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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, 2022

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 001-35403

Verastem, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**27-3269467**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
117 Kendrick Street, Suite 500 Needham, Massachusetts	**02494**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(781) 292-4200**

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value	VSTM	Nasdaq Global Market

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 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). ☒ 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 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 issues 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

Aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2022 was $215,932,064.

The number of shares outstanding of the registrant's common stock as of March 13, 2023 was 200,677,979.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A relating to the Registrant's Annual General Meeting of Shareholders, to be held on May 15, 2023 will be incorporated by reference in this Form 10-K in response to Items 10, 11, 12, 13 and 14 of Part III. The definitive proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2022.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements related to present facts or current conditions or historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. Such statements relate to, among other things, the development and activity of our programs and product candidates, avutometinib (VS-6766) (rapidly accelerated fibrosarcoma ("RAF")/ mitogen-activated protein kinase kinase ("MEK") program) and defactinib (focal adhesion kinase ("FAK") program), the structure of our planned and pending clinical trials, and the timeline and indications for clinical development, regulatory submissions and commercialization of activities. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are not guarantees of future performance and our actual results could differ materially from the results discussed in the forward-looking statements we make. Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the uncertainties inherent in research and development of avutometinib and defactinib, such as negative or unexpected results of clinical trials; whether and when any applications for avutometinib and defactinib may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such other applications that may be filed for avutometinib and defactinib, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted and, if approved, whether avutometinib or defactinib will be commercially successful in such jurisdictions; our ability to obtain, maintain and enforce patent and other intellectual property protection for avutometinib and defactinib; the scope, timing, and outcome of any legal proceedings; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of avutometinib and defactinib; whether preclinical testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that avutometinib or defactinib will cause unexpected safety events, experience manufacturing or supply interruptions or failures, or result in unmanageable safety profiles as compared to their levels of efficacy; that any of our third party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for avutometinib or defactinib; that we will be unable to in-license additional compounds or successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned; that we may not have sufficient cash to fund our contemplated operations; that we may not attract and retain high quality personnel, that we or Chugai Pharmaceutical, Co. Ltd., will fail to fully perform under the license agreement; that our target market for our product candidates might be smaller than we are presently estimating; that we or Secura Bio, Inc. will fail to fully perform under the asset purchase agreement; that we may be unable to make additional draws under our debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates, that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients; and that the duration and impact of COVID-19 may affect, precipitate or exacerbate one or more of the foregoing risks and uncertainties. Other risks and uncertainties include those identified under the heading "Risk Factors" in this Annual Report on Form 10-K for the year ended December 31, 2022, and in any subsequent filings with the Securities and Exchange Commission ("SEC").

As a result of these and other factors, we may not achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. The forward-looking statements contained in this Annual Report on Form 10-K reflect our views as of the date hereof. We do not assume and specifically disclaim any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I

Item 1. Business

OVERVIEW

We are a late-stage development biopharmaceutical company, with an ongoing registration directed trial, committed to advancing new medicines for patients battling cancer. Our pipeline is focused on novel anticancer agents that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, particularly RAF/MEK inhibition and FAK inhibition.

Our most advanced product candidates, avutometinib (VS-6766) and defactinib, are being investigated in both preclinical and clinical studies for the treatment of various solid tumors, including, but not limited to low-grade serous ovarian cancer ("LGSOC"), non-small cell lung cancer ("NSCLC"), colorectal cancer ("CRC"), pancreatic cancer, and melanoma. We believe that avutometinib may be beneficial as a therapeutic, as a single agent or when used together in combination with defactinib, other agents, other pathway inhibitors, or other current and emerging standard of care treatments in cancers that do not adequately respond to currently available therapies.

Avutometinib is an orally available first-in-class unique small molecule RAF/MEK clamp. In contrast to other MEK inhibitors that are commercially available and in development, avutometinib is a dual RAF/MEK clamp that blocks MEK kinase activity and induces the formation of dominant negative RAF-MEK complexes preventing phosphorylation of MEK by A-Raf proto-oncogene, serine/threonine kinase ("ARAF"), B-Raf proto-oncogene serine/threonine kinase ("BRAF") and C-raf proto-oncogene serine/threonine kinase ("CRAF"). MEK-only inhibitors (e.g. trametinib) may have limited efficacy because they induce MEK phosphorylation ("pMEK") by relieving extracellular-signal-regulated-kinase ("ERK")-dependent feedback inhibition of RAF. By inhibiting RAF-mediated phosphorylation of MEK, avutometinib has the advantage of not inducing pMEK. This unique mechanism of avutometinib enables it to inhibit ERK signaling more effectively and may confer enhanced therapeutic activity against mitogen-activated pathway kinase ("MAPK") pathway-driven cancers.

