs.
- *Potential to improve the patient experience as measured by validated Patient Reported Outcomes ("PRO") instruments.* PRO data from our randomized trials demonstrate that patients receiving trilaciclib prior to chemotherapy report less fatigue and improved physical and functional well-being.
- *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.

Preclinical and Clinical Development for trilaciclib

Preclinical development

We have published extensive biochemical, cellular and *in vivo* data on trilaciclib. Our preclinical data show that trilaciclib can induce transient and reversible cell-cycle arrest of HSPCs; helps protect HSPCs from damage caused by chemotherapy; preserves bone marrow and immune system function; improves complete blood count ("CBC") recovery; helps protect from bone marrow exhaustion; prevents myeloid skewing and consequent lymphopenia; activates T-cells in the tumor microenvironment; and enhances chemotherapy and checkpoint inhibitor anti-tumor activity.

We are currently conducting extensive preclinical development work to assess the synergistic potential of trilaciclib with a variety of novel and emerging therapeutic agents to identify synergies to evaluate in future clinical trials.

Completed clinical trials

We have completed eight clinical trials using trilaciclib. (See below for chart and narrative description.)

Indications	Regimen	Status	Phase	Publications
Phase 1 clinical trial in healthy volunteers	Trilaciclib single agent	Phase 1 complete; announced at ASCO 2015 and results published	1	Science Translational Medicine (He et al.), April 2017
1st-line ES-SCLC (study 1 in package insert)	Tecentriq/ carboplatin/ etoposide	COSELA® (trilaciclib) approved to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC.	2	International Journal of Cancer (Daniel *et al.)*, December 2020
1st -line ES-SCLC (study 2 in package insert)	etoposide/ carboplatin		1b/2	Annals of Oncology (Weiss *et al.)* August 2019
2nd /3rd –line ES-SCLC (study 3 in package insert)	topotecan		1b/2	Advances in Therapy (Hart *et al.)*, November 2020
Metastatic Triple Negative Breast Cancer	gemcitabine/ carboplatin	Phase 2 complete; Phase 3 fully enrolled with final OS analysis expected in 3Q 2024.	2	Lancet Oncology (Tan *et al.*), September 2019
1L mUC (Bladder Cancer)	gemcitabine/ carboplatin + avelumab	Phase 2 complete; announced in November 2023	2	To be published
Neoadjuvant TNBC ("Mechanism of Action study")	Chemotherapy +/- pembro	Phase 2 complete; announced at ASCO 2023	2	To be published
1L metastatic Colorectal cancer (CRC)	FOLFOXIRI + bevacizumab	Phase 3 results announced in February 2023. Trial discontinued.	3	To be published

Phase 1 clinical trial in healthy volunteers

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 ("DLTs"), serious adverse events ("SAEs"), AEs, and pharmacokinetics ("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.

Phase 2 clinical trial in ES-SCLC (study 1 in package insert)

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

We evaluated the combination of Genentech's immune checkpoint, anti-PD-L1 antibody Tecentriq with trilaciclib in first-line treatment for patients with ES-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 were to evaluate the safety, OS, myeloprotection, PK, and anti-tumor activity of trilaciclib in combination with Tecentriq and chemotherapy. We completed enrollment in the first quarter of 2018. We reported positive multilineage myeloprotection data and preliminary PFS in November 2018, and presented updated safety and anti-tumor efficacy data at the 2019 ESMO Congress.

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

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

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

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

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

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

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

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

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

Phase 3 clinical trial in metastatic colorectal cancer (PRESERVE 1) - Trial discontinued

PRESERVE 1 was a randomized, placebo-controlled registrational trial of trilaciclib in colorectal cancer (“CRC”). CRC is a large indication commonly treated with 5-FU-based chemotherapy. We have extensive preclinical research demonstrating myeloprotection in 5-FU-based regimens with trilaciclib. PRESERVE 1 evaluated trilaciclib administered in combination with the triplet therapy FOLFOXIRI (5-FU, folinic acid, oxaliplatin and irinotecan) and bevacizumab, which is the most efficacious chemotherapy regimen for most 1L CRC tumors but also highly myelosuppressive compared to doublet therapies including FOLFOX or FOLFIRI.

On February 13, 2023 , we announced topline results from our pivotal Phase 3 PRESERVE 1 trial showing that the trial achieved its co-primary endpoints related to severe neutropenia with statistical significance, including clinically meaningful and statistically significant reductions in both occurrence of severe neutropenia during induction (placebo=20% vs. trilaciclib=1%; p<0.001) and mean duration of severe neutropenia in Cycles 1 through 4 (placebo=1.3 days vs. trilaciclib=0.1 days; p<0.001).

However, despite the achievement of the co-primary endpoints and other secondary measures of myeloprotection and tolerability, early anti-tumor efficacy data, including ORR, favored patients receiving placebo compared to trilaciclib (61% and 50% ORRs, respectively). Given the differential in these anti-tumor efficacy metrics and the low likelihood of achieving the PFS and OS endpoints, we made the decision to discontinue PRESERVE 1. The Data Monitoring Committee (DMC) independently reached the same conclusion.

Other clinical trials of trilaciclib in combination with different chemotherapies in patients with ES-SCLC and triple negative breast cancer did not demonstrate this adverse survival signal.

Phase 2 clinical trial in first line mUC (Bladder Cancer) (PRESERVE 3)

In November 2023, we announced the completion of the Phase 2 trial of trilaciclib in bladder cancer (PRESERVE 3). We concluded the trial following the final fourth quarter protocol defined analyses of survival and plan to report the results at a future medical meeting. PRESERVE 3 was a signal finding study designed to assess the potential additive contribution of trilaciclib to anti-cancer therapy, including in combination with the immune checkpoint inhibitor avelumab alone without chemotherapy during the maintenance part of the study. An overall survival trend in favor of the trilaciclib plus avelumab arm in the maintenance phase was observed, suggesting a potential additive benefit when used in combination with a checkpoint inhibitor. This Phase 2 trial has been concluded and the information may inform future studies in our core areas of focus.

Phase 2 clinical trial to confirm the anti-tumor mechanism of action (MOA) in the tumor microenvironment

In June 2023, we presented final results during the 2023 ASCO meeting from 24 patients enrolled in our Phase 2, single arm mechanism of action study of trilaciclib administered as a single agent to patients with early-stage TNBC prior to receiving trilaciclib and neoadjuvant therapy confirming that trilaciclib can increase the pool of memory T cells in the tumor microenvironment responsible for long term immune surveillance and efficacy. These results highlight the potential for trilaciclib to enhance long term immune surveillance by increasing T cell function and generation of certain memory T cells and demonstrate gene expression profiles that may be associated with improved clinical outcome. These data support earlier findings from this Phase 2 trial demonstrating an increase in the ratio of CD8+ T cells to regulatory T cells (Tregs); a high ratio of CD8+ T cell to Tregs is predictive of overall survival (OS) and is associated with pathologic complete response (pCR). As expected, high rates of pCR were observed in patients with PD-L1(+) tumors and in patients with inflamed tumor immune microenvironments.

Trilaciclib was shown to enhance the number and function of CD8+ T cells in the tumor microenvironment. Seven days after monotherapy with trilaciclib, the number of CD8+ T cells and GZMB+ cells, which is a surrogate marker for T cell function, were enhanced with statistical significance in patients achieving a pCR. There was also an increase in stromal TILs within the tumor microenvironment after a single dose of trilaciclib.

Ongoing clinical trials for trilaciclib

Phase 3 clinical trial in first line Metastatic Triple Negative Breast Cancer (mTNBC) (PRESERVE 2)

Building upon the robust OS benefit observed in the prior Phase 2 study, we initiated PRESERVE 2, a pivotal Phase 3 trial of trilaciclib in patients receiving first-line GC for locally advanced unresectable or mTNBC. Enrollment was completed in this trial in October 2022. This study is evaluating trilaciclib in PD-L1 positive and negative patients and largely replicates the design of the positive Phase 2 trial which demonstrated improved anti-tumor efficacy across patients. Anti-tumor efficacy and myeloprotection endpoints are being assessed in this study. We broadened enrollment of the 1L cohort in this study to also include patients who received checkpoint inhibitors in the neo/adjuvant setting to ensure that we develop clinical experience for trilaciclib in this increasingly relevant patient population. This trial is being conducted across multiple sites in the United States and Europe. We enrolled patients who previously received checkpoint inhibitors in the new/adjuvant setting into the trial, to ensure that we develop clinical experience in this patient population. The primary endpoint is to evaluate the effect of trilaciclib on overall survival (OS) compared with placebo in patients receiving first-line GC. Key secondary endpoints include assessment of the effect of trilaciclib on patients' quality of life compared with placebo. Enrollment in this trial is complete at 187 IL patients.

An interim OS analysis at approximately 80% of events required for the final analysis was conducted in February 2024. The Independent Data Monitoring Committee ("DMC") determined that the trial did not achieve the early stopping criteria and recommended continuation of PRESERVE 2 to the final analysis. The DMC raised no safety concerns nor did it recommend any other changes to the study. The final analysis will be conducted on the intent-to-treat (ITT) population and is estimated to occur in the third quarter of 2024. G1 remains blinded to all data.

We believe that the additional events required for the final analysis and the longer follow up could potentially allow patients to benefit from receiving subsequent anticancer therapies following discontinuation of trilaciclib. This is based on new data we presented at the 2023 San Antonio Breast Cancer Symposium ("SABCS") from patients with mTNBC who participated in our Phase 2 trial (NCT02978716) indicating that patients with mTNBC who received trilaciclib with their cytotoxic chemotherapy during the trial and then received subsequent anticancer therapy ("SACT") after trilaciclib discontinuation exhibit statistically significant and clinically meaningful improvements in median overall survival (OS) (32.7 months versus 12.8 months; p=0.001). Additionally, median OS for patients who received prior trilaciclib was improved from the time they started their first SACT compared to patients who did not receive prior trilaciclib (14.0 months versus 5.8 months; p=0.001). Administering trilaciclib with cytotoxic chemotherapy also led to improved survival in patients unable to receive SACT.

Phase 2 clinical trial in combination with the antibody-drug conjugate ("ADC"), Sacituzumab Govitecan ("SG")

In TNBC, trilaciclib, in combination with gemcitabine and carboplatin, and the ADC, SG, have both shown clinically meaningful and substantial improvements in overall survival. We believe that trilaciclib could act synergistically with ADCs to improve overall patient outcomes with fewer myelosuppressive side effects.

In the fourth quarter of 2021, we initiated this ongoing Phase 2, single arm, open-label study of trilaciclib administered prior to the ADC, SG in patients with unresectable locally advanced or mTNBC in the fourth quarter of 2021. Anti-tumor efficacy and myeloprotective endpoints are being assessed. Objectives included of the myeloprotective effects of trilaciclib, and the anti-tumor efficacy of trilaciclib when administered prior to SG as measured by OS, PFS, ORR, duration of objective response (DOR), and clinical benefit rate (CBR).

In May 2023, we presented results at the ESMO meeting confirming the potential benefit of trilaciclib in reducing adverse events related to the TROP2 ADC, SG. The data suggested a potential for trilaciclib to meaningfully reduce adverse events related to use of SG, including that trilaciclib was well tolerated when administered prior to SG. Safety results showed a clinically meaningful on-target effect of trilaciclib to reduce (>50%) the rates of multiple adverse events compared to the previously published sacituzumab govitecan-hziy single agent safety profile from the ASCENT trial, including myelosuppression (neutropenia, anemia) and diarrhea due to the presence of CDK4/6-expressing cells in the intestinal crypt.

In January 2024, we provided initial efficacy results from the ongoing Phase 2 ADC trial suggesting improved OS among patients receiving trilaciclib in combination with SG. Preliminary data from the ongoing Phase 2 trial of trilaciclib in combination with SG in metastatic TNBC patients suggested clinically meaningful improvements in OS among patients receiving trilaciclib in combination with SG compared to SG alone based on historical data from the ASCENT trial, including (1) current median OS of 17.9 months with trilaciclib vs 12.1 months for SG alone and (2) estimated 12-month survival of 59% of patients receiving trilaciclib in combination with SG, representing a ~20% improvement over SG alone. The clinical benefit rate was similar in both arms: 47% (trilaciclib) vs 45% (SG; historical from ASCENT).

We expect to provide updated OS data from this study in mid-2024.

Post-marketing trial of trilaciclib in 2L ES-SCLC in combination with topotecan

We are conducting an approximately 300 patient post-marketing trial of trilaciclib in 2L ES-SCLC in combination with topotecan (a topoisomerase 1 inhibitor chemotherapy). This is a global study, which is intended to formally evaluate the OS for trilaciclib in combination with topotecan in this 2L ES-SCLC patient population.

Phase 2 Investigator Sponsored Studies ("ISS") of trilaciclib

An ISS is a study that is proposed, developed, and conducted by a qualified sponsor external to G1 Therapeutics who assumes full responsibility for the conduct of the study

G1 is supporting an ISS of trilaciclib and lurbinectedin in patients with 2L ES-SCLC, sponsored by UNC Lineberger. This is a prospective, non-randomized, single-arm Phase 2 study to evaluate trilaciclib administered intravenously prior to lurbinectedin in approximately 30 participants with platinum refractory ES-SCLC evaluating myeloprotection, and efficacy measures (OS, PFS, and ORR), and quality of life assessments. The primary endpoint is the rate of grade 4 neutropenia in any cycle. Secondary endpoints include mean duration (days) of grade 4 neutropenia in cycle 1, OS, PFS, ORR, quality of life assessments, and the use of secondary/reactive supportive measures including G-CSF administration.

G1 is supporting an ISS of trilaciclib in combination with gemcitabine/carboplatin and pembrolizumab, which is being sponsored by Atrium Health Levine Cancer Institute. This is an open label, single-arm, phase 2 study to evaluate trilaciclib, pembrolizumab, gemcitabine and carboplatin administered to approximately 36 participants with locally advanced unresectable or metastatic TNBC evaluating efficacy, safety and tolerability measures.

Regulatory Status for trilaciclib

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

We received Breakthrough Therapy Designation from the FDA in 2019 based on positive myeloprotection data in small cell lung cancer patients from three randomized Phase 2 clinical trials and the New Drug Application (NDA) received priority review. As a condition of approval, we were required to complete certain post-marketing activities. The only remaining post-marketing activity is completion of a clinical trial to assess the impact of trilaciclib on disease progression or survival in patients with ES-SCLC with chemotherapy-induced myelosuppression treated with a platinum/etoposide-containing or topotecan-containing regimen with at least a two year follow up. We have completed site selection for the post-approval clinical trial, site activations are in progress, and the first patient was enrolled in October 2023.

In 2021, the FDA granted Fast Track designation to trilaciclib for use in combination with chemotherapy for the treatment of locally advanced or mTNBC. Fast track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill unmet medical needs. The purpose is to get important new drugs to the patient earlier. A drug that receives Fast Track designation may be eligible for more frequent engagements with the FDA to discuss a drug's clinical development plan, eligibility for Accelerated Approval and Priority Review, and Rolling Review in which completed sections of an NDA can be submitted for FDA review on a rolling basis rather than waiting until all sections of the NDA are completed before the entire application can be reviewed.

We continue to engage in research and clinical development of trilaciclib in order seek regulatory approval to market additional indications in additional tumor types and treatment combinations, including breast cancer.

Lerociclib

Lerociclib is a differentiated clinical-stage oral CDK4/6 inhibitor being developed for use in combination with other targeted therapies in multiple oncology indications. We are not actively pursuing preclinical or clinical development activities for lerociclib. In 2020, we out-licensed the development and commercialization of lerociclib in all indications. See "Business - License Agreements - Exclusive License to Genor for lerociclib in certain licensed territories" section of this Annual Report for more details.

CDK2 Inhibitor

Cyclin-dependent kinase 2 ("CDK2") is an internally discovered inhibitor. We are not actively pursuing preclinical or clinical development activities for CDK2. In 2020, we out-licensed the development and commercialization of CDK2 inhibitor for all human and veterinary uses. See "Business - License Agreements - Exclusive License to Incyclix" section of this Annual Report for more details.

Commercialization

In February 2021, the FDA approved COSELA (trilaciclib) to decrease the incidence of chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for ES-SCLC. Our commercial team includes sales, marketing, market access, strategic accounts and clinical nurse educator functions, as well as product distribution. The G1 to One program serves as a patient hub and provides patient and healthcare provider services.

COSELA is included in two updated National Comprehensive Cancer Network® (“NCCN”) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): The Treatment Guidelines for Small Cell Lung Cancer and the Supportive Care Guidelines for Hematopoietic Growth Factors. Furthermore, COSELA is recommended as a myeloid supportive agent in the updated American Society of Clinical Oncology (“ASCO”) SCLC guidelines for patients with untreated or previously treated ES-SCLC who are undergoing treatment with chemotherapy or chemoimmunotherapy. These guidelines provide evidence-based, consensus-driven recommendations to practicing clinicians to ensure that all patients receive preventive, diagnostic, treatment, and supportive services that are most likely to lead to optimal outcomes. The Centers for Medicare & Medicaid Services ("CMS") issued the permanent J-code for COSELA, allowing providers to bill for it at all sites of care. This standardized the submission and payment of COSELA insurance claims across Medicare, Medicare Advantage, Medicaid, and commercial plans for all hospital outpatient departments, ambulatory surgery centers, and physician offices in the United States using the Healthcare Common Procedure Coding System ("HCPCS") code.

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

Manufacturing

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

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

Competition

The development and commercialization of new drug therapies is highly competitive. We will face competition with respect to all therapeutics we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. Any drug candidates we successfully develop and commercialize will compete with currently marketed drugs and therapies used for treatment of the same indications, and potentially with products currently in development for the same indications. Many of the entities marketing or developing potentially competing products have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing. We believe the key competitive factors affecting the success of any approved product will be its efficacy, safety profile, price, convenience of administration, and level of promotional activity. Accordingly, our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer side effects, are more convenient or are less expensive than any products that we may develop.

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

Intellectual property

Our commercial success depends in part on our ability to obtain, maintain, and enforce proprietary protection in jurisdictions where we seek to commercialize our FDA approved CDK4/6 inhibitor trilaciclib (COSELA) and where our licensees seek to commercialize our proprietary CDK inhibitors, including trilaciclib and clinical candidate lerociclib. We also, where we believe appropriate, seek protection on processes for the production of our CDK4/6 inhibitors, formulations, additional compositions, combinations of our product candidates with other active agents and dosing schedules and regimens. In addition, we plan to seek patent term adjustments, restorations, and/or patent term extensions where applicable in the United States and other jurisdictions. 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 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. 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 product. See "Business - Government Regulation and Product Approval" section of this Annual Report for more details.

Our owned and in-licensed patent estate as of December 31, 2023, on a worldwide basis, includes over 385 granted or pending patent applications in more than 26 patent families with more than 55 granted U.S. patents. Our intellectual property strategy includes patenting our CDK4/6 inhibitors, their uses, and methods of manufacturing. We have obtained more than twenty composition-of-matter patents in the United States on a number of our CDK4/6 inhibitors, including claims that cover trilaciclib and lerociclib, and we continue to seek composition-of-matter patents on additional CDK inhibitors both in the United States and throughout the world. In addition, we have obtained more than eighteen patents in the United States on methods of treatment using a number of our CDK4/6 inhibitors, including claims that cover methods of using trilaciclib and lerociclib. We continue to seek additional patents for our key CDK4/6 inhibitors and their uses in key therapeutic areas.

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.

The term of individual patents depends upon the laws of the countries in which they are obtained. In the countries in which we currently file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application which serves as a priority application. However, the term of a U.S. patent may be extended to compensate for the time required to obtain regulatory approval to sell a drug (a patent term extension) or by delays encountered during patent prosecution that are caused by the United States Patent and Trademark Office ("USPTO") (referred to as patent term adjustment). For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved drugs of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review and diligence during the review process. Patent term extensions cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent covering an approved drug or its method of use may be extended. A similar kind of patent extension, referred to as a Supplementary Protection Certificate, is available in Europe. Legal frameworks are also available in certain other jurisdictions to extend the term of a patent. We have filed for patent term extensions with the United States Patent and Trademark Office seeking the extension of term for patents encompassing trilaciclib.

Trilaciclib patent coverage

We own seven issued U.S. Patents (U.S. 8,598,186; U.S. 8,598,197; U.S. 9,957,276; U.S. 10,189,849; U.S. 10,189,850; U.S. 10,927,120; and U.S. 11,040,042) covering the trilaciclib compositions-of-matter and its pharmaceutical composition. We have listed each of these patents in the Orange Book listing for COSELA. We own corresponding issued patents covering trilaciclib and its pharmaceutical composition in Europe, Canada, Japan, Mexico, China, Macau, Australia, Russia, South Korea, India, Israel, Hong Kong, Brazil, and Singapore. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2031, without regard to any extensions, adjustments, or restorations of term that may be available under national law. We have filed a request for patent term extension under 35 U.S.C. § 156 for a term extension of U.S. 8,598,186, which claims the composition of matter of trilaciclib, which, if granted and elected (as described further below), would extend the term of this patent to December 30, 2034. Our current issued patents covering methods of use of trilaciclib will expire in 2034 to 2039. Our pending applications on additional methods of use of trilaciclib, should they issue, will expire on dates ranging from 2034 to 2042. We plan to file additional applications on aspects of our innovations that may have patent terms that extend beyond these dates.

In addition, we own four issued U.S. Patents (U.S. 9,487,530; U.S. 10,085,992; U.S. 10,966,984; and U.S. 11,717,523) covering the use of trilaciclib to reduce the effect of chemotherapy on healthy cells in a subject being treated for cancer or to treat a subject with cancer in combination with a chemotherapeutic agent, each of which has been listed in the Orange Book listing for COSELA. 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, and the use of trilaciclib to treat cancer, including SCLC, in combination with a chemotherapeutic agent. 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, and the use of trilaciclib to treat TNBC in combination with a chemotherapeutic agent. Patents from this family have issued in Europe, China, Hong Kong, Macau, Canada, and Japan. Patent applications from this family are pending in Europe, Japan, and the United States. 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 request for patent term extension under 35 U.S.C. § 156 for a term extension of U.S. 9,487,530, which claims the use of trilaciclib to reduce the effect of chemotherapy on healthy cells in a subject being treated for, among other things, small cell lung cancer, which, if granted and elected (as described further below), would extend the term of this patent to February 12, 2035. We ultimately intend to elect one patent (U.S. 8,598,186 or U.S. 9,487,530) for extension under 35 U.S.C. § 156.

We have filed applications in the United States, in the European Patent Office (EPO), Canada, China, Hong Kong, Australia, Brazil, Israel, Japan, South Korea, Mexico, New Zealand, Russia, and the regional patent office of the Eurasian Patent Organization (EAPO) that cover the administration of trilaciclib in combination with a checkpoint inhibitor. Patents have been granted or allowed in the United States, Russia, EAPO, Australia, Israel, New Zealand, and Mexico. The granted U.S. Patent (U.S. 11,529,352) has been submitted for listing in the Orange Book listing for COSELA. This granted patent received 595 days of patent term adjustment, and will expire July 23, 2039. The expected year of expiration for other members of 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 trilaciclib inhibitors to treat RB-positive tumors (U.S. 10,925,878). Patents in this family have also issued in China, Hong Kong, and Macau. 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 certain morphic form compositions of trilaciclib. This family has issued in the United States (U.S. 10,988,479) and is pending in the United States, EPO, China, Hong Kong, and Taiwan. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2040, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to the selection of patients for administration of trilaciclib based on tumor type, chemotherapeutic regimen, and immune factors. This family has been filed in the United States, China, Hong Kong, Taiwan, Japan, Canada, Australia, the EPO, and Argentina. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2040, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to the use of our trilaciclib in combination with sacituzumab govitecan for the treatment of patients with advanced and/or metastatic Trop-2 overexpressing cancers. This family has been filed in the United States, Europe, China, Japan, Australia, Canada, Israel, Korea, and Taiwan. The expected year of expiration for this patent family, where issued, valid, and enforceable, is 2042, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own additional patent families that cover various aspects of our commercial manufacture of trilaciclib. These patent families where issued, valid, and enforceable, expire between 2033 and 2039, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

Lerociclib patent coverage

We own six issued U.S. Patents (U.S. 8,598,186; U.S. 8,598,197; U.S. 9,481,691; U.S. 9,957,276; U.S. 10,189,851; and U.S. 10,696,682) covering the lerociclib composition-of-matter and pharmaceutical composition. We own corresponding issued patents covering lerociclib and its pharmaceutical composition in Europe, Canada, Japan, Mexico, China, Macau, Australia, Russia, South Korea, India, Israel, Hong Kong, Brazil, and Singapore. The expected year of expiration for these composition-of-matter patents, where issued, valid and enforceable, is 2031, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family that is directed to the use of lerociclib to treat RB-positive tumors. The family includes four issued U.S. Patents (U.S. 9,527,857; U.S. 10,076,523; U.S. 10,434,104; and U.S. 11,654,148). The ‘857 patent covers the use of lerociclib, to treat RB-positive breast cancer, colon cancer, ovarian cancer, NSCL cancer, prostate cancer, and glioblastoma, the ‘523 patent covers the use of lerociclib to treat Rb-positive breast cancer continuously for 28 days or more, and the ‘104 patent covers the use of lerociclib to treat Rb-positive breast cancer in combination with goserelin. The ‘148 patent covers the treatment of NSCLC or breast cancer by administering lerociclib at least once a day for 24 or more continuous days. Patents in this family have also issued in China, Hong Kong, Macau, and 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 certain hematological cancers. This family includes one issued U.S. Patent (10,709,711). This patent filing has issued in China. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2034, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We have filed patent applications in the United States, Europe, and China that covers the administration of lerociclib in combination with an EGFR inhibitor, for example osimertinib, for the treatment of EGFR-mutant cancers, most notably NSCLC. One application has granted in the United States (U.S. 11,395,821). The expected year of expiration for this patent family, where issued, valid and enforceable, is 2038, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We own a patent family directed to the use of lerociclib in combination with a Bruton’s tyrosine kinase inhibitor or other selected active agents to treat RB-positive tumors. The family includes two granted U.S. patents (U.S. 10,231,969 and U.S. 11,446,295). The expected year of expiration for this patent family, where issued, valid and enforceable, is 2035, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We have filed patent applications in the United States, EPO, China, Hong Kong, Australia, South Korea, and New Zealand that cover morphic forms of lerociclib. Patents have been granted in the United States (U.S. 11,261,193), Australia, New Zealand, China, and India, and allowed in the EPO. The expected year of expiration for this patent family, where issued, valid and enforceable, is 2038, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

We have filed patent applications in the United States, China, Hong Kong, Australia, South Korea, New Zealand, Indonesia, Sri Lanka, Malaysia, Philippines, Singapore, Thailand, and Vietnam that cover dosage regimes of lerociclib. A patent has been granted in the United States (U.S. 11,357,779). The expected year of expiration for this patent family, where issued, valid and enforceable, is 2039, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

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

We own additional patent families that cover various aspects of our commercial manufacture of lerociclib. These patent families where issued, valid, and enforceable, expire between 2033 and 2039, without regard to any extensions, adjustments, or restorations of term that may be available under national law.

License Agreements

We are the sole owner or exclusive licensee of all of our patents and currently filed patent applications that cover the composition of trilaciclib and lerociclib, the manufacture of trilaciclib and lerociclib, and our use or our licensees' use of trilaciclib and lerociclib. We have the exclusive right to prosecute all pending patent families related to trilaciclib and lerociclib in our sole discretion, and, where we have out-licensed patents and patent applications, our licensees have the right to review and comment on all material patent filings, and their review and comments will be considered by us in good faith. In 2023, we were party to four out-licensing agreements concerning our CDK inhibitor technology with each of Simcere, Genor, and Incyclix; however, our fourth out-license agreement with EQRx was terminated in the third quarter of 2023.

Exclusive license to Simcere for trilaciclib in Greater China

On August 3, 2020, we entered into an exclusive license agreement with Simcere for the development and commercialization of trilaciclib in all indications in Greater China (mainland China, Hong Kong, Macau, and Taiwan) (the "Simcere Territory"). Under the license agreement, we granted to Simcere an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to develop, obtain, hold and maintain regulatory approvals for, and commercialize trilaciclib in the Simcere Territory. Since entering into the license agreement, we have received an upfront payment of $14.0 million and an additional $22.0 million for the achievement of development milestones.

On April 28, 2023, we amended the license agreement with Simcere, whereby we received a one-time, non-refundable payment of $30.0 million in exchange for the relief of future royalty payments from the sale of COSELA in Greater China. In addition, the milestone payments under the license agreement were adjusted such that we will be eligible to receive a $5.0 million payment upon Simcere's filing an NDA of TNBC in mainland China and a $13.0 million payment upon Simcere receiving regulatory approval of TNBC in mainland China. Under the amended license agreement, Simcere is not responsible for any sales milestone payments or any royalties accrued after April 28, 2023. Following the amendment, we continue to own all the global development and commercial rights to trilaciclib, excluding Greater China.

During the twelve months ended December 31, 2023, we recognized $30.0 million in revenue from the one-time payment for the relief of future royalty payments, $2.9 million in supply and manufacturing services, $0.6 million in royalty revenue, and $0.7 million in patent and clinical trial reimbursable costs.

Exclusive license to Genor Biopharma Co. Inc. ("Genor") for lerociclib in certain licensed territories

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

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

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

Pursuant to the license agreement, Genor agreed to pay us a non-refundable, upfront cash payment of $6.0 million with the potential to pay an additional $40.0 million upon reaching certain development and commercial milestones. In addition, Genor will pay us tiered royalties ranging from high single to low double-digits based on annual net sales of lerociclib in the Genor Territory. The upfront cash payment was received in July 2020. In September 2020, we transferred to Genor the related technology and know-how that is necessary to develop, seek regulatory approval for, and commercialize lerociclib in the Genor Territory. Genor will be responsible for the development of the product in the Genor Territory and will be responsible, at its sole cost, for obtaining supply of lerociclib to meet its development, regulatory approval, and commercialization obligations under the agreement. Since entering into the license agreement, we have received an upfront payment of $6.0 million and an additional $3.0 million for the achievement of development and commercial milestones. During the twelve months ended December 31, 2023, we did not recognize any revenue related to development milestones.