Avutometinib has been shown to inhibit signaling and proliferation of tumor cell lines with a variety of MAPK pathway alterations including Kirsten rat sarcoma viral oncogene homolog ("KRAS"), neuroblastoma rat sarcoma viral oncogene homolog ("NRAS"), and BRAF mutations, among others. Avutometinib has demonstrated strong antitumor activity in combination with (i) agents targeting parallel pathways (e.g. inhibitors of FAK, CDK4/6 and mTOR), (ii) agents targeting other nodes in the MAPK pathway (e.g. anti-EGFR, SOS1, KRAS G12C, and KRAS G12D inhibitors), (iii) chemotherapy, and (iv) anti-PD-1.

Defactinib is an oral small molecule inhibitor of FAK and proline-rich tyrosine kinase ("PYK2") that is currently being evaluated as a potential combination therapy for various solid tumors. FAK is a non-receptor tyrosine kinase encoded by the protein tyrosine kinase-2 ("PTK-2") gene that is involved in cellular adhesion and, in cancer, metastatic capability. Defactinib targets malignant cells both directly and through modulation of the tumor microenvironment. Defactinib has received orphan drug designation in ovarian cancer in the United States, the European Union, and Australia. Preclinical research by our scientists and collaborators at world-renowned research institutions has described the effect of FAK inhibition as enhancing immune response by decreasing immuno-suppressive cells, increasing cytotoxic T cells and reducing stromal density, which allows tumor-killing immune cells to enter the tumor. Furthermore, it has been shown that FAK activation in response to MAPK inhibitor therapy may bypass MAPK pathway blockade by driving tumor growth through activation of downstream pathways such as RhoA and YAP, supporting the clinical evaluation of avutometinib in combination with defactinib for treatment of cancers harboring MAPK alterations.

The combination of avutometinib and defactinib has been found to be clinically active in some patients with KRAS mutant and KRAS wild-type LGSOC and has received breakthrough designation from the U.S. Food & Drug Administration (the "FDA") for the treatment of all patients with recurrent LGSOC, regardless of KRAS status, after one or more prior lines of therapy including platinum-based chemotherapy.

In the fourth quarter of 2020, we commenced two registration-directed trials investigating avutometinib as a monotherapy and in combination with defactinib. The registration-directed trials are entitled RAMP 201 and RAMP 202. RAMP 201 is an adaptive two-part multicenter, parallel cohort, randomized, open label trial to evaluate the efficacy and safety of avutometinib alone and in combination with defactinib in patients with recurrent LGSOC. RAMP 202 is a Phase 2, adaptive two-part multicenter, parallel cohort, randomized, open-label trial to evaluate the efficacy and safety of avutometinib alone and in combination with defactinib in patients with KRAS G12V NSCLC, following treatment with a platinum-based regimen and immune checkpoint inhibitor. Additionally, and based on preclinical rationale, we added additional cohorts to the RAMP 202 study including KRAS non-G12V NSCLC and BRAF mutant (V600E and non-V600E) NSCLC. Both studies are discussed in greater detail below.

In January 2023, we reported data from a planned interim analysis of Part A of the ongoing RAMP 201 trial among patients with LGSOC treated with avutometinib alone and in combination with defactinib. Part A included randomized eligible patients to receive treatment of avutometinib monotherapy (n=33) or the combination of avutometinib and defactinib (n=31). The combination of avutometinib and defactinib has been declared the go-forward treatment regimen based on a higher rate of confirmed objective responses in a planned interim analysis with prespecified criteria.

Of the 29 patients evaluable for response by blinded independent central review ("BICR") in the combination arm, the initial results showed a confirmed objective response rate ("ORR") of 28% in all patients and 27% vs 29% in KRAS mutant (n=15) and KRAS wild-type (n=14) LGSOC, respectively. Three additional patients with KRAS mutant LGSOC showed an unconfirmed partial response. In addition, the vast majority of patients showed tumor regression, as the overall disease control rate (stable disease plus partial response) was 93%. Most evaluable patients (62%) were still on study treatment on the combination arm at the time of the data cut with a minimum follow-up of five months.

The confirmed ORR for the monotherapy arm by BICR was 7% in evaluable patients (n=30). The overall disease control rate for the monotherapy arm by BICR was 90%. Across both the combination and monotherapy arms, there have been no additional safety signals reported with a continued favorable safety and tolerability profile, with 9% discontinuation due to adverse events in the combination arm.

We will continue future enrollment of RAMP 201 in the combination arm only in all patients with recurrent LGSOC, regardless of their KRAS status. Target enrollment for the combination arm has been achieved. We are planning a RAMP 201 presentation at a scientific medical conference in 2023.

In the fourth quarter of 2022, a type B meeting with the FDA was held to discuss the results to date of the ongoing RAMP 201 trial, confirm the go-forward treatment regimen selection and discuss the regulatory path forward. The combination of avutometinib with defactinib has been selected versus monotherapy as the go-forward treatment in all recurrent LGSOC regardless of KRAS status, acknowledging the demonstrated contribution of defactinib.

We intend to include mature data from the RAMP 201 study and the FRAME study to potentially support filing for accelerated approval in patients with recurrent LGSOC. Both studies are evaluating avutometinib and defactinib in patients with recurrent LGSOC. We are in ongoing discussions with the FDA on the confirmatory study and plan to provide an update after agreement with the FDA. Continued enrollment in the combination arm of RAMP 201 is planned to expand the clinical experience in anticipation of initiation of a confirmatory study.

In October 2022, we reported data from a planned interim analysis of Part A from the RAMP 202 trial among patients with KRAS G12V NSCLC treated with avutometinib or the combination of avutometinib and defactinib. The results did not meet the pre-defined criteria to continue to the trial expansion phase. Among patients with KRAS non-G12V NSCLC, no KRAS subtype was identified for further clinical evaluation of avutometinib with defactinib in this trial.

In September 2021, we entered into a clinical collaboration agreement with Amgen, Inc. ("Amgen") to evaluate the combination of avutometinib with Amgen's KRAS G12C inhibitor LUMAKRAS® (sotorasib) in a Phase 1/2 trial entitled RAMP 203. The Phase 1/2 trial will evaluate the safety, tolerability and efficacy of avutometinib in combination with LUMAKRAS in patients with KRAS G12C NSCLC who have not been

previously treated with a KRAS G12C inhibitor, as well as in patients who have progressed on a KRAS-G12C inhibitor. The study will investigate the potential benefits of a more complete vertical blockade of the MAPK pathway with the combination of avutometinib (RAF/MEK inhibition) with LUMAKRAS (KRAS G12C inhibition) in KRAS G12C locally advanced or metastatic NSCLC. The RAMP 203 trial has advanced to cohort 2 of 4 mg avutometinib in combination with 960 mg of LUMAKRAS.

In November 2021, we entered into a clinical collaboration agreement with Mirati Therapeutics, Inc. ("Mirati") to evaluate the combination of avutometinib with Mirati's KRAS G12C inhibitor KRAZATI® (adagrasib) in a Phase 1/2 trial entitled RAMP 204. The Phase 1/2 trial will evaluate the safety, tolerability and efficacy of avutometinib in combination with KRAZATI in patients with KRAS G12C NSCLC who have progressed on a KRAS G12C inhibitor. The trial will build on preclinical data showing a deeper blockade of MAPK pathway signaling resulting in enhanced anti-tumor efficacy with the combination of KRAZATI (KRAS G12C inhibition) and avutometinib (RAF/MEK inhibition) relative to either agent alone. The RAMP 204 trial is open and enrolling.

In May 2022, we received the first "Therapeutic Accelerator Award" from the Pancreatic Cancer Network ("PanCAN") for up to $3.8 million. The grant is expected to support a Phase 1b/2 clinical trial of avutometinib in combination with defactinib entitled RAMP 205. This Phase 1b/2 trial will evaluate the safety, tolerability and efficacy of GEMZAR® (gemcitabine) and ABRAXANE® (Nab-paclitaxel) in combination with avutometinib and defactinib in patients with previously untreated metastatic adenocarcinoma of the pancreas. The RAMP 205 trial will evaluate whether combining avutometinib (to target mutant KRAS which is mutated in more than 90% of pancreatic tumors) and defactinib (to reduce stromal density and adaptive resistance to avutometinib) to the standard GEMZAR/ABRAXANE regimen improves outcomes for patients with pancreatic cancer. In August 2022, PanCAN agreed to provide us with an additional $0.5 million for the collection and analysis of patient samples. We received $1.0 million of cash proceeds in July 2022. We opened the RAMP 205 trial in the fourth quarter of 2022.