Exclusive license to Incyclix

On May 22, 2020, we entered into a global license agreement with Incyclix, formerly ARC Therapeutics, LLC, for the development and commercialization of a CDK2 inhibitor for all human and veterinary uses. Pursuant to the Incyclix License, Incyclix is currently granted an exclusive, royalty-bearing, license with the right to grant sublicenses to one of our solely-owned patent families. At close, we received consideration in the form of an upfront payment of $1.0 million and an equity interest in Incyclix equal to 10% of its issued and outstanding units valued at $1.1 million. In addition, we may receive a future development milestone payment totaling $2.0 million and royalty payments in the mid-single digits based on net sales of the licensed compound after commercialization. In the first quarter of 2022, Incyclix announced a new round of financing which we did not participate. Following the financing, our equity interest is now approximately 6.5%.

We also have right of first negotiation to re-acquire these assets. In 2021, Incyclix returned three of the four licensed patent families. Under the Incyclix License, Incyclix received the exclusive right to prosecute these patent families in its sole discretion, and we have the right to review and comment on all material patent filings, and our review and comments will be considered by Incyclix in good faith.

Under the Incyclix License, Incyclix is solely responsible for all patent prosecution costs. Incyclix has the first right, but not the obligation, to bring and control any infringement action at its own expense, subject to Incyclix keeping us reasonably informed. Incyclix also has the right to name and join us in any infringement action relating to our patents. In the case of a patent certification in connection with an Abbreviated New Drug Application under the U.S. Hatch Waxman Act, or the substantial equivalent in a foreign country, if Incyclix declines to file a lawsuit, we have the right to bring an infringement action at our own expense. There was no revenue recognized during twelve months ended December 31, 2023.

Exclusive license to EQRx for lerociclib - terminated

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

Under the license agreement, EQRx agreed to pay us a non-refundable, upfront cash payment of $20.0 million with the potential to pay an additional $290.0 million upon reaching certain development and commercial milestones. In addition, EQRx would pay us tiered royalties ranging from mid-single digits to mid-teens based on annual net sales of lerociclib in the EQRx Territory. In September 2020, we transferred to EQRx the related technology and know-how that was necessary to develop, seek regulatory approval for, and commercialize lerociclib in the EQRx Territory. EQRx was responsible for the development of the product in the EQRx Territory. We agreed to continue until completion, as the clinical trial sponsor, our two primary clinical trials and EQRx agreed to reimburse us for all related out-of-pocket costs incurred after the effective date of the license agreement.

On August 1, 2023, we received from EQRx formal notice of termination of the lerociclib license agreement in connection with the acquisition of EQRx by Revolution Medicines, Inc. The notice stated the intention to revert the lerociclib product rights back to us. Under the terms of the license agreement, EQRx was responsible for winding down its development activities. On September 13, 2023, the parties entered into a letter agreement whereby EQRx would pay us $1.6 million to reimburse anticipated wind down costs; the payment was received during the third quarter of 2023. No milestones were previously achieved through the date of termination of the lerociclib license agreement, and as a result of the termination, we will not receive any further milestone payments or future royalties from EQRx.

During the twelve months ended December 31, 2023, we recognized revenue of $1.7 million for the reimbursement of patent and clinical trial costs, including $1.4 million of the $1.6 million payment received during the third quarter of 2023 following notice from EQRx of termination of the license agreement. As of December 31, 2023, the remaining $0.2 million is held as short-term deferred revenue on the balance sheet and will be recognized as revenue as clinical trial costs associated with the wind down are incurred.

In light of the EQRx termination, we directed the abandonment of certain patents and patent applications solely directed to lerociclib, or its use, in certain EQRx territories. No granted patents, however, have been abandoned in the United States.

Government Regulation and Product Approval

Disclosure of clinical trial information

Sponsors of clinical trials of certain FDA-regulated products, including prescription drugs, are required to register and disclose certain clinical trial information on a public registry maintained by the U.S. National Institutes of Health ("NIH"). Information related to the product, patient population, phase of investigation, clinical trial sites and investigator, and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results may be delayed in some cases for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the design and progress of our development programs. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, the government has brought enforcement actions against clinical trial sponsors that fail to comply with such requirements.

Pediatric clinical trials and exclusivity

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

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

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

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as potential animal studies to assess the pharmacokinetic and pharmacodynamic characteristics and potential safety and effectiveness of the product. The conduct of the preclinical tests must comply with certain federal regulations and requirements, including good laboratory practices ("GLP"), for any safety testing. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term nonclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of qualified investigators. Clinical trials must be conducted: (i) under the supervision of one or more qualified investigators and in compliance with federal regulations, including those encompassing good clinical practice ("GCP") requirements that are meant to protect the rights and welfare of study subjects and to define the roles of clinical trial sponsors, investigators, and monitors, and (ii) under protocols detailing the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Congress also recently amended the FDC Act to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must include the sponsor's diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Sponsors must submit a diversity action plan to the FDA by the time the sponsor submits the relevant clinical trial protocol to the agency for review. The FDA may grant a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect Phase 3 trial planning and timing or what specific information FDA will expect in such plans, but if the FDA objects to a sponsor's diversity action plan or otherwise requires significant changes to be made, it could delay initiation of the relevant clinical trial.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time by imposing a clinical hold or impose other sanctions if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial subjects. The clinical trial protocol and informed consent information for subjects in clinical trials must also be submitted for review and approval by an institutional review board, or IRB, before the trial commences. An IRB also monitors the trial on an ongoing basis consistent with regulatory requirements and may require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements or for safety issues or it may impose other conditions on the clinical investigators or the sponsor of the clinical trial.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all nonclinical, clinical, and other testing and a compilation of data relating to the product's chemistry, manufacture, and controls, as well as proposed labeling and information about the product's manufacturing facility or facilities. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of most NDAs is subject to a substantial application user fee and an annual program fee for approved NDAs. In 2024 the fee for an NDA submission with clinical information is over $4 million and the annual program fee for an approved NDA is over $416 thousand. These fees are typically increased annually. Fee waivers or reductions are available in certain circumstances.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. The FDA seeks to review applications for standard review drug products within ten months, and applications for priority review drugs within six months. Priority review can be applied to drugs intended to treat a serious condition and that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists. The review process for both standard and priority reviews may be extended by FDA for three additional months to consider additional, late-submitted information, or information intended to clarify information already provided in the submission in response to FDA review questions.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an external advisory committee, which is typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will typically inspect the facility or the facilities at which the drug is manufactured, unless the facility has recently had an FDA inspection. The FDA also typically inspects the application sponsor. The FDA will not approve the product unless compliance with current good manufacturing practice ("cGMP") requirements is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, or additional nonclinical or clinical study information, in order for the FDA to reconsider the application. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with the accompanying approved prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy ("REMS"), in addition to the approved labeling, to help ensure that the benefits of the drug outweigh its risks. A REMS could include communication plans for healthcare professionals, medication guides for patients, and/or elements to assure safe use ("ETASU"). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, restricted distribution requirements, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS plan is needed, the sponsor of the NDA must submit a proposed REMS plan. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy as described as post marketing commitments or requirements included in the approval letter. Once granted, product approvals may be withdrawn if compliance with regulatory requirements and commitments is not maintained or problems are identified following initial marketing.

Fast track, breakthrough therapy, RTOR, and priority review designations

The FDA is authorized to designate certain products for expedited development or review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation, and priority review designation. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, fast track designation is a process designed to facilitate the development, and expedite the review, of drugs to treat serious or life-threatening diseases and fill an unmet medical need. The designation request may be made at the time of IND submission and generally no later than the pre-NDA meeting. The FDA will respond within 60 calendar days of receipt of the request. Priority review, which is requested at the time of NDA submission, is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists, an initial review within six months after filing as compared to a standard review time of ten months. Although fast track designation and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a fast track designated drug and expedite review of the application for a drug designated for priority review.

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

Specific to oncology drug applications, FDA's Oncology Center of Excellence has developed a program called Real-Time Oncology Review ("RTOR"). RTOR facilitates earlier submission of topline results (i.e., efficacy and safety results from clinical studies before the study report is completed) and datasets, after database lock, to support an earlier start to the agency's review of a marketing application review. The intent of RTOR is to provide FDA reviewers earlier access to data, to identify data quality and potential review issues, and to potentially enable early feedback to the applicant, which can allow for a more streamlined and efficient review process for the product's NDA. Applicants can apply for review under RTOR when the database for a pivotal trial has been locked and the oncology product is eligible under FDA's criteria for the program. Eligibility requires (a) clinical evidence indicating that the drug may demonstrate substantial improvement on one or more clinically relevant endpoints over available therapies; (b) the use of straightforward study designs and easily interpreted clinical trial endpoints (e.g., overall survival, response rates); and (c) that no aspect of the NDA is likely to require a longer review time (e.g., requirement for new REMS or input from an advisory committee). In November 2023, the agency finalized guidance for industry on RTOR.

Fast track designation, breakthrough therapy designation, RTOR, and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

Accelerated approval pathway

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

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

Post-approval requirements

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

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

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

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

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

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

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (the "PDMA") which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. More recently, the Drug Supply Chain Security Act (the "DSCSA") was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that culminated in November 2023. However, FDA announced a one-year stabilization period, until November 2024, to give entities subject to the DSCSA additional time to finalize interoperable tracking systems and to ensure supply chain continuity. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, the FDA released proposed regulations in February 2022 to amend the national standards for licensing of wholesale drug distributors by the states; establish new minimum standards for state licensing third-party logistics providers; and create a federal system for licensure for use in the absence of a state program, each of which is mandated by the DSCSA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Pharmaceutical Coverage, Pricing, and Reimbursement

Sales of our products that are approved by the FDA will depend, in part, on the extent to which the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers, and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved, and it is time consuming and expensive to seek reimbursement from third-party payors. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries.

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

Accordingly, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our FDA-approved products to each payor separately, with no assurance that coverage and adequate payment will be applied consistently or granted at all. The process for determining whether a payor will cover and how much it will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for healthcare providers or less profitable than alternative treatments or if administrative burdens make our products less desirable to use.

In addition, the containment of healthcare costs has become a priority of federal and state governments and the prices of therapeutics have been a focus in this effort. The United States government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. For example, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. In August 2022, President Biden signed into the law the Inflation Reduction Act of 2022 (the "IRA"), which includes (among other things) multiple provisions that may impact the prices of drug products that are both sold into the Medicare program and throughout the United States. A manufacturer of drug products covered by Medicare Parts B or D must now pay a rebate to the federal government if their drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting for payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities and entered into the first set of agreements with pharmaceutical manufacturers to conduct price negotiations in October 2023. However, the IRA's impact on the pharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e.g., the U.S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. Those lawsuits are currently ongoing.

We expect that federal, state and local governments in the U.S. will continue to consider legislation directed at lowering the total cost of healthcare. Individual states in the United States have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, in recent years, several states have formed prescription drug affordability boards ("PDABs"). Much like the IRA's drug price negotiation program, these PDABs have attempted to implement upper payment limits on drugs sold in their respective states in both public and commercial health plans. As an example, in August 2023, Colorado's PDAB announced a list of five prescription drugs that would undergo an affordability review. The effects of these efforts remain uncertain pending the outcomes of several federal lawsuits challenging state authority to regulate prescription drug payment limits.

If third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis. Moreover, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical products. Similar challenges to obtaining coverage and reimbursement for the pharmaceutical products apply to companion diagnostics.

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

Other Healthcare Laws and Regulations

As we are commercializing COSELA and may commercialize other product candidates in the future, we are subject to additional healthcare statutory and regulatory requirements and enforcement by federal government and the states and foreign governments in the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of COSELA and any other product candidates for which we obtain marketing approval. Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. We contract with a third-party service provider to provide COSELA to qualifying uninsured or underinsured patients within the population indicated in our label. Less than 3% of utilization has been through this patient support program.

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

- The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, paying, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The federal Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the federal Anti-Kickback Statute to reach large settlements with healthcare companies based on a variety of financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- The federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalty laws, prohibit, among other things, knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the U.S. government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. Actions under these laws may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. The federal government uses these laws, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of products for unapproved uses and other allegedly unlawful sales and marketing practices;
- The U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created new federal, civil and criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- The Physician Payments Sunshine Act, among other things, requires manufacturers of FDA-approved drugs, devices, biologics and medical supplies covered by Medicare, Medicaid, or the Children’s Health Insurance Program to report to CMS, on an annual basis, information related to payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, chiropractors and certain advanced non-physician healthcare practitioners, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH") and its implementing regulations impose specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA’s privacy and security standards directly applicable to “business associates,” defined as independent contractors or agents of covered entities, which include certain healthcare providers, health plans, and healthcare clearinghouses, that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney’s fees and costs associated with pursuing federal civil actions;
- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers;

- State laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures to the extent that those laws impose requirements that are more stringent than the Physician Payments Sunshine Act, as well as state and local laws that require the registration of pharmaceutical sales representatives; and
- State laws that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

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

Healthcare Reform and potential changes to drug and healthcare laws

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding healthcare systems that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates that obtain marketing approval. The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product or affect our ability to successfully commercialize COSELA for its approved indication(s). If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations. Moreover, among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. See additional disclosures above under "Pharmaceutical Coverage, Pricing, and Reimbursement."

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

As another example, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drugs and biological products covered under Medicare Part B report the product's average sales price ("ASP") to Department of Health and Human Services ("DHHS") beginning on January 1, 2022, subject to enforcement via civil money penalties. More recently, the American Rescue Plan Act of 2021 included a provision that eliminated the statutory cap on rebates that drug manufacturers pay to Medicaid. Beginning in January 2024, Medicaid rebates are no longer being capped at 100 percent of the quarterly average manufacturer price ("AMP").

As noted above under "Pharmaceutical Coverage, Pricing and Reimbursement," individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In December 2020, the U.S. Supreme Court held unanimously that federal law does not preempt the states' ability to regulate pharmacy benefit managers ("PBMs") and other members of the health care and pharmaceutical supply chain, an important decision that has led to more aggressive efforts by states in this area. The Federal Trade Commission ("FTC") in mid-2022 also launched sweeping investigations into the practices of the PBM industry that could lead to additional federal and state legislative or regulatory proposals targeting such entities' operations, pharmacy networks, or financial arrangements. During the current congressional session, numerous PBM reforms are being considered in both the Senate and the House of Representatives; they include diverse legislative proposals such as eliminating rebates; divorcing service fees from the price of a drug, discount, or rebate; prohibiting spread pricing; limiting administrative fees; requiring PBMs to report formulary placement rationale; promoting transparency. Significant efforts to change the PBM industry as it currently exists in the U.S. may affect the entire pharmaceutical supply chain and the business of other stakeholders, including pharmaceutical product developers like us.

Further, in September 2023, the FTC issued a policy statement articulating its view that certain "improper" patent listings by drug developers in FDA's Orange Book represent an unfair trade practice and indicated that industry should be prepared for potential enforcement actions based on its analysis. The FTC followed that action in November 2023 by publicly calling out over 100 "improper" patent listings made by ten large pharmaceutical companies and initiating an FDA administrative process with respect to those patents. It remains to be seen whether the FTC, other governmental agencies, pharmaceutical manufacturers, or other stakeholders continue to prioritize the policy issue of "improper" patent listings and whether significant litigation will develop in this area. Accordingly, regulatory and government interest in biopharmaceutical industry business practices continues to expand and pose a risk of uncertainty.

In the EU, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or EU member state level may result in significant additional requirements or obstacles that may increase our operating costs. For example, in April 2023 the European Commission issued a proposal that will revise and replace the existing general pharmaceutical legislation. If adopted and implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the European Union.

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

U.S. Foreign Corrupt Practices Act

In general, the Foreign Corrupt Practices Act of 1977, as amended, (the "FCPA") prohibits offering to pay, paying, promising to pay, or authorizing the payment of money or anything of value to a foreign official in order to influence any act or decision of the foreign official in his or her official capacity or to secure any other improper advantage in order to obtain or retain business for or with, or in order to direct business to, any person. The prohibitions apply not only to payments made to "any foreign official," but also those made to "any foreign political party or official thereof," to "any candidate for foreign political office" or to any person, while knowing that all or a portion of the payment will be offered, given, or promised to anyone in any of the foregoing categories. "Foreign officials" under the FCPA include officers or employees of a department, agency, or instrumentality of a foreign government. The term "instrumentality" is broad and can include state-owned or state-controlled entities.

Importantly, United States authorities that enforce the FCPA, including the Department of Justice, deem most healthcare professionals and other employees of foreign hospitals, clinics, research facilities and medical schools in countries with public health care or public education systems to be “foreign officials” under the FCPA. When we, or any of our agents, interact with foreign healthcare professionals and researchers in testing and marketing our products abroad, we must have policies and procedures in place sufficient to prevent us and agents acting on our behalf from providing any bribe, gift or gratuity, including excessive or lavish meals, travel or entertainment in connection with marketing our products and services or securing required permits and approvals such as those needed to initiate clinical trials in foreign jurisdictions. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the maintenance of books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and the development and maintenance of an adequate system of internal accounting controls for international operations. The U.S. Securities and Exchange Commission is involved with the books and records provisions of the FCPA.

Europe/Rest of world government regulation

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

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in non-U.S. countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application ("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. In addition, European clinical trials legislation has recently been reformed with the aims of harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Specifically, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) came into application on January 31, 2022 and is directly applicable in all the EU Member States, repealing the previous Clinical Trials Directive 2001/20/EC. The extent to which ongoing clinical trials are governed by the Clinical Trials Regulation depends on when the Clinical Trials Regulation became applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation became applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial. In addition, use of the new EU-wide application procedure being implemented via the Clinical Trial Information System (“CTIS”) became mandatory for new clinical trial application submissions as of February 1, 2023.

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. In April 2023 the European Commission issued a proposal that will revise and replace the existing general pharmaceutical legislation. If adopted and implemented as currently proposed, these revisions will significantly change several aspects of drug development and approval in the EU.

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 ("MAA"). The way in which a medicinal product can be approved in the European Union depends on the nature of the medicinal product.

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

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application by the European Medicines Agency, or EMA, is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use ("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 ("MRP") for the approval of human drugs is an alternative approach to facilitate individual national marketing authorizations within the European Union. Basically, the MRP may be applied for all human drugs for which the centralized procedure is not obligatory. The MRP is applicable to the majority of conventional medicinal products, and is based on the principle of recognition of an already existing national marketing authorization by one or more member states. In the MRP, a marketing authorization for a drug already exists in one or more member states of the E.U. and subsequently marketing authorization applications are made in other European Union member states by referring to the initial marketing authorization. The member state in which the marketing authorization was first granted will then act as the reference member state. The member states where the marketing authorization is subsequently applied for act as concerned member states. After a product assessment is completed by the reference member state, copies of the report are sent to all member states, together with the approved summary of product characteristics, labeling and package leaflet. The concerned member states then have 90 days to recognize the decision of the reference member state and the summary of product characteristics, labeling and package leaflet. National marketing authorizations within individual member states shall be granted within 30 days after acknowledgement of the agreement.

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

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

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

Data privacy and the protection of personal information

We are subject to laws and regulations governing data privacy and the protection of personal information including health information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues which will continue to affect our business. In the United States, we may be subject to state security breach notification laws, state laws protecting the privacy of health and personal information and federal and state consumer protections laws which regulate the collection, use, disclosure and transmission of personal information, including but not limited to the Federal Trade Commission Act. These laws overlap and often conflict and each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues for us. If we fail to comply with applicable laws and regulations, we could be subject to penalties or sanctions, including criminal penalties. Our customers and research partners must comply with laws governing the privacy and security of health information, including the Health Insurance Portability and Accountability Act of 1996 as amended ("HIPAA") and state health information privacy laws. Although we are not directly subject to HIPAA, we could potentially be subject to criminal penalties if we or our agents knowingly receive individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

State laws protecting health and personal information are becoming increasingly stringent. For example, California has implemented the California Confidentiality of Medical Information Act that imposes restrictive requirements regulating the use and disclosure of health information and other personally identifiable information. In addition, the California Consumer Privacy Act ("CCPA") became effective in January of 2020. The CCPA, as amended by the California Privacy Rights Act ("CPRA," and together, the "CCPA") which came into full effect in January of 2023, broadly defines personal information, and creates new privacy rights and protections for Californians, places increased privacy and security obligations on entities handling personal data, and adds civil penalties for violations and a private right of action by data breaches. The CCPA requires covered companies to provide certain disclosures to consumers (including employees and contractors) about its data collection, use, and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CPRA modifies the CCPA significantly including establishing a new regulatory agency, the California Privacy Protection Agency, which is charged with enacting regulations and has expanded enforcement authority. The scope of the new regulations and the effect on operations is still unclear, resulting in further uncertainty, additional costs and expenses in an effort to comply and additional potential for harm and liability for failure to comply.

In addition to the CCPA, new comprehensive privacy and security laws have been proposed in more than half of the states in the U.S., and Congress continues to propose federal privacy legislation. Colorado, Connecticut, Virginia, and Utah all had comprehensive privacy laws that took effect in 2023 and other states have laws taking effect in 2024 and 2025. The effects of these multiple and differing state laws, and other similar state or federal laws, are potentially significant and may require us to modify our data processing practices and policies and incur substantial costs and potential liability in an effort to comply with such legislation.

Europe - Data Privacy

In Europe, our clinical trials may be subject to the General Data Protection Regulation ("GDPR") and the UK GDPR (collectively, the "GDPR") which went into effect in May 2018 and which imposes obligations on companies that operate in our industry with respect to the processing of personal data and the cross-border transfer of such data. The GDPR applies to any company established in the European Economic Area ("EEA") (which includes the European Union ("EU") member states plus Iceland, Liechtenstein, and Norway) and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EEA or the monitoring of the behavior of data subjects in the EEA. The GDPR establishes stringent requirements applicable to the processing of personal data, including strict requirements relating to the validity of consent of data subjects, expanded disclosures about how personal data is used, requirements to conduct data protection impact assessments for "high risk" processing, limitations on retention of personal data, special provisions affording greater protection to and requiring additional compliance measures for "special categories of personal data" including health and genetic information of data subjects, mandatory data breach notification (in certain circumstances), "privacy by design" requirements, and direct obligations on service providers acting as processors. The GDPR also prohibits the international transfer of personal data from the EEA to countries outside of the EEA unless made to a country deemed to have adequate data privacy laws by the European Commission or a data transfer mechanism has been put in place. If our or our partners' or service providers' privacy or data security measures fail to comply with the GDPR requirements, we may be subject to litigation, regulatory investigations, enforcement notices requiring us to change the way we use personal data and/or fines of up to 20 million Euros or up to 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, as well as compensation claims by affected individuals, negative publicity, reputational harm and a potential loss of business and goodwill. The GDPR may also impose additional compliance obligations relating to the transfer of data between us and our affiliates, collaborators, or other business partners. For example, on July 16, 2020, the Court of Justice of the European Union (CJEU), issued a landmark opinion in the case *Maximilian Schrems vs. Facebook* (Case C-311/18), called *Schrems II.* This decision (a) calls into question commonly relied upon data transfer mechanisms as between the EU member states and the United States (such as the Standard Contractual Clauses) and (b) invalidates the EU-U.S. Privacy Shield on which many companies had relied as an acceptable mechanism for transferring such data from the EU to the United States.

On July 10, 2023, The European Commission adopted an adequacy decision for a new mechanism for transferring data from the EU to the United States – the EU-US Data Privacy Framework (the "Framework"). The Framework provides EU individuals with several new rights, including the right to obtain access to their data, or obtain correction or deletion of incorrect or unlawfully handled data. The adequacy decision followed the signing of an executive order introducing new binding safeguards to address the points raised in the *Schrems II* decision. Notably, the new obligations were geared to ensure that data can be accessed by US intelligence agencies only to the extent necessary and proportionate and to establish an independent and impartial redress mechanism to handle complaints from Europeans concerning the collection of their data for national security purposes. The European Commission will continually review developments in the US along with its adequacy decision. Adequacy decisions can be adapted or even withdrawn in the event of developments affecting the level of protection in the applicable jurisdiction. Future actions of EU data protection authorities are difficult to predict. Reliance on the Framework to enable cross-border transfers without certain contractual and other representations is dependent upon certification to the Framework, which we have not yet done.

Relatedly, the United Kingdom ("UK") formally left the European Union on January 31, 2020 (commonly referred to as Brexit). In the UK, the Data Protection Act 2018 "implements" and compliments the GDPR, and is effective in the UK. On June 28, 2021, the European Commission adopted an adequacy decision in respect of transfers of personal data to the UK for a four year period (until June 27, 2025). Similarly, the UK has determined that it considers all of the European Economic Area to be adequate for the purposes of data protection. This ensures that data flows between the UK and the EU remain unaffected. The UK has likewise adopted a UK Extension to the Framework on the same terms as the European Commission for data transfers between the US and the UK, but we have not yet certified to the Framework.

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

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

Orange book listing

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent that has claims that cover the applicant's product or method of therapeutic use. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an ANDA. The ANDA requests permission to market a drug product that has the same active ingredients in the same strengths and dosage form as the RLD and has been shown through bioequivalence testing to be therapeutically equivalent to the RLD. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, nonclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the innovator drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug referenced by the ANDA applicant if the FDA's listing for the generic drug in the Orange Book indicates that it is "therapeutically equivalent" to the RLD.

In contrast, Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. A Section 505(b)(2) applicant may eliminate the need to conduct certain preclinical or clinical studies, if it can establish that reliance on studies conducted for a previously approved product is scientifically appropriate. Unlike the ANDA pathway used by developers of bioequivalent versions of innovator drugs, which does not allow applicants to submit new clinical data other than bioavailability or bioequivalence data, the 505(b)(2) regulatory pathway does not preclude the possibility that a follow-on applicant would need to conduct additional clinical trials or nonclinical studies; for example, it may be seeking approval to market a previously approved drug for new indications or for a new patient population that would require new clinical data to demonstrate safety or effectiveness.

When an ANDA applicant submits its application to the FDA, it is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement, certifying that its proposed ANDA label does not contain or carve out any language regarding the patented method-of-use, rather than certify to a listed method-of-use patent. Moreover, to the extent that the Section 505(b)(2) NDA applicant is relying on studies conducted for an already approved product, the applicant also is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

If the applicant does not challenge the innovator's listed patents, FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

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

Non-Patent Exclusivity

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

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

Upon approval of the first COSELA marketing application in February 2021, the drug product secured a 5-year period of NCE exclusivity. This exclusivity period will expire on February 12, 2026.

Patent term extension

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent term extension. The allowable patent term extension is calculated as half of the drug’s testing phase—the time between when the IND becomes effective and NDA submission—and all of the review phase—the time between NDA submission and approval, up to a maximum of five years. The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the Patent and Trademark Office (PTO) must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

On April 8, 2021, we filed a request for patent term extension pursuant to 35 U.S.C. § 156 on two of our trilaciclib (COSELA) Orange Book listed patents (U.S. 8,598,186 and U.S. 9,487,530). The ‘186 patent claims the composition of matter of trilaciclib (COSELA). The ‘530 patent claims the use of trilaciclib (COSELA) to reduce the effect of chemotherapy on healthy cells in a subject being treated for, among other things, small cell lung cancer. For the ‘186 patent, we requested an extension of 1,162 days. For the ‘530 patent, we requested an extension of 335 days.

On February 28, 2022, the USPTO informed the FDA that we had requested a patent term extension on the ‘186 patent and ‘530 patent and that the subject matter of the patents would be eligible for extension. On September 21, 2022, the FDA informed the USPTO that COSELA was the subject of a new drug application (NDA), was reviewed by the FDA before commercial marketing, and the patent term extension request was timely filed, all in compliance with 35 U.S.C. § 156. On February 7, 2023, the USPTO informed the FDA that the ‘186 patent and ‘530 patent were eligible for patent term extension and requested that the FDA calculate the regulatory review period. On November 28, 2023, pursuant to 35 U.S.C. § 156(d)(2)(A), the FDA informed the USPTO and published its determination of COSELA’s regulatory review period in the Federal Register (88 Fed. Reg. 83140 (Nov. 28, 2023)), agreeing with our calculations. Anyone with knowledge that any of the dates as published in the Federal Register are incorrect may request that the FDA redetermine the extension calculations by January 29, 2024 (60 days from publication) or petition the FDA for a determination regarding whether we acted with due diligence during the regulatory review period by May 28, 2024 (180-days from publication). If no comment or petition is filed within the time period provided, the FDA will notify the USPTO that the period for filing a due diligence petition pursuant to the publication has expired and that the FDA therefore considers its determination of the regulatory review period for COSELA to be final. Following notification from the FDA, the USPTO will proceed with the final patent term extension eligibility determination.

After reviewing the information provided by the FDA, if the USPTO determines the patents are eligible for extension, the USPTO will then calculate the length of extension for which the patents are eligible. A Notice of Final Determination will be mailed to us which states the length of extension for which the patents have been determined to be eligible and the calculations used to determine the length of extension. The Notice of Final Determination provides a period, usually one month, in which we can request reconsideration of any aspect of the USPTO’s determination as to eligibility or the length of extension.

Under 35 U.S.C. 156, only one patent may be extended for a single regulatory review period for COSELA. The USPTO will provide a period of time (usually one month) for us to elect the patent for which extension is desired following the receipt of the Notice of Final Determination. We ultimately intend to elect one patent for extension. To the extent U.S. 8,598,186 is elected, the term is expected to be extended to December 30, 2034. To the extent U.S. 9,487,530 is elected, the term is expected to be extended to February 12, 2035.