Avutometinib and defactinib are currently being investigated in combination with immunotherapeutic and other agents through investigator sponsored trials ("ISTs").

OUR FOCUS

We are focused on the development and commercialization of anticancer kinase inhibitors for optimized efficacy and safety – primarily as orally available drugs and drug candidates that are designed to treat various forms of cancer. Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. The American Cancer Society estimated that in the United States in 2022, over 1.9 million new cases of cancer were diagnosed and more than 600,000 people died from the disease. Current treatments for cancer include surgery, radiation therapy, chemotherapy, hormonal therapy, immunotherapy, cell therapy, and targeted therapy. Notwithstanding years of intensive research and clinical use, these current treatments often fail to cure cancer. For example, conventional chemotherapy works by stopping tumor growth by disrupting the cell cycle leading to cell death. Chemotherapies are effective at killing cancer cells because cancer cells generally grow more rapidly than normal cells. However, chemotherapies also target fast-growing normal cells of the body, such as blood cells, hair follicles, and the cells lining the mouth, stomach, and intestines. As a result, they have a range of side effects and although the treatments may succeed at initially decreasing tumor burden, they ultimately fail to kill all the cancer cells and/or to effectively disrupt the tumor microenvironment , potentially resulting in eventual disease progression.

Accordingly, cancer remains one of the world's most serious health problems and is the second most common cause of death in the United States after heart disease. For example, the National Cancer Institute's Surveillance, Epidemiology, and End Results Program ("NCI"; "SEER") reported that in 2022 there were approximately 19,880 new cases of ovarian cancer, 236,740 new cases of lung cancer, 151,030 new cases of colorectal cancer and 62,210 new cases of pancreatic cancer in the United States.

With the application of new technologies and key discoveries, we believe that we are now entering an era of cancer research characterized by a more sophisticated understanding of the biology of cancer. We believe that the potential of oral, targeted therapies, along with the rapidly advancing field of immunotherapy, or using the body's immune system to fight cancer, present the opportunity to develop more effective cancer treatments.

We leverage our expertise in translational research and deep understanding of cancer treatment pathways as well as strategic partnerships to identify, develop and deliver effective options to address unmet needs. We believe the best way for us to help patients living with cancer is by advancing newly emerging mechanisms of the disease and developing novel therapies that target these mechanisms.

Despite significant advances in the treatment of cancer, unmet needs persist. KRAS has long been one of the most elusive cancer-causing proteins. KRAS mutant tumors are present in about 30% of all human cancers, have historically presented a difficult treatment challenge, and are often associated with significantly worse prognosis. Since the discovery of KRAS almost four decades ago, researchers have persistently tried, and failed, to develop therapies that effectively block the cancer-promoting effects of KRAS mutation. Challenges associated with identifying new treatment options for these types of cancers include resistance to single agents, identifying tolerable combination regimens with MEK inhibitors, and new KRAS inhibitors in development addressing only a minority of all KRAS mutated cancers.

Our focus is targeting cancer cells both directly and indirectly by way of the tumor microenvironment.

Low Grade Serous Ovarian Cancer ("LGSOC")

LGSOC is a slow-growing cancer with a high mortality rate. It is estimated that approximately 70% of LGSOC tumors are driven by mutations in MAPK pathway-associated genes, with approximately 30% of patients harboring KRAS mutations and an additional approximately 40% of patients harboring mutations in other MAPK pathway associated genes. There are an estimated 6,000 patients in the United States and 80,000 worldwide living with this disease. Approximately half of those diagnosed are in their 20s-40s. LGSOC has a median survival rate of 10 years, with 85% of patients experiencing recurrence and enduring severe pain and complications as the disease progresses. Despite low response rates, chemotherapy continues to be the standard of care for this disease. Most prior research has focused on high grade serous ovarian cancer ("HGSOC"). However, LGSOC is clinically, histologically and molecularly unique from HGSOC with limited treatments available.