Environmental, Health, and Safety Regulation

We are subject to numerous federal, state and local environmental, health and safety (“EHS”), laws and regulations relating to, among other matters, safe working conditions, product stewardship, environmental protection, and handling or disposition of products, including those governing the generation, storage, handling, use, transportation, release, and disposal of hazardous or potentially hazardous materials, medical waste, and infectious materials that may be handled by our research laboratories. Some of these laws and regulations also require us to obtain licenses or permits to conduct our operations. If we fail to comply with such laws or obtain and comply with the applicable permits, we could face substantial fines or possible revocation of our permits or limitations on our ability to conduct our operations. Certain of our development and manufacturing activities involve use of hazardous materials, and we believe we are in compliance with the applicable environmental laws, regulations, permits, and licenses. However, we cannot ensure that EHS liabilities will not develop in the future. EHS laws and regulations are complex, change frequently and have tended to become more stringent over time. Although the costs to comply with applicable laws and regulations, have not been material, we cannot predict the impact on our business of new or amended laws or regulations or any changes in the way existing and future laws and regulations are interpreted or enforced, nor can we ensure we will be able to obtain or maintain any required licenses or permits.

Human Capital

As of December 31, 2023, we had 100 full-time employees, including 72 mapped to selling, general and administrative functions, 25 mapped to research and development functions and three mapped to costs of goods sold functions. Of these full-time employees, 17 had an MD, PhD or PharmD. We have no collective bargaining agreements with our employees, and we have not experienced any work stoppages. We expect headcount to fluctuate slightly as we continue to develop our products and commercialize COSELA. We consider our relations with our employees to be good and were named by Triangle Business Journal as one of the Best Places to Work in 2023 for the second year in a row.

Diversity and Inclusion

Diversity and inclusion are an important part of our culture. We seek to build a diverse and inclusive workplace where we can leverage our collective cognitive and other diversity. We conduct routine pay equity analysis to determine we have pay equity across gender and race in similar jobs, accounting for factors such as role, experience, education and level. We also have a Culture Committee comprised of employees across departments, who focus on employee engagement, building a more diverse and inclusive organization, and other initiatives throughout the year.

Compensation and Benefits

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

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 carries significant risks. Before investing, carefully review the risks and uncertainties outlined in this Annual Report, including our financial statements and related notes. These risks are not exhaustive, and others not currently known to us could also impact our business and reputation. If any of these risks materialize, it could harm our business, financial condition, liquidity, cash flows, or results of operations, potentially leading to a decline in the price of our common stock and a loss of part or all of your investment.

Summary Risk Factors

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

Risks related to the commercialization of COSELA

- We depend almost entirely on the commercial success of COSELA.
- COSELA may fail to achieve the degree of market acceptance for commercial success.
- We may not be able to effectively sell or market COSELA, or generate substantial product revenues.
- COSELA may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies.
- We face substantial competition.
- We must comply with post-approval development and regulatory requirements to maintain FDA approval of COSELA.
- 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.
- Any significant cost increases or shortages in the supply of chemotherapy products containing platinum/etoposide or topotecan could have an adverse impact on our customers' abilities to order and administer COSELA

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

- We may need substantial additional funding.
- We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights.
- Our level of indebtedness and debt service obligations could adversely affect our financial condition.

Risks related to development of COSELA:

- If we are unable to successfully develop and commercialize COSELA, our business will be materially harmed.
- Delays in the enrollment of patients in clinical trials, may delay or prevent our plans.
- Initial success in our ongoing clinical trials may not be indicative of results obtained when these trials are completed.
- We may incur additional costs or experience delays in completing the development and may ultimately be unable to obtain the approval COSELA in additional indications.

Risks related to additional marketing approvals of COSELA:

- If we are not able to obtain, or if there are delays in obtaining the additional required marketing approvals, we will not be able to broadly commercialize COSELA, and our ability to generate revenue will be materially impaired.
- COSELA is subject to extensive post-marketing regulatory requirements and could be subject to additional 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 COSELA.

- COSELA may cause undesirable side effects that could delay or prevent additional marketing approvals, limit the commercial profile of additional approved labels, or result in significant negative consequences following additional marketing approvals, if any.

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.

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 COSELA. 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 additional marketing approval for or commercialize COSELA, and our business could be substantially harmed.
- We contract with third parties for the manufacture of COSELA for preclinical studies and clinical trials. This reliance on third parties increases the risk that we will not have sufficient quantities of COSELA or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- The third parties upon which we rely for the supply of the drug substance and drug product are our sole sources of supply and have limited capacity, and the loss of any of these suppliers could harm our business.

Risks related to our intellectual property:

- If we are unable to obtain, enforce, and maintain intellectual property protection for our current or future 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.
- We may become involved in administrative adversarial proceedings in the U.S. PTO or in the patent offices of foreign countries brought by a third party to attempt to cancel or invalidate our patent rights, which could be expensive, time consuming and cause a loss of patent rights.
- We may have to file one or more lawsuits in court to prevent a third party from selling a product or using a product in a manner that infringes our patent, which could be expensive, time consuming and unsuccessful, and ultimately result in the loss of our proprietary market.
- Applicable regulatory authorities, including the FDA and the USPTO in the United States, may not agree with our assessment of whether applicable extensions should be granted, and even if granted, the length of such extensions. Further, 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.
- 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.

Risks related to our common stock:

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

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

Risks related to the commercialization of COSELA

We depend almost entirely on the commercial success of COSELA. There is no assurance that our commercialization efforts in the U.S. for COSELA will succeed or that we will be able to generate revenues necessary to support our goals.

There is no guarantee that we will be successful in our commercialization efforts with respect to COSELA. There is no assurance that the sales of COSELA will grow on the timing we anticipate. We may encounter delays or hurdles related to our sales efforts that affect the amount of revenue generated and the timing of such revenue.

Our business currently depends heavily on our ability to successfully commercialize COSELA in the U.S. to treat patients with ES-SCLC. There is no guarantee that the infrastructure, systems, processes, policies, personnel, relationships and materials we have built for the commercialization of COSELA in the U.S. will be sufficient for us to achieve success at the levels we expect. Our results may also be negatively impacted if we have not adequately sized our field teams, if our physician segmentation and targeting strategy is inadequate, or if we encounter deficiencies or inefficiencies in our infrastructure or processes. These issues could hinder our ability to successfully commercialize COSELA, generate significant revenues or profits, or meet our expectations regarding revenue or profit amounts or timing. Any issues or hurdles related to our commercialization efforts may materially adversely affect our business, results of operations, financial condition and prospects.

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

Our COSELA commercialization efforts may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Healthcare providers may not accept a change in treatment paradigm for patients with ES-SCLC. We may also encounter challenges related to reimbursement of COSELA including potential limitations in the scope, breadth, availability, or amount of reimbursement covering COSELA. Similarly, healthcare settings or patients may determine that the financial burdens of treatment are not acceptable. If COSELA does not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of COSELA and will depend on a number of factors, including:

- the timing of our receipt of any additional 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 COSELA;
- adverse publicity about COSELA, including the discontinuation of the trials, or favorable publicity about competing products;
- our ability to offer COSELA 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 COSELA together with other medications.

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

If we are unable to enhance our sales or marketing capabilities, we may not be able to effectively sell or market COSELA or generate substantial product revenues.

To achieve commercial success for COSELA, we must continue to develop our sales, marketing, managerial, and other non-technical capabilities.

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

- our inability to 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 COSELA;
- 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 are not successful in commercializing COSELA, 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.

If market opportunities for COSELA are smaller than we estimate or if any FDA approval that we receive for additional indications for COSELA is based on a narrower definition of the patient population, our revenues may be substantially lower than we estimate.

We are focused on the development and commercialization of COSELA. We have estimated the number of people who have cancer or will develop cancer and have estimated the amount of approved patient populations who could benefit from COSELA. However, our estimates, which have been developed from a number of sources, may ultimately be inaccurate. Our estimates may change because of novel studies, the number of potential patients may be fewer than contemplated, any additional indications for COSELA approved by FDA may be based on a narrower definition of the patient population than we have estimated, patients may not be receptive to treatment with COSELA, patients may select our competitors' products instead of ours, or it may be more difficult to identify the potential patient population than anticipated, all of which could cause the market opportunities for COSELA to be more limited than we predicted and adversely impact our business and profitability.

COSELA 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 COSELA in a particular country, but then be subject to price regulations that delay our commercial launch, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of COSELA in that country. Adverse pricing limitations may hinder our ability to recoup our investment in COSELA.

Our ability to commercialize COSELA successfully also will depend in part on the extent to which coverage and reimbursement for COSELA 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 Centers for Medicare & Medicaid Services ("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 CMS policies or decisions 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 COSELA and, if coverage is available, the level of payments. Reimbursement may impact the demand for, or the price of, COSELA. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize COSELA.

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 medicines by determining standards of care. 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 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 or any of our future partners violate the rules or regulations pertaining to promotion and advertising of COSELA, we or they may be subject to disciplinary action by the FDA's Office of Prescription Drug Promotion or other regulatory authorities.

The FDA's Office of Prescription Drug Promotion ("OPDP"), is responsible for reviewing prescription drug advertising and promotional labeling to ensure that the information contained in these materials is not false or misleading. There are specific disclosure requirements, and the applicable regulations mandate that advertisements cannot be false or misleading or omit material facts about the product. Prescription drug promotional materials must present a fair balance between the drug's effectiveness and the risks associated with its use. Most enforcement letters from OPDP cite inadequate disclosure of risk information or misleading presentations about a product's efficacy. In addition, although physicians may prescribe legally available products for off-label uses under professional practice guidelines, manufacturers may not market or promote such uses. Companies may, however, share truthful and not misleading information that is consistent with the product's labeling.

OPDP prioritizes its actions based on the degree of risk to the public health, and often focuses on newly introduced drugs and those associated with significant health risks. OPDP issues two types of public letters for drug advertising violations: untitled letters and warning letters. Untitled letters alert companies of potential violations and direct them to refrain from future violations, while warning letters are issued for more serious offenses and typically request corrective actions be taken by the company. Although we have not received any such letters from OPDP, we or any of our future partners may inadvertently violate OPDP's rules and regulations in the future, which may have a negative impact on our business.

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 COSELA 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 COSELA. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. COSELA competes with (a) existing growth factor support treatments, and (b) multiple approved drugs or drugs that may be approved in the future for indications for which we may develop COSELA.

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

As a condition of the initial marketing approval of COSELA, we were required to (i) conduct a study in a sufficient number of adult patients with extensive stage-small cell lung cancer undergoing chemotherapy to evaluate the impact of COSELA on disease progression or survival in patients with chemotherapy-induced myelosuppression treated with a platinum/etoposide-containing regimen or topotecan-containing regimen with at least 2 years of follow-up, (ii) conduct an in vitro metabolism study and CYP phenotyping study at clinically relevant concentrations to appropriately determine major metabolic pathway for COSELA, and characterize the formation of the major circulating metabolite of trilaciclib, M8, using the purified M8 compound with a validated bioanalytical method, (iii) conduct an in vitro Drug-Drug Interaction (DDI) study to evaluate the major circulating metabolite of COSELA, M8, as an inhibitor for major CYP enzymes and drug transporters, and (iv) conduct a clinical trial to evaluate the effect of hepatic impairment on the pharmacokinetics and safety of COSELA. Except for the clinical study noted in (i) above, we have completed the other post-marketing requirements attached to our NDA approval and submitted them to the FDA for review.

The FDA may withdraw approval of COSELA if evidence generated from the post-approval studies demonstrates that COSELA is not shown to be safe or effective under the conditions of use, we disseminate false or misleading promotional materials relating thereto, among other potential administrative actions that could be taken against the drug product or against our company.

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

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

- the federal Anti-Kickback Statute which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, in return for, either the referral of an individual or the purchase, lease, or order, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;
- the federal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making or causing to be made 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 or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, 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 Payments Sunshine Act, which requires certain require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with certain exceptions, to report annually to CMS information related to payments and other "transfers of value" to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain advanced nonphysician practitioners, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- HIPAA, as amended by HITECH 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;
- some state laws that require pharmaceutical companies to report information on the pricing of certain drug products; and some state and local laws that require the registration of pharmaceutical sales representatives; 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 current and future business arrangements with third parties will comply with applicable healthcare and privacy laws and regulations will involve ongoing 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 penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government-funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. Defending against any such actions can be costly and time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business are found to violate applicable laws or regulations, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

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 EU, 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 COSELA to other available therapies. If reimbursement of COSELA is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Any significant cost increases or shortages in platinum/etoposide or topotecan chemotherapy could hinder our customers' ability to order and administer COSELA, potentially affecting its sales.

As COSELA's efficacy relies on its administration in conjunction with specific chemotherapy regimens containing platinum/etoposide or topotecan, any significant cost increases or supply shortages of these chemotherapy products could have an adverse impact on our customers' abilities to order and administer COSELA, and as a result, could impact the sales of COSELA.

If manufacturers face production challenges for these chemotherapy products due to supply chain disruptions or manufacturing issues, or if customers struggle to obtain an adequate supply due to price fluctuations or shortages, they may reduce orders of COSELA. This could lead to treatment delays or disruptions for ES-SCLC, affecting patient outcomes and treatment schedules.

As of the date of this report, the FDA has reported shortages in the supply of certain platinum-based chemotherapy products, including Cisplatin (since February 2023) and Carboplatin (since April 2023). We are actively monitoring any issues related to the availability of these chemotherapy products and their potential impact on the use of COSELA. Any significant disruption in the supply chain or demand for these chemotherapy products could adversely impact our sales of COSELA and therefore adversely affect our business, results of operations, and financial conditions.

Risks related to our financial position and need for additional capital

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.

Developing pharmaceutical drugs is a capital-intensive venture. We expect increasing expenses for our ongoing activities, particularly as we support commercial activities, conduct clinical trials, and seek marketing approval for, COSELA in any additional indications. For example, we expect to incur significant COSELA commercialization expenses related to product sales, marketing, manufacturing and distribution. We may also need to raise additional funds to pursue new indications and/or geographies for COSELA or otherwise if we expand more rapidly than currently anticipated. 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 and to achieve our business objectives. 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.

Because the length of time and activities associated with successful commercialization, research and development of COSELA is highly uncertain, we are unable to estimate the actual funds we will require. Our future capital needs will depend on several factors and could increase significantly due to various reasons, including:

- the costs of commercialization activities, including product sales, marketing, manufacturing and distribution of COSELA for which we received marketing approval or any of our product candidates for which we receive marketing approval;
- the scope, progress, results and costs of nonclinical development, laboratory testing and clinical trials for COSELA;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of COSELA;
- the extent to which we enter into non-exclusive, jointly funded clinical research collaboration arrangements, if any, for the development of COSELA 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 agreements 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, and the terms of such in-licenses;
- the potential benefit of the NMPA's conditional approval for our products and product candidates and our ability to provide comprehensive clinical data from post-approval clinical research;
- revenue received from commercial sales of COSELA and any future product candidates;
- our ability to meet the required financial covenants under our loan agreement;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- global economic uncertainty, rising inflation, rising interest rates, market disruptions and volatility in commodity prices.

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

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

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

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 $48.0 million for the year ended December 31, 2023, $147.6 million for the year ended December 31, 2022, and $148.4 million for the year ended December 31, 2021. As of December 31, 2023, we had an accumulated deficit of $780.0 million. It may be several years, if ever, before we become profitable. To date, we have financed our operations primarily through proceeds from our initial public offering, our follow-on stock offerings, our loan agreement with Hercules Capital, Inc. ("Hercules") and proceeds from our license agreements. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future.

To date, inflation has not had a material impact on our business, but if the global inflationary trends continue, we expect appreciable increases in clinical trial, selling, labor, and other operating costs. If our costs were to become subject to significant inflationary pressures, we may not be able to fully offset such higher costs through price increases of our product. Our inability or failure to do so could adversely affect our business, financial condition and results of operations.

In addition, currently there is a conflict involving Russia and Ukraine and a conflict involving Israel and Hamas, and these conflicts may directly or indirectly impact our contract research organizations, clinical data management organizations, and clinical investigators' ability to conduct certain of our trials in Eastern European countries, and may increase our product development costs and materially harm our business.

The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate our research and development, commercial activities, and selling, general and administrative expenses will continue to increase in connection with our ongoing and future activities.

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

To become and remain profitable, we must develop and commercialize products with significant market potential.

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. A decline in the value of our company could also cause you to lose all or part of your investment.

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

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

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

As of December 31, 2023, the Company has $50.0 million outstanding under our loan agreement with Hercules (the "Hercules Loan Agreement"), with a maturity date of November 1, 2026. Our obligations under the Hercules Loan Agreement are secured by a blanket lien on substantially all of the Company’s assets, including a security interest in the intellectual property.

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

If we were to become unable to pay, when due, the principal of, interest on, or other amounts due in respect of, our indebtedness, our financial condition would be adversely affected. Further, under the Hercules Loan Agreement, we are subject to certain restrictive covenants that, among other things, subject to exceptions, restrict the Company’s ability to do the following things: declare dividends or redeem or repurchase equity interests; incur additional liens; make loans and investments; incur additional indebtedness; engage in mergers, acquisitions, and asset sales; transact with affiliates; undergo a change in control; and add or change business locations. As of December 31, 2023, we were in compliance with all covenants. If we breach any of these restrictive covenants or are unable to pay our indebtedness under the Hercules Loan Agreement when due, this could result in a default under the Hercules Loan Agreement. In such event, Hercules may elect (after the expiration of any applicable notice or grace periods) to declare all outstanding borrowings, together with accrued and unpaid interest and other amounts payable under the Hercules Loan Agreement, to be immediately due and payable. Any such occurrence would have an adverse impact on our financial condition. See "Management's Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources - Loan and Security Agreement" section of this Annual Report for more details.

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 waste. 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.

Our ability to use our net operating loss carryforwards and other tax attributes may be limited, and changes in tax laws could adversely impact our business and financial position.

The Internal Revenue Service or other tax authority may review and adjust our net operating loss and tax credit carryforwards pursuant to the Internal Revenue Code of 1986 (the "Code"). In the event of an "ownership change" under Section 382 of the Code ("Section 382"), we may be subject to annual limitations on our ability to utilize net operating loss and tax credit carryforwards. An ownership change constitutes a change in the ownership interest of significant shareholders in excess of 50% on a cumulative basis over a three-year period. In April 2019, the Company completed an evaluation study as to whether an "ownership change" had occurred and determined that the limitation would be approximately $8.0 million on federal net operating loss carryforwards, $1.2 million on state net operating loss carryforwards, and $0.1 million on R&D tax credit carryforwards. The carryforward amounts reported above have already been reduced for these limitations. We continue to maintain a valuation allowance on the remaining NOLs as we believe that it is more likely than not that all of the deferred tax asset associated with the NOLs will not be realized regardless of whether an "ownership change" has occurred. As of December 31, 2023, our federal and state net operating loss carryforwards amounted to $550.7 million and $401.2 million, respectively. Other changes in the ownership of our stock may have caused an ownership change in the past or could cause one in the future. Additional ownership changes under Section 382 could further limit our ability to reduce future tax liabilities by utilizing our net operating loss carryforwards.

In addition, our capacity to utilize our net operating loss carryforwards and other tax attributes could be limited due to statutory and regulatory changes. For example, among other things, the Tax Cuts and Jobs Act of 2017 (the "TCJA") comprehensively changed U.S. federal tax rates, permitted capital expenditures to be expensed, and restricted tax deductions for net interest expense and net operating losses. The CARES Act of 2020 was enacted to restore the ailing U.S. economy during the COVID-19 pandemic. Among other things, the CARES Act temporarily eased the TCJA's restrictions on net interest expense tax deductions and altered the payroll tax scheme. Congress may enact additional tax legislation, and we cannot predict how future amendments in tax laws and regulations will impact our business and financial position.

Risks related to development of COSELA

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

We have invested substantially all of our efforts and financial resources identifying and developing COSELA. Our ability to generate product revenues will depend on the successful development and commercialization of COSELA for additional indications. COSELA will require additional development, management of development and manufacturing activities, marketing approval in multiple jurisdictions, obtaining manufacturing supply, commercialization activities, substantial investment and significant marketing efforts.

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:

- maintain robust sales, distribution and marketing capabilities, either on our own or in collaboration with strategic partners;
- gain acceptance for COSELA by patients, the medical community and third-party payors;
- compete effectively with other therapies;
- execute development activities for COSELA, including successful completion of clinical trials;
- obtain required marketing approvals for the development and commercialization of additional indications for COSELA, which may become more difficult considering the discontinuation of clinical trials;

- obtain, maintain, and enforce patent and trade secret protection and regulatory exclusivity for COSELA and ensure that we do not infringe the valid patent rights of third parties;
- protect, leverage and expand our intellectual property portfolio;
- establish and maintain clinical and commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical and commercial manufacturing;
- obtain., maintain, and enforce healthcare coverage and adequate reimbursement;
- maintain a continued acceptable safety profile for COSELA;
- develop and maintain any strategic relationships;
- enforce and defend intellectual property rights and claims; and
- manage our spending as costs and expenses increase due to preclinical development, clinical trials, marketing approvals and commercialization.

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

If we experience delays or difficulties in the enrollment of patients in any future clinical trials, development of additional indications for COSELA may be delayed or prevented, which would have a material adverse effect on our business.

Identifying and qualifying patients to participate in future clinical trials for additional indications for COSELA is critical to our success. We may not be able to initiate or continue future clinical trials for COSELA if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. 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 COSELA 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.

Congress also recently amended the FDC Act to require sponsors of a Phase 3 clinical trial, or other "pivotal study" of a new drug to support marketing authorization, to design and submit a diversity action plan for such clinical trial. The action plan must describe appropriate diversity goals for enrollment, as well as a rationale for the goals and a description of how the sponsor will meet them. Accordingly, we must submit a diversity action plan to the FDA by the time we submit a Phase 3 trial, or pivotal study, protocol to the agency for review, unless we are able to obtain a waiver for some or all of the requirements for a diversity action plan. It is unknown at this time how the diversity action plan may affect the planning and timing of any future Phase 3 trial for our product candidates or what specific information FDA will expect in such plans. However, initiation of such trials may be delayed if the FDA objects to our proposed diversity action plans for any future Phase 3 trial for our product candidates, and we may experience difficulties recruiting a diverse population of patients in attempting to fulfill the requirements of any approved diversity action plan.

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 development of additional indications for COSELA and the 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.

Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published or reported. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of COSELA and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, COSELA may be harmed, which could harm our business, operating results, prospects or financial condition.

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 COSELA in clinical trials. There can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of COSELA. 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.

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 COSELA in additional indications or in non-US markets.

The risk of failure in drug development is high. Before obtaining marketing approval from regulatory authorities for the sale of COSELA, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety and efficacy of COSELA in humans for each of its intended uses. 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 COSELA 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.

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 in additional indications or commercialize COSELA. 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 or statistical analysis plan 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;
- delays in reaching, or failure to reach, agreement with the FDA on a pivotal study's mandatory diversity action plan;
- 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 COSELA 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 COSELA may be larger 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, an IRB, or a Data Safety Monitoring Board, 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 COSELA or other materials necessary to conduct clinical trials 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 COSELA in additional indications. 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 COSELA beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of COSELA 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 COSELA in additional indications;
- 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 COSELA or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize COSELA and may harm our business and results of operations.

We may not be able to identify additional therapeutic indications for COSELA or to expand our portfolio of product candidates.

We are conducting a number of clinical trials to identify new therapeutic indications for COSELA and to expand our portfolio of product candidates. However, we may be unsuccessful in developing additional therapeutic indications for COSELA. For example, our early anti-tumor efficacy data in colorectal cancer showed patients receiving placebo are favored compared to trilaciclib and led to the decision to discontinue PRESERVE 1. In addition, we may be unsuccessful in developing COSELA for breast cancer. Moreover, such clinical trials require the use of significant financial, human, and technical resources. Even if we are able to identify new opportunities, COSELA will not be commercially available in these indications for a number of years due to extensive clinical testing requirements and regulatory approvals. Additionally, we may focus our limited efforts and resources on a new therapeutic indication that is ultimately unsuccessful. Therefore, we cannot guarantee that we will ever be able to identify and develop additional therapeutic indications for COSELA or expand our portfolio of product candidates, which could adversely impact our future growth and prospects.

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

COSELA is a short-acting intravenous CDK4/6 inhibitor. The use of a CDK4/6 inhibitor to decrease the incidence of chemotherapy-induced myelosuppression is a novel approach. Even though COSELA has demonstrated positive results in clinical trials for ES-SCLC, we may not succeed in demonstrating safety and efficacy of COSELA in additional indications.

Advancing COSELA creates significant challenges for us, including:

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

Risks related to marketing approval of COSELA for additional indications

If we are not able to obtain, or if there are delays in obtaining, additional required marketing approvals for COSELA, we will not be able to commercialize it in other indications, and our ability to generate revenue will be materially impaired.

Before we can commercialize COSELA in additional indications, each additional indication must be approved by the FDA pursuant to a supplemental 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 COSELA in additional indications will prevent us from commercializing it in those indications. For example, our early anti-tumor efficacy data in colorectal cancer showed patients receiving placebo were favored compared to trilaciclib and led to the decision to discontinue PRESERVE 1. 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 nonclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish product 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 relevant regulatory authorities. In each proposed indication for use, COSELA 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 limit commercial use. Regulatory authorities also 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 nonclinical studies or clinical trials. COSELA may be delayed in receiving, or fail to receive, marketing approval in additional indications 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 COSELA is safe and effective for each 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 COSELA'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 COSELA may not be sufficient to support the submission of an NDA, sNDA, MAA or other submission to obtain marketing approval in the United States or elsewhere;
- third-party manufacturers or our clinical or commercial product 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 for additional indications, regulatory authorities may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a label that does not include the labeling claims necessary or desirable for the successful commercialization of COSELA. Any of the foregoing scenarios could materially harm the commercial prospects of COSELA.

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

If COSELA is approved for additional indications, it may 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.

Commercialization activities for COSELA, 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 nonclinical 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. See risks described above, under "If we or any of our future partners violate the rules or regulations pertaining to promotion and advertising of COSELA, we or they may be subject to disciplinary action by the FDA's Office of Prescription Drug Promotion or other regulatory authorities."

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 EU or applicable local country requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with the EU or applicable local country 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 additional indications for COSELA. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize COSELA 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 COSELA, restrict or regulate post-approval activities and affect our ability to profitably sell COSELA.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("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 ASP 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. More recently, the 2021 Consolidated Appropriations Act signed into law on December 27, 2020 incorporated extensive healthcare provisions and amendments to existing laws, including a requirement that all manufacturers of drug products covered under Medicare Part B report the product's ASP to CMS beginning on January 1, 2022, subject to enforcement via civil monetary penalties.

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 COSELA 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 Infrastructure Investment and Jobs Act may impact our future strategies and results of operations as it pertains to COSELA. Passed by the 117th United States Congress and signed into law by President Joe Biden on November 15, 2021, the Infrastructure Investment and Jobs Act is landmark legislation which may significantly impact the pharmaceutical industry. As another example, the American Rescue Plan Act of 2021 included a provision that eliminated the statutory cap on rebates that drug manufacturers pay to Medicaid. Beginning in January 2024, Medicaid rebates are no longer being capped at 100 percent of the quarterly AMP.

Moreover, there have been several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to bring more transparency to drug pricing, reduce the costs of drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. One significant example of recent legislative action is the Inflation Reduction Act of 2022 (the "IRA"), which was signed into law in August 2022 and included several measures intended to lower the cost of prescription drugs. Specifically, the IRA authorizes and directs CMS to set drug price caps for certain high-cost Medicare Part B and Part D qualified drugs. A manufacturer of drug products covered by Medicare Parts B or D must now pay a rebate to the federal government if their drug product's price increases faster than the rate of inflation. This calculation is made on a drug product by drug product basis and the amount of the rebate owed to the federal government is directly dependent on the volume of a drug product that is paid for by Medicare Parts B or D. Additionally, starting for payment year 2026, CMS will negotiate drug prices annually for a select number of single source Part D drugs without generic competition. CMS will also negotiate drug prices for a select number of Part B drugs starting for payment year 2028. If a drug product is selected by CMS for negotiation, it is expected that the revenue generated from such drug will decrease. CMS has begun to implement these new authorities and entered into the first set of agreements with pharmaceutical manufacturers to conduct price negotiations in October 2023. However, the IRA's impact on the pharmaceutical industry in the United States remains uncertain, in part because multiple large pharmaceutical companies and other stakeholders (e.g., the U.S. Chamber of Commerce) have initiated federal lawsuits against CMS arguing the program is unconstitutional for a variety of reasons, among other complaints. Those lawsuits are currently ongoing. In addition, the IRA creates significant changes to the Medicare Part D benefit design by capping Part D beneficiaries' annual out-of-pocket spending at $2,000 beginning in 2025. The IRA is still subject to rulemaking (with more information to come via guidance documents from the responsible federal agencies) and at this time, we cannot be sure whether additional or related legislation or rulemaking will be issued or enacted, or what impact, if any, such changes will have on the profitability of COSELA, in the future.

We expect that the IRA, as well as other federal 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.

We also expect that state and local governments in the U.S. will continue to consider legislation directed at lowering the total cost of healthcare. Individual states in the United States have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, in recent years, several states have formed PDABs. Much like the IRA's drug price negotiation program, these PDABs have attempted to implement upper payment limits on drugs sold in their respective states in both public and commercial health plans. As an example, in August 2023, Colorado's PDAB announced a list of five prescription drugs that would undergo an affordability review. The effects of these efforts remain uncertain pending the outcomes of several federal lawsuits challenging state authority to regulate prescription drug payment limits.

In addition, 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 product may cause undesirable side effects that could delay or prevent its marketing approval for additional indications, limit its commercial profile, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product could cause us or the FDA or other regulatory authorities to interrupt, delay or halt our clinical trials for any additional indications 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 in additional indications. Results of our ongoing clinical trials could reveal a high and unacceptable severity and prevalence of these or other side effects we may observe when trilaciclib is administered in the other tumor types and treatment combinations. 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 for any or all additional 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 trilaciclib may only be uncovered with a significantly larger number of patients exposed to the product. If our product receives marketing approval in additional indications and we or others identify undesirable side effects caused by such product (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;
- 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 is distributed or administered, conduct additional clinical trials or change the labeling of the product;
- 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 the product from the marketplace after it is approved;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product; and
- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of COSELA in ES-SCLC and could substantially increase the costs of gaining marketing approval for COSELA in additional indications and significantly impact our ability to successfully commercialize COSELA and generate revenues in other tumor types and treatment combinations.

We may incur material losses and costs as a result of product liability and warranty claims that may be brought against us and recalls, which may adversely affect our results of operations and financial condition. Furthermore, as a pharmaceutical company, we face an inherent risk of damage to our reputation if one or more of our products are, or are alleged to be, defective.

Our business exposes us to potential product liability risks that are inherent in the design, manufacture and marketing of prescription medical products. In particular, COSELA is used to treat seriously ill cancer patients who are undergoing chemotherapy. Manufacturing defects or inadequate disclosure of product-related risks with respect to COSELA or other products we may commercialize in the future could result in an unsafe condition or injury to, or death of, the patient. As a result, we face an inherent risk of damage to our reputation if one or more of our products are, or are alleged to be, defective. Although we carry product liability insurance, we may be exposed to product liability and warranty claims in the event that our products actually or allegedly fail to perform as expected or the use of our products results, or is alleged to result, in bodily injury. The outcome of litigation, particularly any class-action lawsuits, is difficult to quantify. Plaintiffs often seek recovery of very large or indeterminate amounts, including punitive damages. The magnitude of the potential losses relating to these lawsuits may remain unknown for substantial periods of time and the cost to defend against any such litigation may be significant. Accordingly, we could experience material warranty or product liability losses in the future and incur significant costs to defend these claims.

In addition, if any of our products are, or are alleged to be, defective or unsafe, we may voluntarily initiate, or be required by FDA or other applicable regulators, to initiate a recall of that product from the marketplace. In the event of a recall, we may experience lost sales and be exposed to individual or class-action litigation claims and reputational risk. Product liability, warranty and recall costs may have a material adverse effect on our business, financial condition and results of operations.

The FDA and other government agencies could prevent the timely development and commercialization of new indications of COSELA due to concerns about the quality of data from clinical trials performed in China.

Numerous factors, including regulatory and policy changes, could impact the likelihood and timing of obtaining FDA approval of additional indications for COSELA. The FDA has recently expressed reservations regarding the quality of data from clinical trials conducted in China for the development of cancer treatments. In August 2020, we entered into a license agreement with Simcere, which was amended on April 28, 2023, for the development of COSELA in Greater China. In addition, we have collaborated with Simcere in China to help us develop additional indications for COSELA. We are dependent on Simcere's ability to comply with applicable foreign and U.S. regulatory requirements. There can be no assurance that the FDA, EMA or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction, including any trials conducted in China. This may require us to modify our current clinical trials to exclude the data from China or perform additional clinical trials without Simcere's assistance, which could be expensive and time-consuming. A delay in obtaining the required regulatory approvals could in turn lead to delays in the development of additional indications for COSELA, which could adversely affect us financially.

The government of the People's Republic of China ("PRC") may determine that our licensing agreement with Simcere is not in compliance with applicable PRC laws, rules and regulations.

There are uncertainties regarding the interpretation and application of PRC laws, rules and regulations, including, but not limited to, the laws, rules and regulations governing the validity and enforcement of our licensing agreement with Simcere. Because the interpretations of many laws, regulations and rules are not always uniform, the interpretation of statutes and regulations may be subject to government policies reflecting domestic political agendas and enforcement of existing laws or contracts based on existing law may be uncertain and sporadic. We cannot assure you that the PRC regulatory authorities will not determine that our licensing agreement with Simcere in China does not violate PRC laws, rules or regulations. If the PRC regulatory authorities determine that this licensing agreement is in violation of applicable PRC laws, rules or regulations, it may become invalid or unenforceable, which will adversely affect our operations. The PRC has broad discretion in dealing with violations of laws and regulations, including levying fines, revoking business and other licenses and requiring actions necessary for compliance. In particular, licenses and permits issued or granted by relevant governmental agencies may be revoked at a later time by other regulatory agencies. We cannot predict the effect of the interpretation of existing or new PRC laws or regulations on our business. Any of these or similar actions could significantly disrupt our operations or restrict us from conducting a substantial portion of our operations, which could materially and adversely affect our business, financial condition and results of operations.

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 in foreign markets. In order to market and sell our product in the EU and many other jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. 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 product 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 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 in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product 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 COSELA could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

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

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

We are a commercial-stage biopharmaceutical company, and, as of December 31, 2023, had 100 employees, which includes seven executive officers. We are highly dependent on the commercialization, research and development, clinical, and business development expertise of our executive officers, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

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 or from universities and research institutions for the hiring of scientific and clinical personnel. 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.

Changes in funding for the FDA, the SEC and other government agencies, or shutdowns, travel restrictions or furloughs, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, travel restrictions, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. Average review times at the FDA have fluctuated in recent years. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including most recently beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital to properly capitalize and continue our operations.

Public health threats could have a material impact on our business, financial condition and results of operations, including our commercial operations and sales, clinical trials and non-clinical trials.

The COVID-19 worldwide pandemic, which was recently declared no longer a public health emergency both globally and in the United States, presented substantial public health and economic challenges and affected our employees, customers, patients, physicians and other healthcare providers, communities and business operations, as well as the U.S. and global economies and financial markets. International and U.S. governmental authorities in impacted regions took multiple and diverse actions in an effort to slow the spread of COVID-19 and variants of the virus, including issuing varying forms of "stay-at-home" orders. Such measures taken by the governmental authorities to respond to any future epidemic or pandemic disease outbreaks could severely impact our ability to successfully commercialize COSELA or develop and commercialize COSELA in additional indications, disrupt the supply chain and the manufacture or shipment of drug substances and finished drug product for use in our clinical trials and research and non-clinical studies and, delay, limit or prevent our employees from continuing research and development activities, impede our clinical trial initiation and recruitment and the ability of patients to continue in clinical trials, including due to measures taken that may limit social interaction or prevent reopening of high-transmission settings, impede testing, monitoring, data collection and analysis and other related activities, any of which could delay our non-clinical studies and clinical trials and increase our development costs, and have a material adverse effect on our business, financial condition and results of operations. Any future epidemic or pandemic disease outbreak, including any resurgence of COVID-19, could also potentially further affect the operations of the FDA or other regulatory authorities, which could result in delays in meetings related to our planned clinical trials. Any future epidemic disease outbreak may have an adverse impact on global economic conditions which could have an adverse effect on our business and financial condition, including impairing our ability to raise capital when needed.

We may fail to comply with evolving privacy and data protection laws, which could adversely affect our business, results of operations and financial condition.

In California, the California Consumer Privacy Act ("CCPA"), which became effective in 2020, broadly defines personal information, gives California residents expanded individual privacy rights and protections and provides for civil penalties for violations and a private right of action for data breaches. Further, the California Privacy Rights Act ("CPRA"), which became effective in 2023 and amends the CCPA, creates additional obligations with respect to processing and storing personal information. We continue to monitor developments related to the CCPA and anticipate additional costs and expenses associated with CPRA compliance as regulations are enacted by the California Privacy Protection Agency. While there is an exception for protected health information that is subject to HIPAA and clinical trial regulations, the CCPA may impact our business activities as a "Business" defined under the CCPA. Unlike other state privacy laws, the CCPA also regulates personal information collected in a business to business and in human resources contexts. Further, there continues to be some uncertainly about how provisions of the CCPA and the new regulations will be interpreted and how the law will be enforced.

In addition to the CCPA, broad consumer privacy laws recently went into effect in Virginia on January 1, 2023, in Colorado and Connecticut on July 1, 2023, and in Utah on December 31, 2023. New privacy laws will also become effective in Florida, Montana and Texas in 2024, in Tennessee and Iowa in 2025, and in Indiana in 2026 and numerous other states are considering new privacy laws. Furthermore, other U.S. states, such as New York, Massachusetts, and Utah have enacted stringent data security laws and numerous other states have proposed similar privacy laws.

The existence of differing comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly and may require us to modify our data processing practices and policies and to incur substantial costs and potential liability in an effort to comply with such legislation.

In the EU and the UK, we may also face particular privacy, data security, and data protection risks in connection with requirements of the GDPR. The GDPR applies to any company established in the EU as well as to those outside the EU if they collect and use personal data in connection with the offering of goods or services to individuals in the EU or the monitoring of their behavior. We currently conduct clinical trials and engage in regulatory and commercial operations in the EEA and the UK. As a result, The GDPR imposes a broad range of data protection obligations on companies subject to the GDPR, including, for example, imposing obligations on companies around how they process personal data, stricter requirements relating to processing health and other sensitive data, ensuring there is a legal basis to justify the processing of personal data, stricter requirements relating to obtaining consent of individuals, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements, implementing safeguards to protect the security and confidentiality of personal data, taking certain measures on engagement with third parties, restrictions on transfers outside of the EU to third countries deemed to lack adequate privacy protections (such as the U.S.), and has created onerous new obligations and liabilities on services providers or data processors. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. Moreover, data subjects can claim damages resulting from infringement of the GDPR. The GDPR further grants non-profit organizations the right to bring claims on behalf of data subjects. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of personal data, such as healthcare data or other sensitive information, could greatly increase our cost of providing our products and services or even prevent us from offering certain services in jurisdictions that we may operate in. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Ensuring our continued compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

In particular, member states of the EEA (the "Member States") have implemented national laws which may partially deviate from the GDPR and impose different and more restrictive obligations from country to country, so that we do not expect to operate in a uniform legal landscape in the EU. Also, as it relates to processing and transfer of genetic data, the GDPR specifically allows the Member States to enact laws that impose additional and more specific requirements or restrictions, and European laws have historically differed quite substantially in this field, leading to additional uncertainty.

In addition, we must also ensure that we maintain adequate safeguards to enable the transfer of personal data outside of the EEA, in particular to the U.S., in compliance with EEA data protection laws. We expect that we will continue to face uncertainty as to whether our efforts to comply with our obligations under European privacy laws will be sufficient. The EU and U.S. have adopted an adequacy decision for the EU U.S. Data Privacy Framework, which entered into force on July 11, 2023. This Framework provides that the protection of personal data transferred between the EU and the U.S. is comparable to that offered in the EU. This provides a further avenue to ensuring transfers to the U.S. are carried out in accordance with the GDPR. The Framework could be subject to legal challenge like its predecessor frameworks, and we have not yet certified participation with the Framework.

Many jurisdictions outside of Europe are considering and/or enacting comprehensive data protection legislation that could have an impact on market expansion and clinical trials. For example, we are the named sponsor for two clinical trials in China and developments in privacy and data security in China may require adjustments to our business practices with respect to these personal information protection laws and regulations.

We also continue to see jurisdictions imposing data localization laws. These regulations may interfere with our intended business activities, inhibit our ability to expand into those markets or prohibit us from continuing to offer services in those markets without significant additional costs.

Because the interpretation and application of many privacy and data protection laws (including those state laws in the U.S. and the GDPR), commercial frameworks, and standards are uncertain, it is possible that these laws, frameworks, and standards may be interpreted and applied in a manner that is inconsistent with our existing data management practices and policies. If so, in addition to the possibility of fines, lawsuits, breach of contract claims, and other claims and penalties, we could be required to fundamentally change our business activities and practices or modify our solutions, which could have an adverse effect on our business. Any inability to adequately address privacy and security concerns, even if unfounded, or comply with applicable privacy and security or data security laws, regulations, and policies, could result in additional cost and liability to us, damage our reputation, inhibit our ability to conduct trials, and adversely affect our business.

Our business and operations could suffer in the event of system failures, cyberattacks, or deficiency in our cyber security.

We rely on information technology systems and networks, including third-party "cloud-based" service providers, and our third-party CROs, to process, transmit and store electronic information in connection with our business activities. This includes crucial systems such as email, other communication tools, electronic document repositories, and archives. 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. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. There have been no cybersecurity incidents that have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition.

We have little or no control over the security measures and computer systems of our third-party CROs, clinical trial sites and other contractors and consultants and we may have insufficient recourse against such third parties in the event that they become subject to disruptions or security breaches, and may have to expend significant resources to mitigate the impact of such an event. 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 COSELA 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, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our COSELA could be delayed.

We take measures to protect sensitive data from unauthorized access, use or disclosure, but our information technology and infrastructure may be vulnerable to attacks by hackers or viruses or breached due to personnel error, malfeasance, or other malicious or inadvertent disruptions. Any such access, breach, or other loss of information could result in legal claims or proceedings, liability under domestic or foreign privacy, data protection, and data security laws and could subject us to fines and penalties or class action litigation. The costs related to significant security breaches or disruptions could be material and could exceed the limits of the cybersecurity insurance we maintain against such risks.

The interplay of federal and state laws may be subject to varying interpretations by courts and government agencies, creating complex compliance issues for us and data we receive, use and share, potentially exposing us to additional expense, adverse publicity and liability. Further, as regulatory focus on privacy issues continues to increase and laws and regulations concerning the protection of personal information expand and become more complex, these potential risks to our business could intensify. Changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, for the treatment of health and patient data, along with increased customer demands for enhanced data security infrastructure, could greatly increase our cost of providing our products, decrease demand for our products, reduce our revenues and/or subject us to additional liabilities.

Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information, and personal data.

Issues in the development and use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability, or other adverse consequences to our business operations. We may adopt and integrate generative artificial intelligence tools into our systems for specific use cases reviewed by legal and information security. Our vendors may incorporate generative artificial intelligence tools into their offerings, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If we, our vendors, or our third-party partners experience an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

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

To manage our anticipated expansion, we must continue to implement and improve our managerial, operational and financial systems, and continue to recruit and train additional qualified personnel. Our management may need to divert a disproportionate amount of its attention away from its day-to-day activities and devote a substantial amount of time to managing these growth activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees, which may increase our expenses or reduce our ability to generate or increase our revenue. The expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of our product. Our future financial performance and our ability to commercialize our product, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future expansion of our company.

We may 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 a specific product. As a result, we may forgo or delay pursuit of opportunities with other product candidates that later prove to have greater commercial potential, which 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.

Our employees, principal investigators, clinical trial site personnel, 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, clinical trial site personnel, 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. 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 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 or the third parties upon which we depend may be adversely affected by general political, unstable market and economic conditions and other events beyond our control and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

We have become increasingly subject to the risks arising from adverse changes in market and economic and political conditions, both domestically and globally, including trends toward protectionism and nationalism, other unfavorable changes in economic conditions, as well as disruptions in global credit and financial markets, such as failures and instability in U.S. and international banking systems, downgrades of the U.S. credit rating, rising interest rates, slower economic growth or a recession, and other events beyond our control, such as epidemics, political instability, and armed conflicts and wars, including the ongoing conflict between Russia and Ukraine and the war between Israel and Hamas.

The U.S. debt ceiling and budget deficit concerns have increased the possibility of credit-rating downgrades and economic slowdowns, or a recession in the United States. On August 1, 2023, Fitch Ratings downgraded the United States' long-term foreign currency issuer default rating to AA+ from AAA as a result of these repeated debt ceiling and budget deficit concerns. The impact of this or any further downgrades to the U.S. government's sovereign credit rating or its perceived creditworthiness could adversely affect the U.S. and global financial markets and economic conditions.

If the equity and credit markets deteriorate, it may make any necessary equity or debt financing more difficult to secure, more costly or more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could harm our growth strategy, financial performance and stock price and could require us to delay or abandon plans with respect to our business, including clinical development plans. If the financial institutions with which we do business enter receivership or become insolvent in the future, there is no guarantee that the Department of the Treasury, the Federal Reserve and the Federal Deposit Insurance Corporation ("FDIC") will intercede to provide us and other depositors with access to balances in excess of the $250,000 FDIC insurance limit, that we would be able to access our existing cash, cash equivalents and investments, that we would be able to maintain any required letters of credit or other credit support arrangements, or that we would be able to adequately fund our business for a prolonged period of time or at all, any of which could have a material adverse effect on our business, financial condition and results of operations. We cannot predict the impact that the high market volatility and instability of the banking sector more broadly could have on economic activity and our business in particular. In addition, there is a risk that one or more of our current service providers, manufacturers or other third parties with which we conduct business may not survive difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

The effects of current and future economic and political conditions and other events beyond our control on us, patients, our third party vendors, including clinical trial sites, and our partners could severely disrupt our operations and have a material adverse effect on our business. If the critical infrastructure of a third party vendor was disrupted, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans.

Political uncertainty may have an adverse impact on our operating performance and results of operations.

General political uncertainty may have an adverse impact on our operating performance and results of operations. In particular, the United States continues to experience significant political events that cast uncertainty on global financial and economic markets, especially in light of the upcoming presidential election. It is presently unclear exactly what actions a new administration in the United States would implement, and if implemented, how these actions may impact the pharmaceutical industry in the United States.

Climate change or legal, regulatory or market measures to address climate change may negatively affect our business, results of operations, cash flows and prospects.

We believe that climate change has the potential to negatively affect our business. We are exposed to physical risks (such as extreme weather conditions), risks in transitioning to a low-carbon economy (such as additional legal or regulatory requirements, changes in technology, market risk and reputational risk) and social and human effects (such as population dislocations and harm to health and well-being) associated with climate change. These risks can be either acute (short-term) or chronic (long-term).

The adverse impacts of climate change include increased frequency and severity of natural disasters and extreme weather events. Extreme weather poses physical risks to our facilities as well as those of our suppliers, such as physical damage to facilities, loss or spoilage of inventory, and business interruption. Other potential physical impacts due to climate change include reduced access to high-quality water in certain regions and the loss of biodiversity, which could impact future product development. These risks could disrupt our operations and supply chains, which may result in increased costs.

New legal or regulatory requirements may be enacted to prevent, mitigate, or adapt to the implications of a changing climate and its effects on the environment. These regulations could result in us being subject to new or expanded carbon pricing or taxes, increased compliance costs, restrictions on greenhouse gas emissions, investment in new technologies, increased carbon disclosure and transparency, upgrade of facilities to meet new building codes, and the redesign of utility systems, which could increase our operating costs. Our supply chain would likely be subject to these same transitional risks and would likely pass along any increased costs to us.

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.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Adequate internal control over financial reporting is necessary for us to provide reliable financial reports and, together with effective disclosure controls and procedures, are designed to prevent or detect material misstatements due to fraud or error. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing conducted by us in connection with Section 404 of the Sarbanes-Oxley Act, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inadequate internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock and make it more difficult for us to effectively market and sell our service to new and existing customers.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business.

We have a hybrid in-person and remote workforce, which could subject us to certain operational challenges and risks and potential harm to our business.

We expect to continue to be subject to the challenges and risks of having a remote workforce, as well as challenges and risks from operating with a hybrid workforce. For example, certain security systems in remote workplaces may be less secure than those used in our offices, which may subject us to increased security risks and expose us to risks of data or financial loss and associated disruptions to our business operations. Members of our workforce who work remotely may not have access to technology that is as robust as that in our offices, so the networks, information systems, applications, and other tools available to those remote workers to be more limited or less reliable than in our offices. We may also be exposed to risks associated with the locations of remote workers, including compliance with local laws and regulations or exposure to compromised internet infrastructure. Allowing members of our workforce to work remotely may create intellectual property risk if employees create intellectual property on our behalf while residing in a jurisdiction with unenforced or uncertain intellectual property laws. Our hybrid work model may also subject us to other operational challenges and risks. For example, hybrid working may adversely affect our ability to recruit and retain personnel who prefer a fully remote or fully in-person work environment. Operating our business with both remote and in-person workers, or workers who work in flexible locations and on flexible schedules, could have a negative impact on our corporate culture, decrease the ability of our workforce to collaborate and communicate effectively, or decrease innovation and productivity. If we are unable to manage these challenges, our business could be harmed or otherwise negatively impacted.

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 COSELA. 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 commercialize our product or obtain marketing approval for additional indications, 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 and our clinical trial sites personnel, to conduct or otherwise support clinical trials for COSELA. We rely heavily on these parties for performance of clinical trials for our product. Nevertheless, we are and will continue to 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, our clinical trial sites and our CROs are 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 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, our clinical sites 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 produced under cGMPs. Our failure or the failure of our investigators, our clinical trial sites 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 our product 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 COSELA, 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 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 in additional indications or successfully commercialize COSELA. As a result, we believe that our financial results and the commercial prospects for COSELA 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 COSELA for nonclinical studies, clinical trials, and commercial supply. This reliance on third parties increases the risk that we will not have sufficient quantities of COSELA or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

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

The facilities used to manufacture COSELA (drug substance and drug product) must be approved by the FDA (and comparable foreign regulatory authority depending on where marketing authorizations are filed) before marketing authorizations are approved. Often, but not always, these inspections are triggered by marketing authorization submissions. We are completely dependent on our contract manufacturers for compliance with current Good Manufacturing Practices (cGMPs) in connection with the manufacture of our product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and to the regulatory requirements of the FDA or comparable foreign regulatory authority, then we will not be able to use the products produced at their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel outside of contractual obligations and periodic independent audits of their quality systems. If the FDA or comparable foreign regulatory authority finds that these facilities do not comply with cGMP, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market COSELA. 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 or drugs, if approved, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business and supplies of COSELA.

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

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

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

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

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

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

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

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

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

In order to conduct large-scale clinical trials of COSELA, or successfully commercialize COSELA, we will need to manufacture them in large quantities. We, or any of our manufacturing partners, may be unable to successfully increase the manufacturing capacity of COSELA in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any manufacturing partners, are unable to successfully scale up the manufacture COSELA in sufficient quality and quantity, the development, testing, and clinical trials of the product 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.

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

Our drug development programs and the potential commercialization of COSELA will require substantial additional cash to fund expenses. We may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of COSELA.

We have entered into license agreements with third-parties, and may continue to selectively pursue strategic collaborations, for the development and commercialization of our products.

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

We face significant competition in seeking additional appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product, the costs and complexities of manufacturing and delivering such product 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. 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 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 COSELA or bring it 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 a product 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 our intellectual property

If we are unable to obtain, maintain, and enforce 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, maintain, and enforce 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 COSELA and its uses, pharmaceutical formulations and dosages, and processes for the manufacture of it. 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. 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. Recent United States Supreme Court and Federal Circuit rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, recent Federal Circuit rulings such as *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1340 (Fed. Cir. 2010) (en banc), *Wyeth & Cordis Corp. v. Abbott Labs*, 720 F.3d 1380 (Fed. Cir. 2013), *Enzo Life Scis., Inc. v. Roche Molecular Sys.*, 928 F.3d 1340 (Fed. Cir. 2019), and *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149 (Fed. Cir. 2019), and *Amgen Inc. v. Sanofi*, 598 U.S. 594 (2023) have significantly heightened the standard for securing broad claims to pharmaceutical and biological products. In addition, recent Federal Circuit rulings such as *In re Cellect*, 81 F.4th 1216 (Fed. Cir. 2023) have expanded the bases for invalidating a patent under the judicially created doctrine of obviousness-type double patenting. 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.

The recently-passed Inflation Reduction Act may impact our future strategies and results of operations as it pertains to COSELA. Passed by the 117th United States Congress and signed into law by President Joe Biden on August 16, 2022, the Inflation Reduction Act of 2022 is landmark legislation which may significantly impact the pharmaceutical industry.

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 products.

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.

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 marketplace. 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 COSELA is a small molecule, after commercialization it 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 ("ANDA") to the FDA to obtain approval to sell our drug using bioequivalence data only. Under the Hatch Waxman Act, we have listed all of our patents that cover COSELA and 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 trilaciclib has been deemed a new chemical entity. 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.

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

We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights covering our products and technology, including inter parties review proceedings before the U.S. PTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. For example, we are aware that many companies, universities, and institutions, including competitors, have filed patent applications and received issued patents in our general areas of CDK 4/6 inhibitors and their uses in methods of treatment and combinations with other drugs as well as their processes of manufacture. If we are found to infringe a third party's intellectual property rights, we could be required to litigate the validity or enforceability of the third-party asserted patent, which may be expensive, time-consuming and distracting to the company, and which litigation we may lose. We may, instead of litigating, seek to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing COSELA 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 COSELA and lerociclib 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 COSELA, 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 COSELA, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market it. 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 ("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 ("WTO"), which administers TRIPS, voted to extend the exemption against enforcing pharmaceutical drug patents in least developed countries until 2033. We currently have no patents or pending applications 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.

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 products, 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.

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 ("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.

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.

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.

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.

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 products or 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;
- 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.

Forecasting potential sales for COSELA is difficult, and if our projections are inaccurate, our business may be harmed and our stock price may be adversely affected.

Our business planning requires us to forecast or make assumptions regarding product demand and revenues for COSELA, despite numerous uncertainties. These uncertainties may be increased if we rely on third parties to conduct commercial activities in certain jurisdictions and provide us with accurate and timely information. Actual results may differ materially from projected results for various reasons, including the following, as well as risks identified in other risk factors:

- the efficacy and safety of COSELA, including as relative to marketed products and drug candidates in development by third parties;
- pricing (including discounting and other promotions), reimbursement, product returns or recalls, competition, labeling, adverse events and other items that impact commercialization;
- the rate of adoption in the particular market, including fluctuations in demand for various reasons;
- potential market size;
- lack of patient and physician familiarity with the drug product;
- lack of patient use and physician prescribing history;
- lack of commercialization experience with COSELA;
- uncertainty relating to when COSELA may become commercially available to patients in a particular jurisdiction and rate of adoption; and
- products provided without compensation through patient support programs or product sample programs, may not eventually result in or contribute to revenue-producing prescriptions.

We expect that our revenues from sales of COSELA will be based in part on estimates, judgment and accounting policies. Any incorrect estimates or disagreements with regulators or others regarding such estimates, judgment or accounting policies may result in changes to our guidance, projections or previously reported results. Expected and actual product sales and quarterly and other results may greatly fluctuate, including in the near-term, and such fluctuations can adversely affect the price of our common stock, perceptions of our ability to forecast demand and revenues, and our ability to maintain and fund our operations. The metrics that we are tracking in order to evaluate the success of our sales efforts may not correlate to commercial success, particularly given the challenging market for COSELA.

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

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

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

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

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

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

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

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

We 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 1C. Cybersecurity.

We recognize the critical importance of maintaining the trust and confidence of customers, patients, business partners and employees toward our business and are committed to protecting the confidentiality, integrity and availability of our business operations and systems. Our board of directors is actively involved in oversight of our risk management activities, and cybersecurity represents an important element of our overall approach to risk management. Our cybersecurity policies, standards, processes and practices are based on recognized frameworks established by the National Institute of Standards and Technology ("NIST") and other applicable industry standards. In general, we seek to address cybersecurity risks through a comprehensive, cross-functional approach that is focused on preserving the confidentiality, security and availability of the information that we collect and store by identifying, preventing and mitigating cybersecurity threats and effectively responding to cybersecurity incidents when they occur.

Cybersecurity Risk Management and Strategy; Effect of Risk

We face risks related to cybersecurity such as unauthorized access, cybersecurity attacks and other security incidents, including as perpetrated by hackers and unintentional damage or disruption to hardware and software systems, loss of data, and misappropriation of confidential information. To identify and assess material risks from cybersecurity threats, we maintain a comprehensive cybersecurity program to ensure our systems are effective and prepared for information security risks, including regular oversight of our programs for security monitoring for internal and external threats to ensure the confidentiality and integrity of our information assets. We consider risks from cybersecurity threats alongside other company risks as part of our overall risk assessment process. We employ a range of tools and services, including regular network and endpoint monitoring, audits, vulnerability assessments, penetration testing, threat modeling and tabletop exercises to inform our risk identification and assessment. As discussed in more detail under “Cybersecurity Governance” below, our board of directors provides oversight of our cybersecurity risk management and strategy processes, which are led by our General Counsel and Chief Compliance Officer, Vice President, Information Technology and Associate Director of Information Technology Operations, and Chief Operations Officer.

We also identify our cybersecurity threat risks by comparing our processes to standards set by NIST, as well as by engaging experts to attempt to infiltrate our information systems. To provide for the availability of critical data and systems, maintain regulatory compliance, manage our material risks from cybersecurity threats, and protect against and respond to cybersecurity incidents, we undertake the following activities:

- monitor emerging data protection laws and implement changes to our processes that are designed to comply with such laws;
- through our policies, practices and contracts (as applicable), require employees, as well as third parties that provide services on our behalf, to treat confidential information and data with care;
- employ technical safeguards that are designed to protect our information systems from cybersecurity threats, including firewalls, intrusion prevention and detection systems, anti-malware functionality and access controls, which are evaluated and improved through vulnerability assessments and cybersecurity threat intelligence;
- provide regular, mandatory training for our employees and contractors regarding cybersecurity threats as a means to equip them with effective tools to address cybersecurity threats, and to communicate our evolving information security policies, standards, processes and practices;
- conduct regular phishing email simulations for all employees and contractors with access to our email systems to enhance awareness and responsiveness to possible threats;
- conduct at least annual cybersecurity management and incident training for employees involved in our systems and processes that handle sensitive data;
- conduct annual tabletop exercises facilitated by a third party to simulate a response to a cybersecurity incident and use the findings to improve our processes and technologies;
- review and revise our incident response plan at least annually to ensure that it is current with respect to our technology and current risks;

- leverage the NIST incident handling framework to help us identify, protect, detect, respond and recover when there is an actual or potential cybersecurity incident;
- carry information security risk insurance that provides protection against the potential losses arising from a cybersecurity incident;
- review privileged network and application accounts every three (3) months for appropriate access privileges, and review user accounts every six (6) months; and
- review and test our disaster recovery plan annually to confirm effective and efficient recovery processes are in place to support business continuity in the event of a disaster.

Our incident response plan coordinates the activities we take to prepare for, detect, respond to and recover from cybersecurity incidents, which include processes to triage, assess severity for, escalate, contain, investigate and remediate the incident, as well as to comply with potentially applicable legal obligations and mitigate damage to our business and reputation.

As part of the above processes, we regularly engage with consultants and other third party advisors, including annually having a third-party review our cybersecurity program to help identify areas for continued focus, improvement and compliance.

Our processes also address cybersecurity threat risks associated with our use of third-party service providers, including our suppliers and manufacturers or who have access to patient and employee data or our systems. In addition, cybersecurity considerations affect the selection and oversight of our third-party service providers. We perform diligence on third parties that have access to our systems, data or facilities that house such systems or data, and continually monitor cybersecurity threat risks identified through such diligence. When we identify a vendor who may pose a cybersecurity threat risk, we will require those third parties to agree by contract to manage their cybersecurity risks in specified ways, and to agree to be subject to cybersecurity audits.

We describe whether and how risks from identified cybersecurity threats, including as a result of any previous cybersecurity incidents, have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition, under the heading "*Our business and operations could suffer in the event of system failures, cyberattacks, or deficiency in our cyber security*," which disclosures are incorporated by reference herein.

In the last three fiscal years, we have not experienced any material cybersecurity incidents. We did not incur any expenses related to penalties and settlements.

Cybersecurity Governance; Management

Cybersecurity is an important part of our risk management processes and an area of focus for our board of directors and management. In general, our board of directors oversees risk management activities designed and implemented by our management, and considers specific risks, including, for example, risks associated with our strategic plan, business operations, and capital structure. Our board of directors executes its oversight responsibility for risk management both directly and through delegating oversight of certain of these risks, including those from cybersecurity threats, to its audit committee.

On an annual basis, our board of directors receives an update from management of our cybersecurity threat risk management and strategy processes covering topics such as data security posture, results from third-party assessments, progress towards pre-determined risk-mitigation-related goals, our incident response plan, and material cybersecurity threat risks or incidents and developments, as well as the steps management has taken to respond to such risks. In such sessions, our board of directors generally receives materials that include a cybersecurity scorecard and other materials discussing current and emerging material cybersecurity threat risks, and describing our ability to mitigate those risks, as well as recent developments, evolving standards, technological developments and information security considerations arising with respect to our peers and third parties, and discusses such matters with our Vice President, Information Technology. Our board of directors also receive prompt and timely information regarding any cybersecurity incident that meets establishing reporting thresholds, as well as ongoing updates regarding any such incident until it has been addressed.

Members of our board of directors may also engage in conversations with management on cybersecurity-related news events and discuss any updates to our cybersecurity risk management and strategy programs.

Our cybersecurity risk management and strategy processes, which are discussed in greater detail above, are led by our Vice President, Information Technology, Associate Director of Information Technology Operations, General Counsel and Chief Compliance Officer, and Chief Operations Officer. Such individuals have collectively over 30 years of prior work experience in various roles involving managing information security, developing cybersecurity strategy, implementing effective information and cybersecurity programs, as well as several relevant degrees. These management team members are informed about and monitor the prevention, mitigation, detection, and remediation of cybersecurity incidents through their management of, and participation in, the cybersecurity risk management and strategy processes described above, including the operation of our incident response plan. As discussed above, our Vice President of Information Technology and Associate Director of Information Technology Operations report to our board of directors about cybersecurity threat risks, among other cybersecurity related matters, on an annual basis.

Item 2. Properties.

Our corporate headquarters is located at 700 Park Offices Drive in Research Triangle Park, North Carolina ("700 Building"), where we lease approximately 60,000 square feet of laboratory and office space. This lease on our corporate headquarters commenced in September 2019 and expires on September 30, 2027. On November 1, 2023, we entered into a sublease agreement with a third party for the third floor of the 700 Building, the term of which commences on January 1, 2024 and expires on August 31, 2027. None of our leases are material to our business operations. We believe our facility is adequate for our current needs and that suitable additional or substitute space would be available if needed.

Item 3. Legal Proceedings.

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

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

Holders

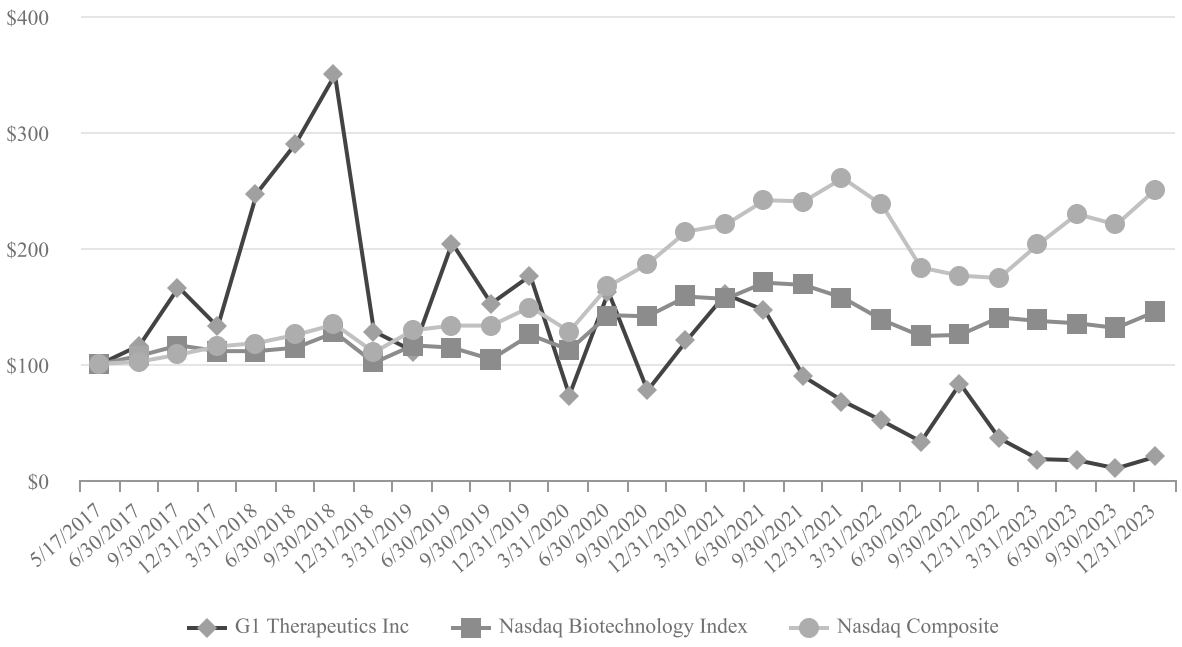
As of February 26, 2024, there were approximately 10 stockholders of record of our common stock. Holders of record are defined as those stockholders whose shares are registered in their names in our stock records and do not include beneficial owners of common stock whose shares are held in the names of brokers, dealers or clearing agencies.

Stock Performance Graph

This performance graph is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing by us under the Securities Act of 1933, as amended (the "Securities Act") or the Securities Exchange Act of 1934, as amended (the "Exchange Act"), 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, 2023. Our relative performance is then compared with the Nasdaq Composite Index and the Nasdaq Biotechnology Index.

Recent Sales of Unregistered Securities

None.

Equity Compensation Plans

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

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our equity securities during the fiscal year 2023.

Item 6. [Reserved]

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

You should read the following discussion and analysis of our financial condition and results of operations together with our 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.

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 selling, general and administrative support for these operations as well as securing intellectual property protection for our products. Currently, COSELA is our only product approved for sale. We began generating revenue for the net product sales from COSELA in March of 2021. We recorded $46.3 million, $31.3 million, and $11.1 million of net product sales from COSELA for the years ended December 31, 2023, 2022, and 2021, respectively. We recorded $36.2 million, $20.0 million, and $20.4 million of license revenue for the years ended December 31, 2023, 2022, and 2021, respectively. To date, we have financed our operations primarily through the sale of equity securities, our loan agreement with Hercules, and licensing arrangements. Under our licensing arrangements, we are eligible to receive certain development and sales-based milestones. Our ability to earn these milestones and the timing of achieving these milestones is primarily dependent upon the outcome of the licensee's activities and is uncertain at this time.

As of December 31, 2023, we had cash and cash equivalents of $32.2 million and marketable securities of $49.9 million. Since inception we have incurred net losses. As of December 31, 2023, we had an accumulated deficit of $780.0 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs, our commercial launch of COSELA, and from selling, general and administrative expenses associated with our operations. We expect to continue to incur significant expenses and increasing operating losses. As disclosed in the Liquidity and Capital Resources section, as of the date of issuance of these financial statements, we expect that our cash and cash equivalents and marketable securities as of December 31, 2023 will be sufficient to fund our planned operations and remain in compliance with our objective financial covenants for at least the next 12 months from the date of issuance of these financial statements. To date, inflation has not had a material impact on our business, but if the global inflationary trends continue, we expect appreciable increases in clinical trial, selling, labor, and other operating costs. If our costs were to become subject to significant inflationary pressures, we may not be able to fully offset such higher costs through price increases of our product. Our inability or failure to do so could adversely affect our business, financial condition and results of operations.

In addition, currently there is a conflict involving Russia and Ukraine and a conflict involving Israel and Hamas, and these conflicts may directly or indirectly impact our contract research organizations, clinical data management organizations, and clinical investigators' ability to conduct certain of our trials in Eastern European countries, and may increase our product development costs and materially harm our business.

We also expect to continue incurring costs for research and development, commercial activities, and selling, general and administrative expenses, in connection with our ongoing and future initiatives as we:

- continue development of trilaciclib, including continuation of ongoing clinical trials;
- seek additional marketing approvals for trilaciclib upon successful completion of clinical trials;
- grow our sales, marketing and distribution infrastructure to commercialize COSELA and any future products for which we may obtain marketing approval;
- achieve market acceptance of our product in the medical community and with third-party payors;
- maintain, expand and protect our intellectual property portfolio;
- enter into collaboration arrangements, if any, for the development of our product or in-license other products and technologies;
- add personnel to support our product development and planned future commercialization efforts; and
- continue to incur increased costs as a result of operating as a public company.

Components of our Results of Operations

Revenues

On February 12, 2021, COSELA was approved by the FDA and we began generating revenue for the product sales of COSELA in March 2021. Prior to the approval of COSELA, our revenues have been derived from our license agreements.

Pursuant to the exclusive license agreement with Simcere, during the twelve months ended December 31, 2023, we recognized $2.9 million in supply and manufacturing services, $0.6 million in royalty revenue, and $0.7 million in patent and clinical trial reimbursable costs. We did not receive any development milestones during the twelve months ended December 31, 2023. On April 28, 2023, we amended the license agreement with Simcere, whereby we received a one-time, non-refundable payment of $30.0 million in exchange for the relief of future royalty payments from the sale of COSELA in Greater China, which was recognized as license revenue during the period. See "Business - License Agreements - Exclusive license to Simcere for trilaciclib in Greater China" section of this Annual Report for more details.

Pursuant to the exclusive license agreement with EQRx, during the twelve months ended December 31, 2023, we recognized revenue of $1.7 million for the reimbursement of EQRx patent and clinical trial costs, including $1.4 million of the $1.6 million payment received during the third quarter of 2023 following notice from EQRx of termination of the license agreement. As of December 31, 2023, the remaining $0.2 million is held as short-term deferred revenue on the balance sheet and will be recognized as revenue as clinical trial costs associated with the wind down are incurred. No milestones were previously achieved through the date of termination of the lerociclib license agreement, and as a result of the termination, we will not receive any further milestone payments or future royalties from EQRx. See "Business - License Agreements - Exclusive license to EQRx for lerociclib" section of this Annual Report for more details.

Pursuant to the exclusive license agreement with Genor, we have the potential to receive $40.0 million upon reaching development and commercial milestones, and receive tiered royalties ranging from high single to low double-digits based on annual net sales of lerociclib in the Genor Territory. We did not receive any development milestones during the twelve months ended December 31, 2023. See "Business - License Agreements - Exclusive license to Genor for lerociclib" section of this Annual Report for more details.

Pursuant to the exclusive license agreement with Incyclix, we are entitled to receive an additional milestone payment and sales-based royalties, and have right of first negotiation to re-acquire these assets. We did not receive the development milestone payment during the twelve months ended December 31, 2023. See "Business - License Agreements - Exclusive license to Incyclix" section of this Annual Report for more details.

Operating expenses

We classify our operating expenses into three categories: cost of goods sold, research and development and selling, 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. In addition, costs to sell and market COSELA are included within selling, general and administrative expense categories.

Cost of goods sold

Cost of goods sold includes direct and indirect costs related to the manufacturing and distribution of COSELA, including third-party manufacturing costs, packaging services, freight-in, third-party logistics costs associated with COSELA, and personnel costs. Cost of goods sold may also include period costs related to certain inventory manufacturing services and inventory adjustment charges for excess and obsolete inventory.

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 product for preclinical studies and clinical trials;
- fees paid to consultants and other third parties who support our product development; and
- allocated facility-related costs and overhead.

The successful development of our products is highly uncertain. Products 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 as we conduct later stage clinical trials. However, we do not believe that it is possible at this time to accurately project total program-specific 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 products 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;
- 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.

Selling, general and administrative expenses

Selling, 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 selling, general and administrative expenses include facility-related costs not otherwise allocated to research and development expense, professional fees, commercialization costs, expenses associated with obtaining and maintaining patents and costs of our information systems. We anticipate that our selling, general and administrative expenses will continue to increase in the future as we continue to expand our research and development and commercialization of COSELA.

Total other income (expense), net

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

Income taxes

To date, we have not been required to pay U.S. federal or state income due to our significant net operating losses. Income tax expense was recognized in 2023, 2022, and 2021 related to the foreign withholding taxes incurred as a result of the payments received under the Simcere license agreement during each year.

Critical accounting policies and significant judgments and estimates

This discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

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

Revenue Recognition

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

License Revenue

Licenses of Intellectual Property

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

Milestone Payments

At the inception of each arrangement that includes developmental and regulatory milestone payments, we evaluate whether the achievement of each milestone specifically relates to our efforts to satisfy a performance obligation or transfer a distinct good or service within a performance obligation. We evaluate each milestone to determine when and how much of the milestone to include in the transaction price. We first estimate the amount of the milestone payment that we could receive using either the expected value or the most likely amount approach. We primarily use the most likely amount approach as that approach is generally most predictive for milestone payments with a binary outcome. Then, we consider whether any portion of that estimated amount is subject to the variable consideration constraint (that is, whether it is probable that a significant reversal of cumulative revenue would not occur upon resolution of the uncertainty). We update the estimate of variable consideration included in the transaction price at each reporting date which includes updating the assessment of the likely amount of consideration and the application of the constraint to reflect current facts and circumstances. For regulatory milestones, we recognize revenue at a point in time upon approval, as that is when achievement of the milestone is considered probable. We assess milestones as they are achieved to determine whether they are tied to any other performance obligations in the respective license agreements.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). During the twelve months ended December 31, 2023, the Company recognized $0.6 million in revenue related to sales-based royalties under the Simcere license agreement prior to the amendment on April 28, 2023.

Product Sales, Net

We sell COSELA to specialty distributors in the U.S. and, in accordance with ASC 606, recognize revenue at the point in time when the customer is deemed to have obtained control of the product. The customer is deemed to have obtained control of the product at the time of physical receipt of the product at the customers' distribution facilities, or Free on Board ("FOB") destination, the terms of which are designated in the contract.

Product sales are recorded at the net selling price, which includes estimates of variable consideration for which reserves are established for (a) rebates and chargebacks, (b) co-pay assistance programs, (c) distribution fees, (d) product returns, (e) GPO fees, and (f) other discounts. Where appropriate, these estimates take into consideration a range of possible outcomes for relevant factors such as current contractual and statutory requirements, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which it is entitled based on the terms of the applicable contract. The amount of variable consideration may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from estimates, we adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Liabilities related to co-pay assistance, rebates, returns, and GPO fees are classified as "Accrued Expenses" in the Balance Sheets. Discounts such as chargebacks and specialty distributor fees are recorded as a reduction to trade accounts receivable, which is included in "Accounts Receivable" in the Balance Sheets.

Forms of Variable Consideration

Rebates and Chargebacks*:* We estimate reductions to product sales for Public Health Service Institutions, such as Medicaid, Medicare and Veterans Administration ("VA") programs, as well as certain other qualifying federal and state government programs, and other group purchasing organizations. We estimate these reductions based upon our contracts with government agencies and other organizations, statutorily defined discounts and estimated payor mix. These organizations purchase directly from our specialty distributors at a discount and the specialty distributors charge us back the difference between the wholesaler price and the discounted price. Our liability for Medicaid rebates consists of estimates for claims that a state will make. We reserve for this discounted pricing is based on expected sales to qualified healthcare providers and the chargebacks that customers have already claimed.

Co-pay assistance: Eligible patients who have commercial insurance may receive assistance from us to reduce the patient's out of pocket costs. Liabilities for co-pay assistance are calculated by actual program participation from third-party administrators.

Distribution Fees: We have written contracts with its customers that include terms for distribution fees and costs for inventory management. We estimate and record distribution fees due to its customers based on gross sales.

Product Returns: We generally offer a right of return based on the product's expiration date and certain spoilage and damaged instances. We estimate the amount of product sales that may be returned and record the estimate as a reduction of product sales in the period the related product sales are recognized. Our estimates for expected returns are based primarily on an ongoing analysis of sales information and visibility into the inventory remaining in the distribution channel.

Cost of Goods Sold

Cost of goods sold includes direct and indirect costs related to the manufacturing and distribution of COSELA, including third-party manufacturing costs, packaging services, freight-in, third-party logistics costs associated with COSELA, and our personnel costs. Cost of goods sold may also include period costs related to certain inventory manufacturing services and inventory adjustment charges for excess and obsolete inventory.

Accrued research and development expenses

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

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

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

Debt

The Company classifies its loan payable in current or long-term liabilities based on the timing of scheduled principal payments. The Loan Agreement with Hercules contains events of default, including a material adverse change, which is subjectively defined, in the Company's business, payment defaults, and breaches of covenants following any applicable cure period. In the event of default by the Company under the Loan Agreement, the Company may be required to repay all amounts then outstanding under the Loan Agreement. The Company has determined that subjective acceleration under the material adverse events clause included in the Loan Agreement is not probable and, therefore, has classified the outstanding principal amount in long-term liabilities based on the timing of scheduled principal payments.

Stock-based compensation

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

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

We recorded non-cash stock-based compensation expense of $14.5 million, $20.6 million and $22.3 million for the twelve months ended December 31, 2023, 2022 and 2021, 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:

- the expected stock price volatility assumptions for our stock options were determined by examining the historical volatilities for industry peers, as we did not have sufficient history to estimate volatility using only our common stock; in 2019, we began incorporating our historical stock price in conjunction with selected similar publicly traded companies; we continued to use the guideline peer group volatility information until April 2023, when the historical volatility of our common stock became sufficient to measure expected volatility for future option grants;
- the assumed dividend yield of zero is based on our expectation of not paying dividends for the foreseeable future;
- our estimates of expected term used in the Black-Scholes option-pricing model were based on the estimated time from the grant date to the date of exercise;
- we determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant; and
- we account for forfeitures as they occur, rather than estimating forfeitures as of an award's grant date.

See "Note 9 – Stock-Based Compensation" to the accompanying audited financial statements included in Item 15 of this Annual Report for the weighted average assumptions used in the Black-Scholes option-pricing model for awards granted in the twelve months ended December 31, 2023, 2022 and 2021.

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

Income taxes

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

At December 31, 2023, we have federal net operating loss carryforwards ("NOLs") of approximately $550.7 million, which are available to offset future taxable income. Of the $550.7 million available, $93.5 million will begin to expire in 2029. The remaining $457.2 million has an indefinite carryforward period. Under the Tax Cuts and Jobs Act ("Tax Act"), federal NOLs arising after December 31, 2017 may be carried forward indefinitely. However, for NOLs arising after December 31, 2017, NOL carryforwards will be limited to 80% of taxable income. Our NOLs generated in 2017 and in prior years will not be subject to the 80% limitation under the Tax Act. In addition, we had state net operating loss carryforwards totaling approximately $401.2 million, which are available to offset future state taxable income. The state net operating loss carryforwards are inclusive of North Carolina net operating losses, which are recorded at zero benefit, as discussed in the income tax footnote. State net operating losses begin to expire in 2024. Because we had incurred cumulative net operating losses since inception, all tax years remain open to examination by U.S. federal and state income tax authorities. As of December 31, 2023, we also had federal research and development (R&D) credit carryforwards of approximately $23.4 million available to offset future income tax which begin to expire in 2035.

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

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

Results of operations

Comparison of the twelve months ended December 31, 2023 and December 31, 2022

	Twelve Months Ended December 31,		Change
	2023	2022	$
		(in thousands)	
Revenues			
Product sales, net	$ 46,344	$ 31,337	$ 15,007
License revenue	36,167	19,964	16,203
Total revenues	82,511	51,301	31,210
Operating expenses			
Cost of goods sold	7,195	3,748	3,447
Research and development	43,711	83,316	(39,605)
Selling, general and administrative	71,132	100,415	(29,283)
Total operating expenses	122,038	187,479	(65,441)
Loss from operations	(39,527)	(136,178)	96,651
Other income (expense)			
Interest income	2,473	748	1,725
Interest expense	(10,038)	(10,432)	394
Other income (expense)	2,240	3	2,237
Total other income (expense), net	(5,325)	(9,681)	4,356
Loss before income taxes	(44,852)	(145,859)	101,007
Income tax expense	3,115	1,700	1,415
Net loss	$ (47,967)	$ (147,559)	$ 99,592

Product sales, net

Product sales, net was $46.3 million and $31.3 million for the twelve months ended December 31, 2023 and 2022, respectively. The increase of $15.0 million, or 48%, was primarily due to increased sales volume as we continued our commercialization efforts.

License revenue

License revenue was $36.2 million and $20.0 million for the twelve months ended December 31, 2023 and 2022, respectively. License revenue increased $16.2 million, or 81%. License revenue recognized in the current year was primarily related to $30.0 million in revenue from the one-time payment for the relief of future royalty payments, $2.9 million in supply and manufacturing services, and $0.6 million in royalty revenue from Simcere. Additionally, we recognized $2.5 million in license revenue related to patent and clinical trial costs reimbursed by EQRx and Simcere.

Cost of goods sold

Cost of goods sold was $7.2 million and $3.7 million for the twelve months ended December 31, 2023 and 2022, respectively. The increase of $3.5 million, or 95%, was primarily due to an increase in inventory write-offs and an increase in units sold.

Research and development

Research and development expenses were $43.7 million for the twelve months ended December 31, 2023 as compared to $83.3 million for the twelve months ended December 31, 2022. The decrease of $39.6 million, or 48%, was primarily due to a decrease of $37.3 million in our clinical program costs, a decrease of $2.0 million for manufacturing of active pharmaceutical ingredients and drug product to support our clinical trials, and a decrease of $0.3 million in pre-clinical and discovery costs. The following table summarizes our research and development expenses allocated to trilaciclib, lerociclib, and unallocated research and development expenses for the periods indicated:

	Twelve Months Ended December 31,	
	2023	2022
	(in thousands)	
Clinical Program Expenses—trilaciclib	$ 39,747	$ 73,498
Clinical Program Expenses—rintodestrant	7	2,110
Clinical Program Expenses—lerociclib	1,095	2,553
Chemical Manufacturing and Development	739	2,707
Discovery, Pre-Clinical and Other Expenses	2,123	2,448
Total Research and Development Expenses	$ 43,711	$ 83,316

Selling, general and administrative

Selling, general and administrative expenses were $71.1 million for the twelve months ended December 31, 2023 as compared to $100.4 million for the twelve months ended December 31, 2022. The decrease of $29.3 million, or 29%, was due to decreases of $14.6 million in commercialization activities, $10.1 million in personnel costs due to a reduction in force, $1.1 million in professional fees, $2.4 million in medical affairs costs related to trilaciclib, and $1.1 million in audit, IT, legal, office and other administrative expenses.

Total other income (expense), net

Total other income (expense), net was $(5.3) million for the twelve months ended December 31, 2023 as compared to $(9.7) million for twelve months ended December 31, 2022. The change of $4.4 million, or 45%, was primarily driven by an increase of $1.7 million in interest income, an increase of $2.2 million in other income, and a decrease of $0.4 million in interest expense on the loan payable due to reduction of principal outstanding following the principal repayment in the second quarter of 2023.

Income tax expense

Income tax expense was $3.1 million for the twelve months ended December 31, 2023. as compared to $1.7 million for the twelve months ended December 31, 2022. The increase of $1.4 million, or 82%, was primarily driven by the foreign tax withheld on the one-time payment for the relief of future royalty payments received from Simcere during the first half of 2023.

Comparison of the year ended December 31, 2022 and December 31, 2021

	Year Ended December 31,		Change
	2022	2021	$
		(in thousands)	
Revenues			
Product sales, net	$ 31,337	$ 11,120	$ 20,217
License revenue	19,964	20,356	(392)
Total revenues	51,301	31,476	19,825
Operating expenses			
Cost of goods sold	3,748	2,016	1,732
Research and development	83,316	76,225	7,091
Selling, general and administrative	100,415	95,692	4,723
Total operating expenses	187,479	173,933	13,546
Loss from operations	(136,178)	(142,457)	6,279
Other income (expense)			
Interest income	748	43	705
Interest expense	(10,432)	(4,667)	(5,765)
Other income (expense)	3	(346)	349
Total other income (expense), net	(9,681)	(4,970)	(4,711)
Loss before income taxes	(145,859)	(147,427)	1,568
Income tax expense	1,700	925	775
Net loss	$ (147,559)	$ (148,352)	$ 793

Product sales, net

Product sales, net was $31.3 million and $11.1 million for the years ended December 31, 2022 and December 31, 2021, respectively. The increase of $20.2 million, or 182%, was primarily due to increased sales volume as we continued our commercialization efforts. We received FDA approval of COSELA on February 12, 2021 and the product has been commercially available since March 2, 2021.

License revenue

License revenue was $20.0 million and $20.4 million for the years ended December 31, 2022 and December 31, 2021, respectively. License revenue decreased $0.4 million, or 2% License revenue recognized in the current year was primarily related to $14.0 million in milestone payments from Simcere. We also recognized $2.4 million and $2.3 million in clinical trial costs reimbursed by EQRx and Simcere, respectively. Additionally, we recognized $1.3 million in supply, manufacturing services and patent reimbursable costs from EQRx, Genor, and Simcere. License revenue recognized in the prior year was primarily related to $11.0 million in milestone payments from Genor and Simcere. We also recognized $2.5 million and $1.0 million in clinical trial costs reimbursed by EQRx and Simcere, respectively. Additionally, we recognized $5.9 million in supply, manufacturing services and patent reimbursable costs from EQRx, Genor, and Simcere.

Cost of goods sold

Cost of goods sold was $3.7 million and $2.0 million for the years ended December 31, 2022 and December 31, 2021, respectively. The increase of $1.7 million, or 85%, was primarily due to an increase in units sold and an increase in overhead.

Research and development

Research and development expenses were $83.3 million for the year ended December 31, 2022 as compared to $76.2 million for the year ended December 31, 2021. The increase of $7.1 million, or 9%, was primarily due to an increase of $10.8 million in our clinical program costs, offset by a decrease of $3.2 million for manufacturing of active pharmaceutical ingredient and drug product to support our clinical trials and a decrease of $0.5 million in external costs related to discovery and preclinical development. The following table summarizes our research and development expenses allocated to trilaciclib, rintodestrant, lerociclib, and unallocated research and development expenses for the periods indicated:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Clinical Program Expenses—trilaciclib	$ 73,498	$ 60,911
Clinical Program Expenses—rintodestrant	2,110	3,132
Clinical Program Expenses—lerociclib	2,553	3,330
Chemical Manufacturing and Development	2,707	5,883
Discovery, Pre-Clinical and Other Expenses	2,448	2,969
Total Research and Development Expenses	$ 83,316	$ 76,225

Selling, general and administrative

Selling, general and administrative expenses were $100.4 million for the year ended December 31, 2022 as compared to $95.7 million for the year ended December 31, 2021. The increase of $4.7 million, or 5% was due to an increase of $12.5 million in personnel related costs due to increased headcount, and an increase of $2.6 million in office and other administrative expenses, of which $1.7 million related to travel expenses. These increases were offset by a decrease of $7.3 million in commercialization activities, a decrease of $1.7 million in information technology systems and related expenses, and a decrease of $1.4 million in medical affairs costs related to trilaciclib, professional services, and taxes.

Total other income (expense), net

Total other income (expense), net was $(9.7) million for the year ended December 31, 2022 as compared to $(5.0) million for the year ended December 31, 2021. The change of $4.7 million, or 94%, was primarily driven by an increase in interest expense on loan payable due to higher principal balance in 2022 as compared to 2021.

Income tax expense

Income tax expense was $1.7 million for the year ended December 31, 2022 as compared to $0.9 million for the year ended December 31, 2021. The increase of $0.8 million, or 89%, in foreign tax withholdings incurred is a result of an increase in license revenue recognized from Simcere as compared to the prior year.

Liquidity and Capital Resources

We have experienced net losses since our inception, and have an accumulated deficit of $780.0 million and $732.0 million as of December 31, 2023 and December 31, 2022, respectively. We expect to incur losses and have negative net cash flows from operating activities as we execute on our strategy including engaging in further research and development activities, particularly conducting non-clinical studies and clinical trials. Our success depends on the ability to successfully commercialize our technologies to support our operations and strategic plan. As of the date of issuance of these financial statements, we expect that our cash and cash equivalents and marketable securities as of December 31, 2023 will be sufficient to fund our planned operations and remain in compliance with our objective financial covenants for at least the next 12 months from the date of issuance of these financial statements. 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. There can be no assurances that we will be able to secure such additional financing if at all, or on terms that are satisfactory to us, and that it will be sufficient to meet our needs. In the event we are not successful in obtaining sufficient funding, this could force us to delay, limit, or reduce our product development, commercialization efforts or other operations. Our financial statements have been prepared assuming that we 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. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above. In connection with the Loan Payable described in Note 7, we are required to remain in compliance with a minimum cash covenant and are subject to a conditional borrowing base measured on a trailing three-month net revenue basis, which begins with the financial reporting for the period ending June 30, 2023, and has been tested monthly thereafter. The lender also has the ability to call debt based on a material adverse change clause, which is subjectively defined. As of December 31, 2023, we are in compliance with the minimum cash covenant and the conditional borrowing base requirements. If we do not maintain unrestricted cash equal to at least 35% of the outstanding or do not comply with the conditional borrowing base requirements or the subjective acceleration clauses are triggered under the agreement, then the lender may call the debt, resulting in us immediately needing additional funds.

To date, we have funded our operations primarily through proceeds from our initial public offering, our follow-on stock offerings, our Loan Agreement with Hercules, and proceeds from our license agreements. Under our licensing arrangements, we are eligible to receive certain development and sales-based milestones. Our ability to earn these milestones and the timing of achieving these milestones is primarily dependent upon the outcome of the licensee's activities and are uncertain at this time.

Shelf registration statement

On July 2, 2021, we filed an automatically effective shelf registration statement (the "2021 Form S-3") with the Securities and Exchange Commission (the "SEC"). Each issuance under the shelf registration statement would have required the filing of a prospectus supplement identifying the amount and terms of securities to be issued. The 2021 Form S-3 did not limit the amount of securities that could have been issued thereunder.

At the time of the filing of our Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 23, 2022, we no longer qualified as a "well-known seasoned issuer" as such term is defined in Rule 405 under the Securities Act. As a result, in February 2022, we amended the 2021 Form S-3 to register for sale up to $300.0 million of any combination of our common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that we may determine. The 2021 Form S-3, as amended, will remain in effect for up to three years from the date it originally became effective, which was July 2, 2021.

At-the-market offerings

In connection with the 2021 Form S-3, as amended, we entered into a sales agreement for "at the market offerings" with Cowen and Company, LLC ("Cowen") acting as our agent (the "2022 Sales Agreement"), which allows us to issue and sell shares of common stock pursuant to the amended 2021 Form S-3 for total gross sales proceeds of up to $100.0 million from time to time through Cowen.

As of the date hereof, we have not sold any shares of common stock or other securities under the 2022 Sales Agreement.

Loan and Security Agreement

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

On March 31, 2021, we entered into a First Amendment to Loan and Security Agreement (the "First Amendment") with Hercules whereby we drew the remaining $10.0 million of the first tranche and the interest rate and financial covenants were amended. Unless loan advances exceeded $40.0 million, no financial covenants were required.

On November 1, 2021, we entered into a Second Amendment to the Loan and Security Agreement (the "Second Amendment") with Hercules, under which Hercules agreed to lend us up to $150.0 million, to be made available in a series of tranches, subject to certain terms and conditions. The first tranche was increased to $100.0 million. At close of the Second Amendment, we borrowed an additional $45.0 million from the first tranche. We had the right to request that Hercules make the remaining $25.0 million term loan advances under the first tranche to us by September 15, 2022, which we did not exercise. No principal payments were due during an interest-only period, commencing on the close of the Second Amendment and continuing through December 1, 2024. The interest only period may be extended through December 1, 2025, in quarterly increments, subject to compliance with covenants of the Second Amendment. Following the interest only period, we agreed to repay the principal balance and interest of the advances in equal monthly installments through the maturity date of November 1, 2026.

On June 24, 2022, we entered into a Third Amendment to Loan and Security Agreement (the "Third Amendment") with Hercules which extended the time for drawing the remainder of the first tranche advance of up to $25.0 million from September 15, 2022 to December 31, 2022, which we did not exercise. The Third Amendment also added a minimum cash covenant whereby we must maintain unrestricted cash equal to at least 50% of the outstanding debt, and such percentage shall decrease upon us achieving specified net product revenue of COSELA. It further provides for a minimum revenue covenant that, beginning August 15, 2022, with the reporting of the financial results for the second fiscal quarter ended June 30, 2022, and tested monthly, we must have achieved net product revenue of COSELA of at least 80% of the amounts projected in our forecast. Testing of the minimum revenue covenant shall be waived at any time in which either (a) our market capitalization exceeds $750.0 million and we maintain unrestricted cash equal to at least 50% of the total amounts funded, or (b) we maintain unrestricted cash equal to at least 100% of the total amounts funded.

On November 1, 2022, we entered into a Fourth Amendment to Loan and Security Agreement (the "Fourth Amendment") with Hercules. The Fourth Amendment extended the time for drawing the Tranche 1D Advance (as defined in the Loan Agreement) of up to $25.0 million from December 31, 2022 to June 30, 2023. The Fourth Amendment continues to provide for a minimum revenue covenant, tested monthly, where we must achieve net product revenue of COSELA of at least 80% of the amounts projected in our forecast. The Fourth Amendment also amended the minimum cash covenant such that if the outstanding debt is less than or equal to $75.0 million, we must maintain unrestricted cash equal to at least 65% of the outstanding debt in addition to meeting the required revenue covenant. In addition, if the outstanding debt is greater than $75.0 million, we must maintain unrestricted cash equal to at least 70% of the outstanding debt while meeting the revenue covenant. If we achieve the specified net revenue of COSELA, the cash percentage will decrease to 45% of the outstanding debt. Testing of the minimum revenue covenant shall be waived at any time in which either (a) our market capitalization exceeds $750.0 million and we maintain unrestricted cash equal to at least 50% of the total amounts funded, or (b) we maintain unrestricted cash equal to at least 100% of the total amounts funded. The Fourth Amendment also re-set the prepayment premiums associated with any prepayment of the loans under the Loan Agreement.

On June 6, 2023, we entered into a Fifth Amendment to Loan and Security Agreement (the "Fifth Amendment") with Hercules, under which Hercules agreed to lend us up to $75.0 million, subject to specified conditions. In conjunction with the closing of the Fifth Amendment, we repaid $25.0 million of the outstanding debt such that the total loan amount outstanding upon closing of the Fifth Amendment was $50.0 million. The Fifth Amendment eliminated advances under Tranches 2 and 3 and increased the advance available under Tranche 4 from $15.0 million to $25.0 million and extended the time for drawing the Tranche 4 Advance (as defined in the Loan and Security Agreement) from June 30, 2024 to December 15, 2024. The Fifth Amendment adjusted the minimum cash covenant such that we must maintain unrestricted cash equal to at least 35% of the outstanding debt at all times. The Fifth Amendment removed the existing minimum revenue covenant and provided for a conditional borrowing base limit such that, beginning with the financial reporting for the period ended June 30, 2023, and tested monthly, our debt outstanding shall not exceed certain thresholds of trailing three months net product revenue of COSELA.

Hercules also has the ability to call debt based on a material adverse change clause, which is subjectively defined. If we are not in compliance with the minimum cash covenant, conditional borrowing base requirements, or the subjective acceleration clauses are triggered under the agreement, then Hercules may call the debt resulting in us immediately needing additional funds. We have determined that subjective acceleration under the material adverse events clause included in the Loan Agreement is not probable and, therefore, have classified the outstanding principal amount in long-term liabilities based on the timing of scheduled principal payments. As of December 31, 2023, and as of the date of the issuance of these financial statements, we were not in default under the Loan Agreement as we remained in compliance with the minimum cash covenant, the conditional borrowing base requirements, and have not been notified of an event of default by the lender under the Loan Agreement.

License Agreements

On May 22, 2020, we entered into a global license agreement with Incyclix, formerly ARC Therapeutics, LLC, for the development and commercialization of a CDK2 inhibitor for all human and veterinary uses. On June 15, 2020, we entered into an exclusive license agreement with Genor for the development and commercialization of lerociclib in the Genor Territory. On July 22, 2020, we entered into an exclusive license agreement with EQRx for the development and commercialization of lerociclib in the EQRx Territory. The license agreement with EQRx was terminated during the previous quarter. On August 3, 2020, we entered into an exclusive license agreement with Simcere for the development and commercialization of trilaciclib in all indications in the Simcere Territory. The license agreement with Simcere was amended on April 28, 2023. See "Note 10 – License Revenue" to the accompanying audited financial statements included in Item 15 of this Annual Report for a further description of our license agreements and our relationships with Incyclix, Genor, EQRx, and Simcere.

Cash flows

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

	Twelve Months Ended December 31,		
	2023	2022	2021
	(in thousands)		
Net cash used in operating activities	$ (38,337)	$ (128,620)	$ (132,108)
Net cash provided by/(used in) investing activities	2,810	(50,529)	—
Net cash (used in)/provided by financing activities	(26,912)	52,495	145,863
Net change in cash, cash equivalents, and restricted cash	$ (62,439)	$ (126,654)	$ 13,755

Net cash used in operating activities

During the twelve months ended December 31, 2023, net cash used in operating activities was $38.3 million, which consisted of a net loss of $48.0 million, accretion of discount on available for sale securities of $2.3 million, and a decrease in net operating assets and liabilities of $5.2 million, partially offset by non-cash stock compensation expense of $14.5 million, $1.5 million in amortization of debt issuance costs, $0.6 million of non-cash interest expense, and $0.5 million of depreciation expense.

During the twelve months ended December 31, 2022, net cash used in operating activities was $128.6 million which consisted of a net loss of $147.6 million, accretion of discount on available for sale securities of $0.4 million, and a decrease in net operating assets and liabilities of $5.3 million, partially offset by non-cash stock compensation expense of $20.6 million, $2.2 million in amortization of debt issuance costs, $0.5 million of depreciation expense, $0.9 million of non-cash interest expense, and non-cash equity interest of $0.5 million.

During the twelve months ended December 31, 2021, net cash used in operating activities was $132.1 million, which consisted of a net loss of $148.4 million and a decrease in net operating assets and liabilities of $8.8 million, partially offset by non-cash stock compensation expense of $22.3 million, $1.1 million in amortization of debt issuance costs, $0.6 million of non-cash interest expense, $0.5 million of depreciation expense, non-cash equity interest of $0.4 million, and $0.2 million from loss on extinguishment of debt.

Net cash provided by/(used in) investing activities

During the twelve months ended December 31, 2023, net cash provided by investing activities was $2.8 million, due to marketable securities maturities of $127.5 million, offset by the purchase of $124.7 million in marketable securities.

During the twelve months ended December 31, 2022, net cash used in investing activities was $50.5 million due to the purchase of $65.0 million in marketable securities and $0.5 million of manufacturing equipment placed in service during the year, offset by maturities of $15.0 million in marketable securities.

For the year ended December 31, 2021, there was no cash provided or used in investing activities.

Net cash (used in)/provided by financing activities

During the twelve months ended December 31, 2023, net cash used in financing activities was $26.9 million, which consisted primarily of $26.7 million for repayment of debt and proportionate amount of the end of term fee, and $0.3 million in payment of public offering costs.

During the twelve months ended December 31, 2022, net cash provided by financing activities was $52.5 million, which consisted of $52.3 million in net proceeds from our public offering after deducting cash paid during the year for underwriting discounts and commissions and other expenses, and $0.2 million in net proceeds from the exercise of stock options.

During the twelve months ended December 31, 2021, net cash provided by financing activities was $145.9 million, which consisted of $86.4 million in net proceeds from our ATM offering after deducting cash paid during the year for underwriting discounts and commissions and other expenses, $55.0 million in proceeds from our loan agreement with Hercules, partially offset by $1.4 million in payments related to debt issuances costs, and $5.9 million in net proceeds from the exercise of stock options.

Operating capital requirements and plan of operations

To date, we have generated limited revenue from product sales. We expect our expenses to increase as we continue the development of and seek additional regulatory approvals for trilaciclib, and continue to commercialize COSELA. We are subject to all of the risks inherent in the development of new products, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business.

We believe that our existing cash and cash equivalents and marketable securities will be sufficient to fund our projected cash needs for at least the next 12 months from the date of issuance of the financial statements.

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 agreements 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 and the terms of such in-licenses;
- the costs of commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the potential benefit of the NMPA's conditional approval for our products and product candidates and our ability to provide comprehensive clinical data from post-approval clinical research;
- revenue received from commercial sales of our product candidates;
- our ability to meet the required financial covenants under our loan agreement;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- global economic uncertainty, rising inflation, rising interest rates, market disruptions and volatility in commodity prices.

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. Other than amounts included under the terms of our licensing arrangements and the Loan Agreement with Hercules, which are subject to certain conditions, we do not have any committed external source of funds. We may be bound by ongoing compliance with financial covenants under the Loan Agreement with Hercules. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations, Commitments and Contingencies

Our principal commitments consist of obligations under our clinical trial commitments, consulting fees, operating lease commitments and long-term debt obligations. The following table summarizes these contractual obligations as of December 31, 2023:

	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)	$ 6,534	$ 1,679	$ 3,498	$ 1,357	$ —
Long-term debt obligation, including interest and end of term charge (2)	69,876	9,008	60,868	—	—
Total contractual obligations (3, 4, 5)	$ 76,410	$ 10,687	$ 64,366	$ 1,357	$ —

(1) Represents future minimum lease payments under the non-cancelable lease for our current headquarters in Research Triangle Park, NC. The lease for our current office space commenced in September 2019 for approximately 60,000 square feet of laboratory space and office space in Research Triangle Park, NC. The lease will expire in September 2027, with the Company having the option to renew for an additional five years. The lease for our former headquarters expired in December 2022, no payments were owed or paid related to this lease subsequent to the lease expiration date. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) Amounts in the table reflect payments due under our Fifth Amendment to the Loan and Security Agreement with Hercules with outstanding borrowings of $50.0 million as of December 31, 2023. The amounts in the table above reflect interest-only payments through December 1, 2024 with payments on principal beginning thereafter. For purposes of the table above, interest payments were calculated using an annual interest rate of 14.15%, which was the interest rate in effect as of December 31, 2023. Additionally, the table above includes end of term charges of $2.1 million due on June 1, 2025 and $3.4 million due upon maturity on November 1, 2026. See Note 7 of the financial statements for further discussion of the Hercules loan agreement.

(3) We enter into agreements in the normal course of business with contract research organizations (CROs) for clinical trials and with vendors for preclinical studies and other services and products for operating purposes which are cancellable at any time by us, generally upon 30-60 days prior written notice. As of December 31, 2023, 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.

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

(5) We entered into a three-year co-promotion agreement in the United States and Puerto Rico with Boehringer Ingelheim Pharmaceuticals, Inc., or BI, in June 2020. In December 2021, G1 and BI announced that the parties mutually agreed to end the co-promotion agreement for COSELA, effective March 2022. At that time, we announced that we would hire and deploy our own oncology sales team to accelerate sales activities and help maximize the adoption of COSELA. For two years following the termination, sales payments to BI will be decreased to mid-single digit percentages of net sales. The sales payments will vary based on the level of net sales in an applicable year following the termination. Our obligations to make sales payments under the co-promotion agreement will terminate in March 2024.

Off-Balance Sheet Arrangements

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

Recent Accounting Pronouncements

For a discussion of recent accounting pronouncements, refer to Note 2, *Basis of Presentation and Summary of Significant Accounting Policies*, to our financial statements appearing elsewhere in this Annual Report on Form 10-K.

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, which are affected by changes in the general level of U.S. interest rates. We had cash and cash equivalents of $32.2 million and marketable securities of $49.9 million as of December 31, 2023. Cash and cash equivalents consist of deposits in banks, including checking accounts and money market accounts and funds. Marketable securities consist of U.S. Treasury bills. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. Due to the short-term nature of our cash equivalents, a sudden change in interest rates would not be expected to have a material effect on our business, financial condition or results of operations.

We also have exposure to market risk on our Loan Agreement with Hercules. Our Loan Agreement (as such is amended from time to time) accrues interest from its date of issue at a variable interest rate equal to the greater of either (i) (a) the prime rate as reported in The Wall Street Journal, plus (b) 5.65%, and (ii) 9.15%. As of December 31, 2023, $50.0 million of principal was outstanding under the Loan Agreement with Hercules. See "Management's Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources - Loan and Security Agreement" section of this Annual Report for more details.

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

Inflation generally affects us by increasing our cost of labor. We do not believe that inflation had a material effect on our business, financial condition, or results of operations during the three and twelve months ended December 31, 2023.

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 Exchange Act 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, 2023, 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 Exchange Act). 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, 2023, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Controls Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the fourth quarter of 2023 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, 2023.

Item 9B. Other Information.

During the three months ended December 31, 2023, none of our directors or officers (as defined in Rule 16a-1(f) of the Securities Exchange Act of 1934, as amended), adopted, terminated or modified a Rule 10b5-1 trading arrangement or non-Rule 10b5-1 trading arrangement (as such terms are defined in Item 408 of Regulation S-K of the Securities Act of 1933, as amended).

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated herein by reference from the Company's Proxy Statement for the 2024 Annual Meeting of Stockholders, which will be filed with the SEC within 120 days after the end of our 2023 fiscal year pursuant to Regulation 14A for our 2024 Annual Meeting of Stockholders (the "Proxy Statement"), except for the information provided under the caption "Pay Versus Performance." The additional information required by this Item is included under the captions "Management and Corporate Governance," "Election of Directors," "Certain Relationships and Related Party Transactions," and other information included in the Proxy Statement and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this item is incorporated herein by reference from the Proxy Statement under the captions "Compensation of Named Executive Officers and Director," "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.

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	Certificate of Correction to G1 Therapeutics, Inc.'s Amended and Restated Certificate of Incorporation filed on May 22, 2017, dated June 30, 2021, filed as Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed on July 2, 2021 (File No. 001-38096), and incorporated herein by reference.
3.3	Amended and Restated Bylaws of G1 Therapeutics, Inc., dated as of May 22, 2017, filed as Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed on May 26, 2017 (File No. 001-38096), and incorporated herein by reference.
4.1	Specimen Common Stock Certificate, filed as Exhibit 4.1 to the Registrant's Second Amendment to the Registration Statement on Form S-1 filed on May 8, 2017 (File No. 333-217285), and incorporated herein by reference.
4.2	Description of Securities of the Registrant.
10.1^ +	Loan and Security Agreement, by and between the Registrant and Hercules Capital, Inc., dated May 29, 2020, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 filed on August 5, 2020 (File No. 001-38096), and incorporated herein by reference.

10.2	First Amendment to Loan and Security Agreement, by and between the Registrant and Hercules Capital, Inc., dated March 31, 2021, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 filed on May 5, 2021 (File No. 001-38096), and incorporated herein by reference.
10.3^ +	Second Amendment to Loan and Security Agreement, by and between the Registrant and Hercules Capital, Inc., dated November 1, 2021, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 filed on November 3, 2021 (File No. 001-38096), and incorporated herein by reference.
10.4^ +	Third Amendment to Loan and Security Agreement, by and between the Registrant and Hercules Capital, Inc., dated June 24, 2022, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2022 filed on August 3, 2022 (File No. 001-38096), and incorporated herein by reference.
10.5^+	Fourth Amendment to Loan and Security Agreement by and between Registrant and Hercules Capital, Inc., dated November 1, 2022, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 filed on November 2, 2022 (File No. 001-38096), and incorporated herein by reference.
10.6^+**	Fifth Amendment to Loan and Security Agreement by and between Registrant and Hercules Capital, Inc., dated June 6, 2023, filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on June 9, 2023 (File No. 001-38096), and incorporated herein by reference.
10.7+	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.
10.8*	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.
10.9*	Amended and Restated 2021 Inducement Equity Incentive Plan, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2022 filed on May 4, 2022 (File No. 001-38096), and incorporated herein by reference.
10.10*	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.
10.11*	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, Amended and Restated Non-Employee Director Compensation Policy effective as of June 12, 2019, filed as Exhibit 10.1 to the Registrant's Form 8-K filed on June 13, 2019 (File No. 001-38096), and incorporated herein by reference.
10.12*	Second Amended and Restated Non-Employee Director Compensation Policy, filed as Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on June 21, 2021 (File No. 001-38096), and incorporated herein by reference.
10.13*	Employment Agreement by and between Registrant and John E. Bailey, Jr. dated September 29, 2020, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed on November 4, 2020 (File No. 001-38096), and incorporated herein by reference.

10.14*	Senior Advisor Agreement between Registrant and John E. Bailey, Jr. dated September 29, 2020, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed on November 4, 2020 (File No. 001-38096), and incorporated herein by reference.
10.15*	Employment Agreement by and between the Registrant and Mark Avagliano, dated as of July 29, 2019, filed as Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 filed on August 7, 2019 (File No. 001-38096), and incorporated herein by reference.
10.16*	Employment Agreement, by and between the Registrant and Rajesh K. Malik, M.D., dated July 1, 2014, as amended; First Amendment effective May 5, 2017, filed as Exhibit 10.5 to the Registrant's Second Amendment to the Registration Statement on Form S-1 filed on May 8, 2017 (File No. 333-217285), and incorporated herein by reference; and Second Amendment effective June 12, 2019, filed as Exhibit 10.2 to the Registrant's Form 8-K filed on June 13, 2019 (File No. 001-38096), and incorporated herein by reference.
10.17*	Senior Advisor Agreement between Registrant and Jennifer K. Moses dated February 28, 2023, filed as Exhibit 10.22 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2022 filed on March 1, 2023 (File No. 001-38096), and incorporated herein by reference.
10.18*	Employment Agreement by and between the Registrant and Terry Murdock, dated as of August 1, 2017, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 filed on November 8, 2017 (File No. 001-38096) incorporated herein by reference; and First Amendment effective June 12, 2019, filed as Exhibit 10.3 to the Registrant's Form 8-K filed on June 13, 2019 (File No. 001-38096), and incorporated herein by reference.
10.19*	Employment Agreement by and between Registrant and Andrew Perry dated July 28, 2021, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 filed on August 4, 2021 (File No. 001-38096) incorporated herein by reference.
10.20*	Employment Agreement by and between the Registrant and John W. Umstead V, dated as of February 28, 2023, filed as Exhibit 10.25 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2022 filed on March 1, 2023 (File No. 001-38096), and incorporated herein by reference.
10.21*	Senior Advisor Agreement between Registrant and Mark A. Velleca, M.D., Ph.D. dated September 29, 2020, filed as Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 filed on November 4, 2020 (File No. 001-38096), and incorporated herein by reference.
10.22*	First Amendment to Senior Advisor Agreement between Registrant and Mark A. Velleca, M.D., Ph.D., dated as of September 20, 2023, filed as Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 filed on November 1, 2023 (File No. 001-38096), and incorporated herein by reference.
10.23	Sales Agreement by and between the Registrant and Cowen and Company, LLC, dated as of February 23, 2022, filed as Exhibit 10.29 to the Registrant's Annual Report on Form 10-K for the year ended December 31, 2021 filed on February 23, 2022 (File No. 001-38096), and incorporated herein by reference.
10.24*	G1 Therapeutics, Inc. Deferred Compensation Plan for Non-Employee Directors, filed as Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended on June 30, 2023 filed on August 2, 2023 (File No. 001-38096), and incorporated herein by reference.
10.25*†	G1 Therapeutics, Inc. Amended and Restated Clawback Policy

10.26*	Form of Performance Based Restricted Stock Unit Award Agreement under the Amended and Restated 2017 Employee, Director and Consultant Equity Plan, as amended, filed as Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2023 filed on May 3, 2023 (File No. 001-38096), and incorporated herein by reference.
10.27*†	Form of Restricted Stock Unit Agreement under the Amended and Restated 2017 Employee, Director and Consultant Equity Incentive Plan, as amended
10.28*†	Form of Restricted Stock Unit Agreement under the G1 Therapeutics, Inc. Amended and Restated 2021 Inducement Equity Incentive Plan, as amended
10.29*†	Employment Agreement by and between the Registrant and Monica Roberts Thomas, dated as of May 22, 2023
21.1	Subsidiaries of the Registrant, filed as Exhibit 21.1 to the Registrant’s Registration Statement on Form S-1 filed on April 13, 2017 (File No. 333-217285), and incorporated herein by reference.
23.1†	Consent of PricewaterhouseCoopers LLP.
31.1†	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2†	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1†	Certification of Principal Executive Officer Pursuant to 18 U.S.C. § 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2†	Certification of Principal Financial Officer Pursuant to 18 U.S.C. § 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)XBRL Taxonomy Extension Presentation Linkbase Document

* Management contract or compensatory plan or arrangement.

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

^ Certain confidential portions of this Exhibit were omitted by means of marking such portions with brackets ("[***]") because the identified confidential portions (i) are not material and (ii) is the type that the Registrant treats as private or confidential.

+ Certain of the exhibits and schedules to this Exhibit have been omitted in accordance with Regulation S-K Item 601(a)(5). The Registrant agrees to furnish a copy of all omitted exhibit and schedules to the SEC upon its request.

† Filed herewith.

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, 2024

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

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

Name	Title	Date
/s/ John E. Bailey, Jr. **John E. Bailey, Jr.**	President, Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2024
/s/ John W. Umstead V **John W. Umstead V**	Chief Financial Officer (Principal Financial and Accounting Officer)	February 28, 2024
/s/ Garry A. Nicholson **Garry A. Nicholson**	Director	February 28, 2024
/s/ Cynthia L. Flowers **Cynthia L. Flowers**	Director	February 28, 2024
/s/ Jacks Lee **Jacks Lee**	Director	February 28, 2024
/s/ Glenn P. Muir **Glenn P. Muir**	Director	February 28, 2024
/s/ Alicia Secor **Alicia Secor**	Director	February 28, 2024
/s/ Norman E. Sharpless, M.D. **Norman E. Sharpless, M.D.**	Director	February 28, 2024

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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of G1 Therapeutics, Inc. (the "Company") as of December 31, 2023 and 2022, and the related statements of operations, of stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2023, including the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

Emphasis of Matter

As discussed in Note 2 to the financial statements, the Company will require additional financing to fund future operations. Management's evaluation of the events and conditions and plans to mitigate this matter are also described in Note 2.

Critical Audit Matter

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

Accrued External Clinical Study Costs

As described in Notes 2 and 5 to the financial statements, management estimated and accrued research and development expenses including external clinical study costs associated with clinical trial activities. The Company's accrued external clinical study costs were $10.9 million as of December 31, 2023. The process of estimating and accruing expenses involved reviewing contracts and purchase orders, identifying services that have been provided on the Company's behalf, and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual cost. Costs for clinical trial activities were estimated based on an evaluation of the vendors' progress towards completion of specific tasks, using data such as patient enrollment, clinical site activations or information provided by vendors regarding their actual costs incurred. Management determined accrual estimates through reports from and discussion with applicable personnel and outside service providers as to the progress or state of completion of trials, or the services completed.

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

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

/s/ PricewaterhouseCoopers LLP
Raleigh, NC
February 28, 2024

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, 2023	December 31, 2022
Assets		
Current assets		
Cash and cash equivalents	$ 32,218	$ 94,594
Restricted cash	63	63
Marketable securities	49,938	50,476
Accounts receivable and unbilled receivables, net	12,687	11,094
Inventories, net	12,442	16,179
Prepaid expenses and other current assets	7,600	7,094
Total current assets	114,948	179,500
Property and equipment, net	1,476	1,989
Restricted cash	187	250
Operating lease assets	4,908	5,962
Other assets	21	264
Total assets	$ 121,540	$ 187,965
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 3,992	$ 7,431
Accrued expenses	21,893	25,557
Deferred revenue	620	7
Other current liabilities	3,211	2,593
Total current liabilities	29,716	35,588
Loan payable	51,557	77,015
Deferred revenue	500	1,000
Operating lease liabilities	4,340	5,615
Other liabilities	41	—
Total liabilities	86,154	119,218
Stockholders' equity		
Common stock, $0.0001 par value, 120,000,000 shares authorized as of December 31, 2023, and December 31, 2022; 51,952,741 and 51,526,100 shares issued as of December 31, 2023, and December 31, 2022, respectively; 51,926,075 and 51,499,434 shares outstanding as of December 31, 2023, and December 31, 2022, respectively	5	5
Treasury stock, 26,666 shares as of December 31, 2023, and December 31, 2022	(8)	(8)
Additional paid-in capital	815,374	800,768
Accumulated deficit	(779,985)	(732,018)
Total stockholders' equity	35,386	68,747
Total liabilities and stockholders' equity	$ 121,540	$ 187,965

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,		
	2023	2022	2021
Revenues			
Product sales, net	$ 46,344	$ 31,337	$ 11,120
License revenue	36,167	19,964	20,356
Total revenues	82,511	51,301	31,476
Operating expenses			
Cost of goods sold	7,195	3,748	2,016
Research and development	43,711	83,316	76,225
Selling, general and administrative	71,132	100,415	95,692
Total operating expenses	122,038	187,479	173,933
Loss from operations	(39,527)	(136,178)	(142,457)
Other income (expense)			
Interest income	2,473	748	43
Interest expense	(10,038)	(10,432)	(4,667)
Other income (expense)	2,240	3	(346)
Total other income (expense), net	(5,325)	(9,681)	(4,970)
Loss before income taxes	(44,852)	(145,859)	(147,427)
Income tax expense	3,115	1,700	925
Net loss	$ (47,967)	$ (147,559)	$ (148,352)
Net loss per share, basic and diluted	$ (0.93)	$ (3.38)	$ (3.54)
Weighted average common shares outstanding, basic and diluted	51,733,487	43,626,113	41,943,417

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

G1 Therapeutics, Inc.
Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common stock		Treasury stock		Additional paid-in capital	Accumulated deficit	Total stock-holders' equity
	Shares	Amount	Shares	Amount			
Balance at December 31, 2020	**38,140,756**	**$ 4**	**(26,666)**	**$ (8)**	**$ 613,462**	**$ (436,107)**	**$ 177,351**
Public offering (ATM)	3,513,027	—	—	—	86,378	—	86,378
Exercise of common stock options	935,031	—	—	—	5,845	—	5,845
Stock-based compensation	—	—	—	—	22,319	—	22,319
Net loss during year	—	—	—	—	—	(148,352)	(148,352)
Balance at December 31, 2021	**42,588,814**	**$ 4**	**(26,666)**	**$ (8)**	**$ 728,004**	**$ (584,459)**	**$ 143,541**
Public offering	8,573,353	1	—	—	52,020	—	52,021
Exercise of common stock options	206,608	—	—	—	155	—	155
Restricted stock units vested	157,325	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	20,589	—	20,589
Net loss during year	—	—	—	—	—	(147,559)	(147,559)
Balance at December 31, 2022	**51,526,100**	**$ 5**	**(26,666)**	**$ (8)**	**$ 800,768**	**$ (732,018)**	**$ 68,747**
Public offering	—	—	—	—	39	—	39
Exercise of common stock options	165,180	—	—	—	57	—	57
Restricted stock units vested	261,461	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	14,510	—	14,510
Net loss during year	—	—	—	—	—	(47,967)	(47,967)
Balance at December 31, 2023	**51,952,741**	**$ 5**	**(26,666)**	**$ (8)**	**$ 815,374**	**$ (779,985)**	**$ 35,386**

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

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

	Twelve Months Ended December 31,		
	2023	2022	2021
Cash flows from operating activities			
Net loss	$ (47,967)	$ (147,559)	$ (148,352)
Adjustments to reconcile net loss to net cash used in operating activities			
Stock-based compensation	14,510	20,589	22,319
Accretion of discount on available for sale securities	(2,272)	(453)	—
Depreciation and amortization	513	530	469
Amortization of debt issuance costs	1,473	2,233	1,113
Loss on extinguishment of debt	—	—	220
Non-cash interest expense	609	850	591
Non-cash equity interest, net	—	497	370
Change in operating assets and liabilities			
Accounts receivable	(1,593)	(5,406)	(5,451)
Inventories	3,737	(12,708)	(3,471)
Prepaid expenses and other assets	548	7,184	(3,380)
Accounts payable	(3,372)	4,421	(675)
Accrued expenses and other liabilities	(4,636)	1,226	3,345
Deferred revenue	113	(24)	794
Net cash used in operating activities	(38,337)	(128,620)	(132,108)
Cash flows from investing activities			
Purchases of marketable securities	(124,690)	(65,023)	—
Maturities of marketable securities	127,500	15,000	—
Purchases of property and equipment	—	(506)	—
Net cash provided by/(used in) investing activities	2,810	(50,529)	—
Cash flows from financing activities			
Proceeds from stock options exercised	57	155	5,845
Proceeds from loan agreement	—	—	55,000
Payments of debt issuance costs	—	—	(1,360)
Proceeds from public offering, net of underwriting fees and commissions	—	52,383	86,429
Repayment of debt	(26,688)	—	—
Payment of public offering costs	(281)	(43)	(51)
Net cash (used in)/provided by financing activities	(26,912)	52,495	145,863
Net change in cash, cash equivalents and restricted cash	(62,439)	(126,654)	13,755
Cash, cash equivalents and restricted cash			
Beginning of period	94,907	221,561	207,806
End of period	$ 32,468	$ 94,907	$ 221,561
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 8,807	$ 7,924	$ 2,908
Non-cash operating, investing and financing activities			
Upfront project costs and other current assets in accounts payable and accrued expenses	$ —	$ 47	$ —
Public offering costs in accounts payable and accrued expenses	$ —	$ 320	$ —

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

1. Description of Business

G1 Therapeutics, Inc. (the “Company”) is a commercial-stage biopharmaceutical company focused on the development and commercialization of novel small molecule therapeutics for the treatment of patients with cancer. The Company's first product approved by the U.S. Food and Drug Administration (“FDA”), COSELA® (trilaciclib), is the first and only therapy indicated to proactively help protect bone marrow from the damage of chemotherapy (myeloprotection) is the first innovation in managing myeloprotection in decades. COSELA (trilaciclib hydrochloride for injection) is also conditionally approved by the China National Medical Products Administration (NMPA) for marketing in mainland China and is commercialized by the Company's partner, Simcere Pharmaceutical Co., Ltd. ("Simcere"), in Greater China (mainland China, Hong Kong, Macau and Taiwan).

Trilaciclib was developed from a technology platform that targets key cellular pathways including transient arrest of the cell cycle at the G1 phase, prior to the beginning of DNA replication. Controlled administration and clean G1 arrest from transient CDK4/6 inhibition may protect bone marrow and the immune system from cytotoxic damage during treatment. Transient CDK4/6 inhibition also may improve survival in combination with leading and emerging treatments by improving long-term immune surveillance. This can be accomplished through protection of the immune system for improved longer-term function and by potentially increasing the generation of memory T cells, which can provide additional benefit after treatment. The Company is exploring the use of trilaciclib in clinical trials to optimize these potential benefits in combination with leading and emerging treatments for patients. Beyond the Company’s initial ES-SCLC indication in the United States, the Company plans to focus its efforts on two core development paths for trilaciclib in order to optimize the opportunity ahead, including: (1) triple negative breast cancer ("TNBC"), where trilaciclib has demonstrated potential benefits across treatment settings in multiple Phase 2 studies, and (2) in antibody-drug conjugate ("ADC") combinations, in TNBC and potentially other additional tumor types.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

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

The Company has experienced net losses since its inception and has an accumulated deficit of $780.0 million and $732.0 million as of December 31, 2023 and December 31, 2022, respectively. The Company expects to incur losses and have negative net cash flows from operating activities as it executes on its strategy including engaging in further research and development activities, particularly conducting non-clinical studies and clinical trials. The success of the Company depends on the ability to successfully commercialize its technologies to support its operations and strategic plan. Management has evaluated actions already taken, the significance of anticipated continued losses, future cash flow projections, and the ability of the Company to remain in compliance with the financial covenants and requirements as defined within the Loan Agreement (as defined below). Based on the foregoing, as of the date of issuance of these financial statements, the Company expects that its cash and cash equivalents and marketable securities as of December 31, 2023 will be sufficient to fund the Company’s planned operations and remain in compliance with its objective financial covenants for at least the next 12 months from the date of issuance of these financial statements. Until such time, if ever, as the Company can generate substantial revenues, the Company expects to finance its 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. There can be no assurances that the Company will be able to secure such additional financing if at all, or on terms that are satisfactory to the Company, and that it will be sufficient to meet its needs. In the event the Company is not successful in obtaining sufficient funding, this could force it to delay, limit, or reduce its product development, commercialization efforts or other operations. 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. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

In connection with the Loan Payable described in Note 7, the Company is required to be in compliance with a minimum cash covenant and is subject to a conditional borrowing base measured on a trailing three-month net revenue basis, which began with the financial reporting for the period ended June 30, 2023, and has been tested monthly thereafter. The lender also has the ability to call debt based on a material adverse change clause, which is subjectively defined. If the Company is not in compliance with the minimum cash covenant, conditional borrowing base requirements, or the subjective acceleration clauses are triggered under the agreement, then the lender may call the debt resulting in the Company immediately needing additional funds. As of December 31, 2023, the Company is in compliance with the minimum cash covenant and the conditional borrowing base requirements as set forth in the Loan Agreement.

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. On an ongoing basis, the Company's management evaluates its estimates which include, but are not limited to, estimates related to accrued expenses, accrued external clinical costs, net product sales, common stock valuation, stock-based compensation expense and deferred tax asset valuation allowance. Actual results could differ from those estimates.

Cash, Cash Equivalents, and Restricted Cash

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, 2023 consist of amounts on deposit in banks, including checking accounts and money market accounts and funds. Cash deposits are all in financial institutions in the United States. As part of the lease for the office space which commenced on September 2, 2019, the Company obtained a standby letter of credit in the amount of $0.5 million related to the security deposit. This letter of credit is secured by a money market account at the financial institution and is classified as restricted cash on the Company's balance sheet. The letter of credit will be reduced ratably on each anniversary of the commencement of the lease until the end of the lease term. Restricted cash totaled $250 thousand and $313 thousand for the years ended December 31, 2023 and 2022, respectively.

Marketable Securities

The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation at each balance sheet date. The Company classified all of its marketable securities at December 31, 2023 as "available-for-sale" pursuant to ASC Topic 320, Investments – Debt and Equity Securities. Investments not classified as cash equivalents are presented as either short-term or long-term investments based on both their maturities as well as the time period the Company intends to hold such securities. Available-for-sale securities are maintained by an investment manager and primarily consist of fixed income securities. Available-for-sale securities are carried at fair value. Any premium or discount arising at purchase is amortized or accreted to interest income over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other (income) expense, net. As of December 31, 2023, the unrealized gains and losses are not considered to be material.

Accounts Receivable

The Company's accounts receivable consists of amounts due from specialty distributors in the U.S. (collectively, its "customers") related to sales of COSELA and have standard payment terms. Trade receivables are recorded net of the estimated variable consideration for chargebacks based on contractual terms and the Company's expectation regarding the utilization and earnings of the chargebacks and discounts as well as the net amount expected to be collected from the Company's customers. Estimates of the Company's credit losses, of which there are none for the year ended December 31, 2023, are determined based on existing contractual payment terms, individual customer circumstances, and any changes to the economic environment.

In addition, the Company's accounts receivable consists of open invoices issued to its license partners for services rendered by the Company or receivables with its license partners for invoices related to milestones that were completed and recognized as revenue. The Company also has unbilled accounts receivable related to clinical trial reimbursements where the Company has the right to invoice the license partner and accordingly has recognized revenue. Invoicing to the license partner will occur once the Company has been invoiced by the service provider. As of December 31, 2023, unbilled accounts receivable totaled $0.2 million.

Inventories

Inventories are stated at the lower of cost or net realizable value and recognized on a weighted-average cost method. The Company uses actual cost to determine the cost basis for inventory. Inventory is capitalized based on when future economic benefit is expected to be realized. Due to the nature of the Company's supply chain process, inventory that is owned by the Company, is physically stored at third-party warehouses, logistics providers, and contract manufacturers.

Inventory valuation is established based on a number of factors including, but not limited to, finished goods not meeting product specifications, product excess and obsolescence, or application of the lower of cost or net realizable value concepts. The determination of events requiring the establishment of inventory valuation, together with the calculation of the amount of such adjustments may require judgment. The Company analyzes its inventory levels on a periodic basis to determine if any inventory is at risk for expiration prior to sale or has a cost basis that is greater than its estimated future net realizable value. Any adjustments are recognized through cost of goods sold in the period in which they are incurred.

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
Manufacturing 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, 2023, 2022 and 2021, the Company's management evaluated its long-lived assets and determined no impairment charge was needed.

Debt

The Company classifies its loan payable in current or long-term liabilities based on the timing of scheduled principal payments. The loan and security agreement with Hercules Capital, Inc. (as amended, the "Loan Agreement") contains events of default, including a material adverse change, which is subjectively defined, in the Company's business, payment defaults, and breaches of covenants following any applicable cure period. In the event of default by the Company under the Loan Agreement, the Company may be required to repay all amounts then outstanding under the Loan Agreement. The Company has determined that subjective acceleration under the material adverse events clause included in the Loan Agreement is not probable and, therefore, has classified the outstanding principal amount in long-term liabilities based on the timing of scheduled principal payments.

Revenue Recognition

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

License Revenue

Licenses of Intellectual Property

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

Milestone Payments

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

Royalties

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company will recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). During the twelve months ended December 31, 2023, the Company recognized $0.6 million in revenue related to sales-based royalties.

Product Sales, Net

The Company sells COSELA to specialty distributors in the U.S. and, in accordance with ASC 606, recognizes revenue at the point in time when the customer is deemed to have obtained control of the product. The customer is deemed to have obtained control of the product at the time of physical receipt of the product at the customers' distribution facilities, or Free on Board ("FOB") destination, the terms of which are designated in the contract.

Product sales are recorded at the net selling price, which includes estimates of variable consideration for which reserves are established for (a) rebates and chargebacks, (b) co-pay assistance programs, (c) distribution fees, (d) product returns, (e) GPO fees, and (f) other discounts. Where appropriate, these estimates take into consideration a range of possible outcomes for relevant factors such as current contractual and statutory requirements, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the applicable contract. The amount of variable consideration may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from estimates, the Company adjusts these estimates, which would affect net product revenue and earnings in the period such variances become known.

Liabilities related to co-pay assistance, rebates, returns, and GPO fees are classified as "Accrued Expenses" in the Balance Sheets. Discounts such as chargebacks and specialty distributor fees are recorded as a reduction to trade accounts receivable, which is included in "Accounts Receivable" in the Balance Sheets.

Forms of Variable Consideration

Rebates and Chargebacks*:* The Company estimates reductions to product sales for Public Health Service Institutions, such as Medicaid, Medicare and Veterans Administration ("VA") programs, as well as certain other qualifying federal and state government programs, and other group purchasing organizations. The Company estimates these reductions based upon the Company's contracts with government agencies and other organizations, statutorily defined discounts and estimated payor mix. These organizations purchase directly from the Company's specialty distributors at a discount and the specialty distributors charge the Company back the difference between the wholesaler price and the discounted price. The Company's liability for Medicaid rebates consists of estimates for claims that a state will make. The Company's reserve for this discounted pricing is based on expected sales to qualified healthcare providers and the chargebacks that customers have already claimed.

Co-pay assistance: Eligible patients who have commercial insurance may receive assistance from the Company to reduce the patient's out of pocket costs. Liabilities for co-pay assistance are calculated by actual program participation from third-party administrators.

Distribution Fees: The Company has written contracts with its customers that include terms for distribution fees and costs for inventory management. The Company estimates and records distribution fees due to its customers based on gross sales.

Product Returns: The Company generally offers a right of return based on the product's expiration date and certain spoilage and damaged instances. The Company estimates the amount of product sales that may be returned and records the estimate as a reduction of product sales in the period the related product sales are recognized. The Company's estimates for expected returns are based primarily on an ongoing analysis of sales information and visibility into the inventory remaining in the distribution channel.

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.

Cost of Goods Sold

Cost of goods sold includes direct and indirect costs related to the manufacturing and distribution of COSELA, including third-party manufacturing costs, packaging services, freight-in, third-party logistics costs associated with COSELA, and Company personnel costs. Cost of goods sold may also include period costs related to certain inventory manufacturing services and inventory adjustment charges for excess and obsolete inventory.

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 product, costs associated with clinical trials, nonclinical activities, regulatory activities, research-related overhead expenses and fees paid to expert consultants, external service providers and contract research organizations which conduct certain research and development activities on behalf of the Company. Costs incurred in the research and development of products are charged to research and development expense as incurred.

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

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

Fair value of Financial Instruments

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

Level 1	Inputs are unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
Level 2	Inputs include quoted prices for similar assets and liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, inputs other than quoted prices that are observable for the asset or liability and inputs that are derived principally from or corroborated by observable market data by correlation or other means.
Level 3	Unobservable inputs that reflect the Company's estimates of the assumptions that market participants would use in pricing the asset or liability. The Company develops these inputs based on the best information available, including its own data.

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

At December 31, 2023 and 2022 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, 2023
Assets:				
Money market accounts and funds	$ 32,110	$ —	$ —	$ 32,110
Marketable securities:				
U.S. Treasury Bills	49,938	—	—	49,938
Total assets at fair value	$ 82,048	$ —	$ —	$ 82,048

	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, 2022
Assets:				
Money market accounts and funds	$ 84,167	$ —	$ —	$ 84,167
Marketable securities:				
U.S. Treasury Bills	50,476	—	—	50,476
Total assets at fair value	$ 134,643	$ —	$ —	$ 134,643

During the twelve months ended December 31, 2023 and December 31, 2022, there were no changes in valuation methodology.

The Loan Payable (discussed in Note 7), which is classified as a Level 3 liability, has a variable interest rate and the carrying value approximates its fair value. As of December 31, 2023, the carrying value was $51.6 million.

Patent Costs

Costs associated with the submission of patent applications are expensed as incurred given the uncertainty of the future economic benefits of the patents. Patent-related legal expenses included in selling, general and administrative costs were approximately $1.8 million, $1.8 million, and $1.9 million for the years ended December 31, 2023, 2022 and 2021, respectively.

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 also incurs stock-based compensation expense related to restricted stock units (“RSUs”), performance based restricted stock units (“PSUs”), and deferred share units (“DSUs”). The fair value of RSUs, PSUs, and DSUs is determined by the closing market price of the Company’s common stock on the date of grant and then recognized over the requisite service period of the award. As the PSUs have non-market performance and service conditions, compensation expense will be recognized over the requisite service periods if and when the achievement of such performance condition(s) is determined to be probable by the Company. If a performance condition is not determined to be probable or is not met, no stock-based compensation expense is recognized. The Company reassesses the probability of achieving the performance condition(s) at each reporting period. As of December 31, 2023, the Company did not deem the achievement of any performance condition(s) to be probable and no compensation expense related to PSUs was recognized.

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, 2023 and December 31, 2022, 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, 2023 and December 31, 2022, the Company had no such accruals.

Segment Information

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

Comprehensive Loss

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

Leases

The Company determines if an arrangement is a lease at inception. Operating lease assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating leases are included in operating lease assets, other current liabilities, and operating lease liabilities on the Company's balance sheet at December 31, 2023. Operating lease assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at commencement date. As most of the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at commencement date to determine the present value of future payments. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that it will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

Debt Issuance Costs

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

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. The Company did not adopt any new accounting pronouncements during the year ended December 31, 2023, that had a material effect on its financial statements.

In November 2023, the FASB issued ASU 2023-07, "Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures." ASU 2023-07 is intended to improve disclosures about a public entity's reportable segment by requiring additional, more detailed incremental segment information to be disclosed on an annual and interim basis. ASU 2023-07 requires that a public entity with a single reportable segment provide all the disclosures required by the amendments of ASU 2023-07 and all existing segment disclosures in FASB ASC Topic 280. The amendments of ASU 2023-07 require a public entity to disclose, on an annual and interim basis, significant segment expenses that are regularly provided to the chief operating decision maker (CODM) and included within each reported measure of segment profit or loss, and an amount for other segment items by reportable segment and a description of its composition. In additional, ASU 2023-07 requires a public entity to disclose the title and position of the CODM, together with an explanation of how the CODM uses the reported measure(s) of segment profit or loss in assessing segment performance and deciding how to allocate resources. ASU 2023-07 also requires a public entity to provide all annual disclosures about a reportable segment profit or loss and assets currently required under FASB ASC Topic 280 in interim periods. The amendments of ASU 2023-07 are effective for annual periods beginning after December 15, 2023, and for interim periods with fiscal years beginning after December 15, 2024, with early adoption permitted. The Company intends to adopt the amendments of ASU 2023-07 related to annual disclosure requirements effective January 1, 2024, and will present any newly required annual disclosures in its Annual Report on Form 10-K for the year ending December 31, 2024. The Company intends to adopt the amendments of ASU 2023-07 related to interim disclosure requirements effective January 1, 2025, an will present any newly required interim disclosures beginning with its Quarterly Report on Form 10-Q for the period ending March 31, 2025. The Company is currently evaluating the changes to disclosures required by ASU 2023-07; however, adoption of ASU 2023-07 is not expected to have a material impact to its financial position or results of operations.

In December 2023, the FASB issued ASU 2023-09 "Income Taxes (Topic 740): Improvements to Income Tax Disclosures." ASU 2023-09 is intended to improve the disclosures for income taxes to allow investors to better assess, in their capital allocation decisions, how an entity's worldwide operations and related tax risks and tax planning and operational opportunities affect its income tax rate and prospects for future cash flows. The amendments in ASU 2023-09 require consistent categories and greater disaggregation of information in the rate reconciliation disclosure as well as disclosure of income taxes paid disaggregated by jurisdiction. The amendments of ASU 2023-09 are effective for annual periods beginning after December 15, 2024, with early adoption permitted for annual financial statements that have not yet been issued or made available for issuance. The Company intends to adopt the amendments of ASU 2023-09 effective January 1, 2025, and will include the required disclosures in its Annual Report on Form 10-K for the year ending December 31, 2025. The Company is currently evaluating the changes to disclosures required by ASU 2023-09; however, adoption of ASU 2023-09 is not expected to have a material impact to its financial position or results of operations.

3. Inventories

Inventories consist of the following (in thousands):

	December 31, 2023	December 31, 2022
Raw materials	$ 2,422	$ 2,790
Work in process	9,593	10,153
Finished goods	427	3,236
Inventories, net	$ 12,442	$ 16,179

The Company uses third party contract manufacturing organizations for the production of its raw materials, active pharmaceutical ingredients, and finished drug product which the Company owns. The Company evaluates the risk of excess inventory and product expiry by evaluating current and future product demand relative to product shelf life.

4. Property and Equipment

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

	December 31, 2023	December 31, 2022
Computer equipment	$ 327	$ 327
Laboratory equipment	334	334
Furniture and fixtures	866	866
Leasehold improvements	1,782	1,782
Manufacturing equipment	506	506
Accumulated depreciation	(2,339)	(1,826)
Property and equipment, net	$ 1,476	$ 1,989

Depreciation expenses relating to property and equipment were $513 thousand, $530 thousand and $469 thousand for the years ended December 31, 2023, 2022 and 2021, respectively.

5. Accrued Expenses

Accrued expenses are comprised as follows (in thousands):

	December 31, 2023	December 31, 2022
Accrued external research	$ 109	$ 268
Accrued professional fees and other	5,854	4,304
Accrued external clinical study costs	10,944	15,566
Accrued compensation expense	4,986	5,419
Accrued expenses	$ 21,893	$ 25,557

6. Leases

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

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

On March 20, 2020, the Lease was amended to surrender three of the office spaces previously entered into above, with a termination date of May 31, 2020 and in consideration of a termination fee to be paid. The lease payments and term for the remaining occupied space will remain the same. Due to these changes in lease terms for the three office spaces, in March 2020 the Company modified the operating lease liabilities and operating lease assets of these three office spaces to reflect the new terms. The Lease term ended on December 31, 2022 and was not renewed.

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

The tables below reflect the Company's lease position and weighted-average lease terms and discount rates for its operating leases as of December 31, 2023. Operating lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. In determining the present value of lease payments, the Company used its incremental borrowing rate based on the information available at the lease commencement date.

(in thousands)	Classification on the Balance Sheet	December 31, 2023
Assets		
Operating lease assets	Operating lease assets	$ 4,908
Total lease assets		$ 4,908
Liabilities		
Current		
Operating	Other current liabilities	$ 1,276
Non-current		
Operating	Operating lease liabilities	4,340
Total lease liabilities		$ 5,616

Lease Term and Discount Rate	December 31, 2023
Weighted-average remaining lease term (years)	
Operating leases	3.8
Weighted-average discount rate	
Operating leases	8.0 %

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

		Year Ended December 31,		
(in thousands)	Classification	2023	2022	2021
Operating lease costs[1]	Research and development	$ 630	$ 618	$ 799
	Selling, general and administrative	924	1,048	870
Total operating lease costs		$ 1,554	$ 1,666	$ 1,669

[1] Includes variable lease costs which are immaterial.

The table below reconciles the undiscounted cash flow for each of the first five years and total of the remaining years to the operating lease liabilities recorded on the balance sheet as of December 31, 2023 (in thousands):

	Operating leases
Years ending December 31,	
2024	$ 1,679
2025	1,725
2026	1,773
2027	1,357
Total future minimum lease payments	6,534
Less: present value adjustment	(918)
Total operating lease liabilities	$ 5,616

Cash payments included in the measurement of the Company's operating leases were $1.6 million, $1.7 million and $1.7 million for the twelve months ended December 31, 2023, 2022, and 2021, respectively.

On November 1, 2023, the Company entered into an agreement (“Sublease”) to sublease approximately 20,830 square feet of office space at 700 Park Offices Drive in Research Triangle Park, NC. Upon signing of the Sublease, the Company received a security deposit equal to one month's rent, which has been recorded within other non-current liabilities on the balance sheet as of December 31, 2023. The initial fixed rental rate is $24 per rentable square foot of the premises per annum and will increase at a rate of 2.75% per rentable square foot each year. The term of the sublease commences on January 1, 2024, with base rent first becoming due on April 1, 2024, and has an expiration date of August 31, 2027. No sublease income was recognized during the twelve months ended December 31, 2023, 2022, or 2021.

7. Loan Payable

On May 29, 2020, the Company entered into a loan and security agreement (the “Loan Agreement”) with Hercules Capital, Inc. (“Hercules”), under which Hercules agreed to lend the Company up to $100.0 million, to be made available in a series of tranches, subject to certain terms and conditions. The first tranche totals $30.0 million, of which the Company received $20.0 million at closing. Upon initiation of the Phase 3 trial of COSELA for metastatic colorectal cancer and receiving FDA approval for COSELA for small cell lung cancer (the "Performance Milestone”), the second tranche of $20.0 million became available to the Company for drawdown through December 15, 2021. The third tranche of $30.0 million was available through December 31, 2022. The fourth tranche of $20.0 million was available at Hercules’ approval through December 31, 2022. On March 31, 2021, the Company entered into the First Amendment to Loan and Security Agreement (the “First Amendment”) with Hercules whereby the Company drew the remaining $10.0 million of the first tranche and the interest rate and financial covenants were amended. Unless loan advances exceeded $40.0 million, no financial covenants were required.

Amounts initially borrowed under the original terms of the Loan Agreement bore an interest rate equal to the greater of either (i) (a) the prime rate as reported in The Wall Street Journal, plus (b) 6.40%, and (ii) 9.65%. Based on original terms of the Loan Agreement, the Company agreed to make interest only payments through June 1, 2022 and following the interest only period, the Company agreed to repay the principal balance and interest of the advances in equal monthly installments through June 1, 2024. Based on the original terms of the Loan Agreement, upon satisfaction of the Performance Milestone, the interest only period was extended through January 1, 2023 and the maturity date was extended to June 1, 2025. Upon entering into the First Amendment on March 31, 2021, the interest rate was amended to the greater of either (i) (a) the prime rate as reported in The Wall Street Journal, plus (b) 6.20%, and (ii) 9.45%.

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

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

On November 1, 2021, the Company entered into a Second Amendment to Loan and Security Agreement (the "Second Amendment") under which Hercules agreed to lend the Company up to $150.0 million, to be made available in a series of tranches, subject to certain terms and conditions. The first tranche was increased to $100.0 million. At close of the Second Amendment, the Company borrowed an additional $45.0 million from the first tranche. The Company had the right to request that Hercules make the remaining $25.0 million term loan advances under the first tranche to the Company by September 15, 2022, which the Company did not exercise. The second tranche of $20.0 million will become available to the Company upon achievement of $50.0 million trailing six-month net product revenue of COSELA no later than June 30, 2023 and will be available through December 15, 2023. The third tranche of $15.0 million will become available upon achievement of certain development performance milestones and available through December 15, 2023. The fourth tranche of $15.0 million will be available at Hercules' approval through June 30, 2024.

Amounts borrowed under the Second Amendment bore an interest rate equal to the greater of either (i) (a) the prime rate as reported in The Wall Street Journal, plus (b) 5.90%, and (ii) 9.15%. The Company will make interest only payments through December 1, 2024 and may be extended through December 1, 2025, in quarterly increments, subject to compliance with covenants of the Second Amendment. Following the interest only period, the Company will repay the principal balance and interest of the advances in equal monthly installments through November 1, 2026.

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

Upon prepayment or repayment of all or any of the advances under the Second Amendment, the Company will pay (in addition to the prepayment charge) an end of term charge of 6.75% of the aggregate amount funded. The Company will be required to make a final payment to Hercules in the amount of 6.75% of the amounts funded, less any amount previously paid. In addition, the Company will be required to make a payment to Hercules for $2.1 million on the earliest occurrence of (i) June 1, 2025, (ii) the date the Company repays the outstanding principal amount in full, or (iii) the date that the principal amount becomes due and payable in full.

The Second Amendment is secured by substantially all of the Company's assets, including intellectual property, subject to certain exemptions. The Company out-licensed lerociclib as permitted in the Loan Agreement.

The Second Amendment contains a minimum revenue covenant. Beginning August 15, 2022, with the reporting of the financial results for the second fiscal quarter ended June 30, 2022, and tested monthly, the Company must have achieved net product revenue of COSELA of at least 65% of the amounts projected in the Company's forecast. Testing of the minimum revenue covenant shall be waived at any time in which either (a) the Company's market capitalization exceeds $750.0 million and the Company maintains unrestricted cash equal to at least 50% of the total amounts funded, or (b) the Company maintains unrestricted cash equal to at least 100% of the total amounts funded.

The Company evaluated the Second Amendment under the guidance found in ASC 470-50 *Modification and* Extinguishment. The Company concluded that the previous debt under the Loan Agreement was extinguished based on the difference in present value of the cash flows of the Loan Agreement and the Second Amendment. Accordingly, the difference between the carrying value of the Loan Agreement as of November 1, 2021, including the unamortized debt issuance costs, and the fair value of the Second Amendment was recorded as a $0.2 million loss on extinguishment of debt for the twelve months ended December 31, 2021. Fees paid to third parties directly related to the funded portion of the Second Amendment have been capitalized as debt issuance costs and will be amortized to interest expense over the life of the Second Amendment using the effective interest method. Fees paid that were directly related to the unfunded portion is accounted for as a deferred financing charge and amortized to interest expense over the period the unfunded portions are available. The end of term charges associated with the Second Amendment are being accreted through interest expense using the effective interest method over the related term of the debt.

On June 24, 2022, the Company entered into a Third Amendment to Loan and Security Agreement (the "Third Amendment") with Hercules, which extended the time for drawing the remainder of the first tranche advance of up to $25.0 million from September 15, 2022 to December 31, 2022, which the Company did not exercise. The Third Amendment also added a minimum cash covenant whereby the Company must maintain unrestricted cash equal to at least 50% of the outstanding debt, and such percentage shall decrease upon the Company achieving specified net product revenue of COSELA. It further provided for a minimum revenue covenant that, beginning August 15, 2022 with the reporting of the financial results for the second fiscal quarter ended June 30, 2022, and tested monthly, the Company must have achieved net product revenue of COSELA of at least 80% of the amounts projected in the Company's forecast. Testing of the minimum revenue covenant shall be waived at any time in which either (a) the Company's market capitalization exceeds $750.0 million and the Company maintains unrestricted cash equal to at least 50% of the total amounts funded, or (b) the Company maintains unrestricted cash equal to at least 100% of the total amounts funded. The Company evaluated the Third Amendment under the guidance found in ASC 470-50 *Modification and Extinguishment.* The Company concluded that the Third Amendment was a modification and there was no impact to the financial statements.

On November 1, 2022, the Company entered into a Fourth Amendment to Loan and Security Agreement (the "Fourth Amendment") with Hercules, which extended the time for drawing the remainder of the first tranche advance of up to $25.0 million from December 31, 2022 to June 30, 2023. The Fourth Amendment continued to provide for a minimum revenue covenant, tested monthly, where the Company must achieve net product revenue of COSELA of at least 80% of the amounts projected in the Company's forecast. The Fourth Amendment also amended the minimum cash covenant such that if the outstanding debt is less than or equal to $75.0 million, the Company must maintain unrestricted cash equal to at least 65% of the outstanding debt in addition to meeting the required revenue covenant. In addition, if the outstanding debt is greater than $75.0 million, the Company must maintain unrestricted cash equal to at least 70% of the outstanding debt while meeting the revenue covenant. If the Company achieves the specified net revenue of COSELA, the cash percentage will decrease to 45% of the outstanding debt. Testing of the minimum revenue covenant shall be waived at any time in which either (a) the Company's market capitalization exceeds $750.0 million and the Company maintains unrestricted cash equal to at least 50% of the total amounts funded, or (b) the Company maintains unrestricted cash equal to at least 100% of the total amounts funded. The Fourth Amendment also re-set the prepayment premiums associated with any prepayment of the loans under the Loan Agreement. The Company evaluated the Fourth Amendment under the guidance found in ASC 470-50 *Modification and Extinguishment*. The Company concluded that the Fourth Amendment was a modification and there was no impact to the financial statements.

On June 6, 2023, the Company entered into a Fifth Amendment to Loan and Security Agreement (the "Fifth Amendment") with Hercules, under which Hercules agreed to lend the Company up to $75.0 million, subject to specified conditions. In conjunction with the closing of the Fifth Amendment, the Company repaid $25.0 million of the outstanding debt such that the total loan amount outstanding upon closing of the Fifth Amendment is $50.0 million. In addition to the $25.0 million principal prepayment, upon closing of the Fifth Amendment, the Company made a $1.7 million pro-rata payment of the end-of-term charge. The Company continues to be required to make a payment to Hercules for $2.1 million on the earliest occurrence of (i) June 1, 2025, (ii) the date the Company repays the outstanding principal amount in full, or (iii) the date that the principal amount becomes due and payable in full.

The Fifth Amendment eliminated advances under Tranches 2 and 3 and increased the advance available under Tranche 4 from $15.0 million to $25.0 million and extended the time for drawing the Tranche 4 Advance (as defined in the Loan and Security Agreement) from June 30, 2024 to December 15, 2024.

Amounts borrowed under the Fifth Amendment will bear an interest rate equal to the greater of either (i) (a) the prime rate as reported in The Wall Street Journal, plus (b) 5.65%, and (ii) 9.15%. The Company will make interest only payments through December 1, 2024 and may be extended through December 1, 2025, in quarterly increments, subject to conditional borrowing base compliance. Following the interest only period, the Company will repay the principal balance and interest of the advances in equal monthly installments through November 1, 2026.

The Company may prepay advances under the Fifth Amendment, in whole or in part, at any time subject to a prepayment charge equal to (a) 3.0% of the prepayment amount in the first year from the effective date of the Fourth Amendment; (b) 2.0% of the prepayment amount in the second year from the effective date of the Fourth Amendment; and (c) 1.0% of the prepayment amount in the third year from the effective date of the Fourth Amendment. For the avoidance of doubt, no prepayment charge shall be applicable when repayments are required to maintain compliance with the conditional borrowing base limit as discussed below.

The Fifth Amendment amended the minimum cash covenant such that the Company must maintain unrestricted cash equal to at least 35% of the outstanding debt at all times. The minimum cash covenant shall be eliminated upon the Company's achievement of quarterly net product revenue of $45.0 million or trailing six months net product revenue of $85.0 million.

The Fifth Amendment removed the existing minimum revenue covenant and provided for a conditional borrowing base limit, beginning with the financial reporting for the period ended June 30, 2023, and tested monthly thereafter. The Fifth Amendment also provides that the Company's debt outstanding shall not exceed certain thresholds of trailing three month net product revenue of COSELA.

The Company evaluated the Fifth Amendment under the guidance found in ASC 470-50 *Modification and Extinguishment*. The Company concluded that the Fifth Amendment was a modification; accordingly, no gain or loss was recorded. A new effective interest rate of 18.33% was established based on the carrying value of the debt and the revised cash flows. The remaining end of term charges are accreted through interest expense through the maturity date using the updated effective interest rate. The borrowing capacity of the new arrangement is less than the old arrangement. As such, the existing unamortized deferred financing costs of the new arrangement were written off in proportion to the decrease in the borrowing capacity of the unfunded portion of the arrangement. The remaining unamortized deferred financing costs are amortized to interest expense and deferred over the commitment term of the new arrangement.

The Loan Agreement contains events of default, including a material adverse change, which is subjectively defined, in the Company's business, payment defaults, and breaches of covenants following any applicable cure period. In the event of default by the Company under the Loan Agreement, the Company may be required to repay all amounts then outstanding under the Loan Agreement. The Company has determined that subjective acceleration under the material adverse events clause included in the Loan Agreement is not probable and, therefore, has classified the outstanding principal amount in long-term liabilities based on the timing of scheduled principal payments.

As of December 31, 2023, the outstanding debt of $50.0 million does not exceed the required threshold of trailing three month revenue for the period ended December 31, 2023. Additionally, as of December 31, 2023 the Company maintained unrestricted cash equal to more than 35% of the total outstanding debt and has not been notified of an event of default by the lender under the Loan Agreement.

As of December 31, 2023, the future principal payments due under the Loan Agreement, excluding interest, are as follows (in thousands):

	Amount
2024	$ 1,819
2025	23,469
2026	24,712
Total principal outstanding	50,000
End of term charge	2,011
Unamortized debt issuance costs	(454)
Total	$ 51,557

8. Stockholders' Equity

Common stock

The Company's common stock has a par value of 0.0001 per share and consists of 120,000,000 authorized shares as of December 31, 2023 and 2022. 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.

On July 2, 2021, the Company filed an automatic shelf registration statement on Form S-3ASR with the Securities and Exchange Commission (the "SEC"), which became effective upon filing, pursuant to which the Company registered for sale an unlimited amount of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that the Company may determine, so long as the Company continued to satisfy the requirements of a "well-known seasoned issuer" under SEC rules (the "2021 Form S-3"). The 2021 Form S-3 also included a prospectus covering up to an aggregate of $150.0 million in shares of common stock that the Company may issue and sell from time to time through Cowen and Company, LLC ("Cowen"), acting as its agent, pursuant to a sales agreement for "at the market offerings" the Company entered into with Cowen in July 2021 (the "2021 Sales Agreement"). The Company did not sell any shares of common stock under the 2021 Sales Agreement.

At the time of the filing of the Company's Annual Report on Form 10-K for the year ended December 31, 2021 filed with the SEC on February 23, 2022, the Company no longer qualified as a "well-known seasoned issuer" as such term is defined in Rule 405 under the Securities Act. As a result, in February 2022, the Company amended the 2021 Form S-3 to register for sale up to $300.0 million of any combination of its common stock, preferred stock, debt securities, warrants, rights and/or units from time to time and at prices and on terms that the Company may determine. The 2021 Form S-3, as amended, will remain in effect for up to three years from the date it originally became effective, which was July 2, 2021. The amended 2021 Form S-3 also includes a prospectus covering up to an aggregate of $100.0 million in common stock that the Company may issue and sell from time to time, through Cowen acting as its sales agent, pursuant to that certain sales agreement that the Company entered into with Cowen on February 23, 2022 (the "2022 Sales Agreement"). In connection with the Company entering into the 2022 Sales Agreement with Cowen, the Company terminated the 2021 Sales Agreement. As of the date hereof, the Company has not sold any shares of common stock or other securities under the 2022 Sales Agreement for "at the market offerings."

On November 17, 2022, the Company entered into an underwriting agreement related to a public offering of 7,700,000 shares of common stock at a public offering price of $6.50 per share less the underwriting discounts and commissions, pursuant to the shelf registration statement on Form S-3. The Company received approximately $50.1 million in gross proceeds from this offering, before deducting underwriting discounts and commissions and offering expenses. The offering closed on November 22, 2022. In addition, 873,353 shares of common stock were issued upon exercise by the underwriters of their option to purchase additional shares at the same offering price, which closed on December 20, 2022. The gross proceeds from the offering of the aggregate of 8,573,353 shares of the Company's common stock were $55.7 million and net proceeds of $52.0 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

Preferred stock

The Company is authorized to issue 5,000,000 shares of undesignated preferred stock in one or more series. As of December 31, 2023, no shares of preferred stock were issued or outstanding.

Shares Reserved for Future Issuance

The Company has reserved authorized shares of common stock for future issuance as follows:

	December 31, 2023	December 31, 2022
Common stock options outstanding	6,774,186	7,372,028
RSUs outstanding [(1)]	1,613,215	675,406
PSUs outstanding [(1)]	218,450	—
DSUs outstanding [(1)]	50,000	—
Options, RSUs, PSUs and DSUs available for grant under Equity Incentive Plans [(1)]	2,385,034	2,323,539
	11,040,885	10,370,973

[(1)] RSUs, PSUs, and DSUs are further defined in Note 9.

9. Stock-Based Compensation

2011 Equity Incentive Plan

In March 2011, the Company adopted the 2011 Equity Incentive Plan (the "2011 Plan"). The 2011 Plan provided for the direct award or sale of the Company's common stock and for the grant of stock options to employees, directors, officers, consultants and advisors of the Company. The 2011 Plan was subsequently amended in August 2012, October 2013, February 2015, December 2015, April 2016 and November 2016 to allow for the issuance of additional shares of common stock. 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, 2023, and in accordance with the "evergreen" provision of the 2017 Plan, an additional 1,096,553 shares were made available for issuance.

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

In January 2021, the Company began granting RSUs under the 2017 Plan. RSUs are granted at the fair market value of a share of common stock on the date of grant.

In January 2023, the Company began granting PSUs, which are subject to non-market performance and service conditions, to Company executives under the 2017 Plan. PSUs are granted at the fair market value of a share of common stock on the date of grant.

In May 2023, the Company adopted the G1 Therapeutics, Inc. Deferred Compensation Plan for Non-Employee Directors to enable non-employee directors of the Company (each a "Non-Employee Director") to elect to defer annually the receipt of shares that vest in accordance with the terms of RSUs granted under the 2017 Plan (the "Vested RSUs") for service as a Non-Employee Director (the "Deferred Compensation Plan"). The Deferred Compensation Plan is intended to comply with the requirements of Section 409A of the Internal Revenue Code of 1986, as amended. Under the Deferred Compensation Plan, the Non-Employee Directors shall be entitled to file with the Compensation Committee of the Board prior to December 31 of each Plan Year (as defined therein) an election form so as to make an election under the Deferred Compensation Plan effective for the following Plan Year, pursuant to which a Non-Employee Director may elect to defer receipt of shares underlying Vested RSUs with respect to RSUs granted in the following Plan Year. The Deferred Compensation Plan is unfunded and unsecured.

As of December 31, 2023, there were a total of 1,473,163 shares of common stock available for future issuance under the 2017 Plan.

Amended and Restated 2021 Inducement Equity Incentive Plan

In February 2021, the Company adopted the 2021 Inducement Equity Incentive Plan (the "2021 Inducement Plan"). The 2021 Inducement Plan provides for the grant of up to 500,000 non-qualified options, stock grants, and stock-based awards to employees and directors of the Company. The 2021 Inducement Plan does not include an evergreen provision.

In September 2021, the Company adopted the 2021 Sales Force Inducement Equity Incentive Plan (the "2021 Sales Force Inducement Plan"). The 2021 Sales Force Inducement Plan provides for the grant of up to 500,000 non-qualified options, stock grants, and stock-based awards to sales force individuals and support staff that were not previously employees or directors of the Company. The 2021 Sales Force Inducement Plan does not include an evergreen provision.

In March 2022, the Company merged the 2021 Sales Force Inducement Plan into the 2021 Inducement Plan and amended and restated the 2021 Inducement Plan to create the Amended and Restated 2021 Inducement Equity Incentive Plan (the "Amended and Restated 2021 Plan"). In addition, the number of shares reserved for issuance under the Amended and Restated 2021 Plan was increased by 750,000 shares of the Company's common stock, for an aggregate of 1,750,000 shares of the Company's common stock authorized to issue under the Amended and Restated 2021 Plan. The Amended and Restated 2021 Plan does not include an evergreen provision.

As of December 31, 2023, there was a total of 911,870 shares of common stock available for future issuance under the Amended and Restated 2021 Plan.

Stock-based Compensation

The Company recognizes compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant. 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. Share-based awards granted to non-employee directors as compensation for serving on the Company's Board of Directors are accounted for in the same manner as employee share-based compensation awards.

The Company calculates 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 the Company's common stock, the assumed dividend yield, the expected term of the Company's stock options and the fair value of the underlying common stock on the date of grant.

The Company also incurs stock-based compensation expense related to RSUs, PSUs, and DSUs. The fair value of RSUs, PSUs, and DSUs is determined by the closing market price of the Company's common stock on the date of grant and then recognized over the requisite service period of the award. As the PSUs have non-market performance and service conditions, compensation expense will be recognized over the requisite service periods if and when the achievement of such performance condition(s) is determined to be probable by the Company. If a performance condition is not determined to be probable or is not met, no stock-based compensation expense is recognized. The Company reassesses the probability of achieving the performance condition(s) at each reporting period. As of December 31, 2023, the Company did not deem the achievement of any performance condition(s) to be probable and no compensation expense related to PSUs was recognized.

The table below summarizes the stock-based compensation expense recognized in the Company's statement of operations by classification (in thousands):

	Year Ended December 31,		
	2023	2022	2021
Cost of goods sold	$ 243	$ 207	$ 252
Research and development	2,177	3,956	$ 4,811
Selling, general and administrative	12,090	16,426	$ 17,256
Total stock-based compensation expense	$ 14,510	$ 20,589	$ 22,319

Stock options – Black-Scholes inputs

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,		
	2023	2022	2021
Expected volatility	81.4% - 88.4%	76.7% - 81.4%	76.8% - 79.6%
Weighted-average risk free rate	3.4% - 4.2%	1.4% - 4.2%	0.4% - 1.3%
Dividend yield	—%	—%	—%
Expected term (in years)	6.00	6.00	6.00
Weighted-average grant-date fair value per share	$3.47	$6.50	$11.93

The expected term of stock options granted was determined using the simplified method under SAB 107 which represents the mid-point between the vesting term and the contractual term.

The expected stock price volatility assumptions for the Company's stock options were determined by examining the historical volatilities for industry peers as the Company does not have sufficient history to estimate volatility using only its common stock. In 2019, the Company began incorporating its historical stock price in conjunction with selected similar publicly traded companies. The Company continued to use the guideline peer group volatility information until April 2023, when the historical volatility of its common stock became sufficient to measure expected volatility for future option grants.

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

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

Stock Option Activity

The following table is a summary of stock option activity for the twelve months ended December 31, 2023:

			Weighted average	
	Options outstanding	Weighted average exercise price	Remaining contractual for life (Years)	Aggregate intrinsic value
				(in thousands)
Balance as of December 31, 2022	7,372,028	$ 16.15	6.9	$ 3,281
Granted	1,369,330	4.79		
Cancelled	(1,801,992)	18.56		
Exercised	(165,180)	0.34		
Balance as of December 31, 2023	6,774,186	$ 13.60	6.4	$ 944
Exercisable at December 31, 2023	4,813,088	$ 15.80	5.5	$ 859
Vested at December 31, 2023 and expected to vest	6,774,186	$ 13.60	6.4	$ 944

As of December 31, 2023, unrecognized compensation expense related to unvested stock options totaled $9.7 million, which is expected to be recognized over a weighted-average period of approximately 1.9 years.

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.

Restricted Stock Units

The Company's restricted stock units ("RSUs") are considered nonvested share awards and require no payment from the employee. For each RSU, employees receive one common share at the end of the vesting period. Compensation cost is recorded based on the market price of the Company's common stock on the grant date and is recognized on a straight-line basis over the requisite service period.

The following table is a summary of the RSU activity for the twelve months ended December 31, 2023:

	Number of RSUs	Weighted – Average Fair Value per Share
Balance as of December 31, 2022	675,406	$ 12.31
Granted	1,617,050	3.76
Cancelled	(417,780)	6.41
Vested	(261,461)	12.38
Balance as of December 31, 2023	1,613,215	$ 5.25

As of December 31, 2023, there was $5.4 million of total unrecognized compensation cost related to the Company's RSUs that are expected to vest. These costs are expected to be recognized over a weighted-average period of approximately 2.2 years.

Performance Based Restricted Stock Units

The Company's performance based restricted stock units ("PSUs") are considered nonvested share awards and require no payment from the employee. For each PSU, employees receive one common share at the end of the vesting period, subject to non-market performance and service conditions. Compensation cost is recorded based on the market price of the Company's common stock on the grant date and is recognized over the requisite service if and when the achievement of such performance condition(s) is determined to be probable by the Company. The Company reassesses the probability of achieving the performance condition(s) at each reporting period. As of December 31, 2023, the Company did not deem the achievement of any performance condition(s) to be probable and compensation expense related to PSUs was not recognized.

The following table is a summary of the PSU activity for the twelve months ended December 31, 2023:

	Number of PSUs	Weighted – Average Fair Value per Share
Balance as of December 31, 2022	—	$ —
Granted	218,450	5.73
Cancelled	—	—
Vested	—	—
Balance as of December 31, 2023	218,450	$ 5.73

As of December 31, 2023, there was $1.3 million of total unrecognized compensation cost related to the Company's PSUs that are expected to vest. These costs are expected to be recognized over a weighted-average period of approximately 2.0 years.

Deferred Share Units

The Company's DSUs are considered nonvested share awards and require no payment from the holders. For each DSU, holders receive one common share on a future date, generally upon “Separation from Service” (within the meaning of Section 409A of the Code) as a Non-Employee Director of the Company for any reason. Upon settlement, holders will receive one fully paid and non-assessable common share in respect of each vested DSU. Compensation cost is recorded based on the market price of the Company’s common stock on the grant date and is recognized on a straight-line basis over the requisite service period.

The following table is a summary of the DSU activity for the twelve months ended December 31, 2023:

	Number of DSUs	Weighted – Average Fair Value per Share
Balance as of December 31, 2022	—	$ —
Granted	50,000	2.83
Cancelled	—	—
Vested	—	—
Balance as of December 31, 2023	50,000	$ 2.83

As of December 31, 2023, there was $0.1 million of total unrecognized compensation cost related to the Company's DSUs that are expected to vest. These costs are expected to be recognized over a weighted-average period of approximately 0.5 years.

10. License Revenue

Incyclix License Agreement

On May 22, 2020, the Company entered into an exclusive license agreement with Incyclix Bio, LLC (“Incyclix”), formerly ARC Therapeutics, LLC, a company primarily owned by a former board member, whereby the Company granted to Incyclix an exclusive, worldwide, royalty-bearing license, with the right to sublicense, solely to make, have made, use, sell, offer for sale, import, export, and commercialize products related to its cyclin dependent kinase 2 (“CDK2”) inhibitor compounds. At close, the Company received consideration in the form of an upfront payment of $1.0 million and an equity interest in Incyclix equal to 10% of its issued and outstanding units valued at $1.1 million. In addition, the Company may receive a future development milestone payment totaling $2.0 million and royalty payments in the mid-single digits based on net sales of the licensed compound after commercialization. The Company has right of first negotiation to re-acquire these assets. In the first quarter of 2022, Incyclix announced a new round of financing which the Company did not participate. Following the financing, the Company's equity interest is now approximately 6.5%.

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

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

There was no revenue recognized during the twelve months ended December 31, 2023.

Genor License Agreement

On June 15, 2020, the Company entered into an exclusive license agreement with Genor Biopharma Co. Inc. ("Genor") for the development and commercialization of lerociclib in Australia, Bangladesh, China, Hong Kong, India, Indonesia, Macau, Malaysia, Myanmar, New Zealand, Pakistan, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, and Vietnam (the "Genor Territory"). Under the license agreement, the Company granted to Genor an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to develop, obtain, hold and maintain regulatory approvals for, and commercialize lerociclib, in the Genor Territory.

Under the license agreement, Genor agreed to pay the Company a non-refundable, upfront cash payment of $6.0 million with the potential to pay an additional $40.0 million upon reaching certain development and commercial milestones. In addition, Genor will pay the Company tiered royalties ranging from high single to low double-digits based on annual net sales of lerociclib in the Genor Territory. In September 2020, the Company transferred to Genor the related technology and know-how that is necessary to develop, seek regulatory approval for, and commercialize lerociclib in the Genor Territory, which resulted in the recognition of $6.0 million in revenue in accordance with ASC 606. Since then, through December 31, 2022, the Company had recognized an additional $3.0 million in revenue for the achievement of development and commercial milestones as defined by the license agreement.

There was no milestone revenue recognized during the twelve months ended December 31, 2023.

EQRx License Agreement

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

Under the license agreement, EQRx agreed to pay the Company a non-refundable, upfront cash payment of $20.0 million with the potential to pay an additional $290.0 million upon reaching certain development and commercial milestones. In addition, EQRx would pay the Company tiered royalties ranging from mid-single digits to mid-teens based on annual net sales of lerociclib in the EQRx Territory. In September 2020, the Company transferred to EQRx the related technology and know-how that was necessary to develop, seek regulatory approval for, and commercialize lerociclib in the EQRx Territory which resulted in the recognition of $20.0 million in revenue in accordance with ASC 606. EQRx was responsible for the development of the product in the EQRx Territory. The Company agreed to continue until completion, as the clinical trial sponsor, its two primary clinical trials and EQRx agreed to reimburse the Company for all related out-of-pocket costs incurred after the effective date of the license agreement.

On August 1, 2023, the Company received from EQRx formal notice of termination of the lerociclib license agreement in connection with the acquisition of EQRx by Revolution Medicines, Inc. The notice stated the intention to revert the lerociclib product rights back to the Company. Under the terms of the license agreement, EQRx is responsible for winding down its development activities. On September 13, 2023, the parties entered into a letter agreement whereby EQRx would pay the Company $1.6 million to reimburse anticipated wind down costs; the payment was received during the third quarter of 2023. No milestones were previously achieved through the date of termination of the lerociclib license agreement, and as a result of the termination, the Company will not receive any further milestone payments or future royalties from EQRx.

During the twelve months ended December 31, 2023, the Company recognized revenue of $1.7 million for the reimbursement of patent and clinical trial costs, including $1.4 million of the $1.6 million payment received during the third quarter of 2023 following notice from EQRx of termination of the license agreement. As of December 31, 2023, the remaining $0.2 million is held as short-term deferred revenue on the balance sheet and will be recognized as revenue as clinical trial costs associated with the wind down are incurred.

Simcere License Agreement

On August 3, 2020, the Company entered into an exclusive license agreement with Simcere for the development and commercialization of trilaciclib in all indications in Greater China (mainland China, Hong Kong, Macau, and Taiwan) (the "Simcere Territory"). Under the license agreement, the Company granted to Simcere an exclusive, royalty-bearing, non-transferable license, with the right to grant sublicenses, to develop, obtain, hold and maintain regulatory approvals for, and commercialize trilaciclib in the Simcere Territory. Since entering into the license agreement, the Company had received an upfront payment of $14.0 million and an additional $22.0 million for the achievement of development milestones through December 31, 2022.

On April 28, 2023, the Company amended the license agreement with Simcere, whereby the Company received a one-time, non-refundable payment of $30.0 million in exchange for the relief of future royalty payments from the sale of COSELA in Greater China. In addition, the milestone payments under the license agreement were adjusted such that the Company will be eligible to receive a $5.0 million payment upon Simcere's filing an NDA of TNBC in mainland China and a $13.0 million payment upon Simcere receiving regulatory approval of TNBC in mainland China. Under the amended license agreement, Simcere is not responsible for any sales milestone payments or any royalties accrued after April 28, 2023. Following the amendment, the Company continues to own all the global development and commercial rights to trilaciclib, excluding Greater China.

During the twelve months ended December 31, 2023, the Company recognized $30.0 million in revenue from the one-time payment for the relief of future royalty payments, $2.9 million in supply and manufacturing services, $0.6 million in royalty revenue, and $0.7 million in patent and clinical trial reimbursable costs.

11. Net Loss per Common Share

Basic net loss per common share is computed using the weighted average number of common shares outstanding during the period including nominal issuances of common stock warrants. Diluted net loss per common share is computed using the sum of the weighted average number of common shares outstanding during the period and, if dilutive, the weighted average number of potential shares of common stock, including the assumed exercise of stock options, stock warrants and unvested restricted common stock. For the twelve months ended December 31, 2023, 2022 and 2021, 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,		
	2023	2022	2021
Stock options issued and outstanding	7,507,583	7,692,064	7,056,745
Unvested RSUs	1,458,341	636,978	451,138
Unvested PSUs	216,655	—	—
Unvested DSUs	27,260	—	—
Total potential dilutive shares	9,209,839	8,329,042	7,507,883

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

12. Income Taxes

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

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

	Year Ended December 31,		
	2023	2022	2021
Current Expense:			
Federal	$ —	$ —	$ —
State	—	—	—
Foreign	3,115	1,700	925
	3,115	**1,700**	**925**
Deferred Expense:			
Federal	—	—	—
State	—	—	—
Foreign	—	—	—
	$ 3,115	**$ 1,700**	**$ 925**

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,		
	2023	2022	2021
Federal income tax benefit at statutory rate:	$ (9,419)	$ (30,631)	$ (30,960)
Increase (reduction) in income tax resulting from:			
State Income Taxes	(706)	(5,372)	(1,923)
Increase in Valuation Allowance	9,868	36,472	27,618
Stock Compensation	3,873	2,879	108
Research and Development Credit	(2,835)	(3,521)	(3,030)
NC Tax Rate Change	—	—	8,359
Foreign Withholding Tax	3,115	1,700	925
Foreign Tax Deduction	(654)	—	—
Other	(127)	173	(172)
	$ 3,115	$ 1,700	$ 925

On November 18, 2021, North Carolina enacted the 2021 Appropriations Act, which included a gradual corporate income tax rate decrease from the current 2.5% to 0% by 2030. The Company is in a cumulative loss position and does not have significant deferred tax liabilities that can be utilized as a source of taxable income in the future. Therefore, the Company has reduced its North Carolina deferred tax assets, including the NOLs, to zero, as no benefit is expected to be realized from these deferred tax assets prior to 2030 when there would be no income tax in North Carolina. The reduction in the value of the deferred tax assets resulted in $8.4 million of tax expense in the year ended December 31, 2021, which was offset fully by the reduction in the corresponding valuation allowance. To the extent the Company becomes profitable prior to 2030, the Company will recognize an income tax benefit related to the portion of its North Carolina deferred tax assets utilized.

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, 2023 and 2022 (in thousands):

	Year Ended December 31,	
	2023	2022
Deferred tax assets		
Accrued expenses	$ 2,966	$ 4,127
Operating lease liabilities	1,337	1,596
Stock compensation	9,223	10,518
R&D credits	23,351	20,516
Net operating loss carryforwards	120,626	117,896
Nondeductible Interest	3,691	2,178
Research and experimentation costs	21,546	17,945
Other	2,160	571
Deferred tax assets	184,900	175,347
Deferred tax liabilities		
Operating lease assets	(1,160)	(1,410)
Other	—	(65)
Deferred tax liabilities	(1,160)	(1,475)
Valuation allowance	(183,740)	(173,872)
Net deferred tax assets	$ —	$ —

At December 31, 2023 and December 31, 2022, 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 increased $9.9 million from $173.9 million at December 31, 2022 to $183.7 million at December 31, 2023. The increase in valuation allowance was due primarily to the increase in net operating loss carryforwards, capitalized research and experimentation costs, and income tax credits.

The table below summarizes changes in the deferred tax valuation allowance (in thousands):

	2023	2022	2021
Balance at beginning of year	$ 173,872	$ 137,400	$ 109,782
Charges to costs and expenses	9,868	36,472	35,961
Write-offs[1]	—	—	(8,343)
Balance at end of year	$ 183,740	$ 173,872	$ 137,400

1. Includes impact of NC enacted tax rate change

At December 31, 2023, the Company has federal net operating loss carryforwards ("NOLs") of approximately $550.7 million, which are available to offset future taxable income. Of the $550.7 million available, $93.5 million will begin to expire in 2029. The remaining $457.2 million has an indefinite carryforward period. Under the Tax Cuts and Jobs Act ("Tax Act"), federal NOLs arising after December 31, 2017 may be carried forward indefinitely. However, for NOLs arising after December 31, 2017, NOL carryforwards will be limited to 80% of taxable income. The Company's NOLs generated in 2017 and in prior years will not be subject to the 80% limitation under the Tax Act. In addition, the Company has state net operating loss carryforwards totaling approximately $401.2 million, which are available to offset future state taxable income. The state net operating loss carryforwards are inclusive of North Carolina net operating losses, which are recorded at zero benefit, as discussed in this footnote. 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, 2023, the Company also had federal research and development (R&D) credit carryforwards of approximately $23.4 million available to offset future income tax which begin to expire in 2035.

In accordance with FASB ASC 740, *Accounting for Income Taxes*, the Company reflects in the financial statements the benefit of positions taken in a previously filed tax return or expected to be taken in a future tax return only when it is considered 'more-likely-than-not' that the position taken will be sustained by a taxing authority. As of December 31, 2023 and 2022, 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, 2023 and 2022, the Company had no such accruals.

Section 382 Limitation

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

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

13. Related Party Transactions

On September 19, 2023, Mark A. Velleca, M.D., Ph.D., notified the Company of his decision to resign from the Company's Board of Directors, effective as of September 30, 2023. Dr. Velleca was a member of the Board since May 2014. Dr. Velleca's decision to resign was not due to any disagreement with the Company on any matter relating to the Company's operations, policies or practices.

Dr. Velleca will continue to serve as a senior advisor to the Company pursuant to the terms of a Senior Advisor Agreement dated September 29, 2020 (the "Agreement"), as amended by that certain First Amendment to Senior Advisor Agreement, dated as of September 20, 2023 (the "Amendment"). Pursuant to the terms of the Agreement, Dr. Velleca was paid in equal quarterly installments, for his services, of which one final installment of $50,000 has not been paid as of December 31, 2023.

Pursuant to the Amendment, the term of the Agreement has been extended from December 31, 2023 to December 31, 2024. Dr. Velleca will not receive any cash or equity compensation for his services during the period from January 1, 2024 through December 31, 2024 (the "Extended Term"). However, any stock options held by Dr. Velleca will continue to vest in accordance with their terms during the Extended Term.