Currently, avutometinib is being evaluated in combination with defactinib for the treatment of patients with recurrent LGSOC (i) in a Phase 2 registration directed study entitled RAMP 201, and (ii) in the IST entitled FRAME. Avutometinib is also being investigated in combination with defactinib in ISTs to assess efficacy in other gynecological cancers with MAPK pathway mutations (e.g. high-grade and mucinous ovarian cancers, endometrial and cervical cancers).

Non-Small Cell Lung Cancer ("NSCLC")

Lung cancer is the leading cause of cancer-related death in the United States and worldwide. Approximately 15% of lung cancers are small cell lung cancer, approximately 55% are adenocarcinomas, approximately 20% are squamous carcinomas, and about 5% are large cell carcinomas with the remainder being mixed or rare histologies. Approximately 80-85% of lung cancers are NSCLCs, comprising of adenocarcinomas, squamous carcinomas, and large cell carcinomas. Adenocarcinomas most frequently (>50%) have molecular alterations that can be targeted with oral therapies. The most frequent molecular alterations are mutations in the KRAS gene (about 25% of adenocarcinomas) of which KRAS G12C is most common (14%) and G12V second most frequent (7%). Several tyrosine kinase inhibitors are in development for patients with KRAS G12C NSCLC of which the KRAS G12C inhibitors LUMAKRAS (sotorasib) and KRAZATI (adagrasib) are currently approved. LUMAKRAS and KRAZATI have relatively low response rates and short times to progression and thus, number of agents are being combined with the G12C inhibitors including avutometinib in RAMP 203 and RAMP 204, respectively. Currently, avutometinib is being evaluated (i) in combination with Amgen's KRAS-G12C inhibitor LUMAKRAS (sotorasib) in a Phase 1/2 trial in patients with KRAS G12C mutant NSCLC entitled RAMP 203, (ii) in combination with Mirati's KRAZATI (adagrasib) in patients with KRAS G12C mutant NSCLC in a Phase 1/2 trial entitled RAMP 204, and (iii) in combination with everolimus for treatment of patients with NSCLC in an IST.

BRAF mutations, including BRAF class II and class III non-V600E, also occur in NSCLC. Whereas BRAF inhibitors in combination with MEK inhibitors are currently approved for BRAF V600E NSCLC, no targeted therapies are approved for BRAF non-V600E NSCLC. Currently, the combination of avutometinib and defactinib is being evaluated for treatment of patients with BRAF mutant NSCLC including a non-V600E cohort in RAMP 202.

Colorectal Cancer ("CRC")

CRC, also known as bowel cancer, colon cancer, or rectal cancer, is the development of cancer from the colon or rectum (parts of the large intestine). One in 23 men and one in 25 women will be diagnosed with CRC in their lifetime. CRC is the second leading cause of cancer death among people in the United States. The NCI estimates that the number of new incidences of CRC was 37.7 per 100,000 men and women per year based on 2015-2019 cases and the five-year relative survival rate from 2012 to 2018 for patients with CRC was approximately 65%. The individual likelihood of survival depends on how advanced the cancer is, whether or not all the cancer can be removed with surgery, and the person's overall health.

Treatments used for colorectal cancer may include some combination of surgery, radiation therapy, chemotherapy and targeted therapy. Cancers that are confined within the wall of the colon may be curable with surgery, while cancer that has spread widely is usually not curable, with management being directed towards improving quality of life and symptoms. KRAS mutations are present in approximately 45% of CRC and predict lack of response to anti-EGFR antibodies such as cetuximab. Although clinical trials of the KRAS G12C inhibitors LUMAKRAS (sotorasib) and KRAZATI (adagrasib) in combination with anti-EGFR antibodies in KRAS G12C CRC have shown promising activity, KRAS G12C only occurs in 3% of CRCs. Thus, novel therapies are needed for patients with CRC harboring other KRAS mutations including KRAS G12D and KRAS G12V which represent 11% and 9%, respectively. It has been shown that simultaneous targeting of multiple nodes in the MAPK pathway may be necessary for deep and durable response, supporting the clinical evaluation of avutometinib in combination with anti-EGFR for patients with KRAS mutant CRC. Currently, avutometinib in combination with the anti-EGFR antibody cetuximab is being evaluated for the treatment of patients with advanced KRAS mutant CRC in an IST.

Pancreatic Cancer

In 2022, the NCI estimated that pancreatic cancer was the tenth most common cancer diagnosed in the United States and that the disease represented the third leading cause of cancer-related death in the country. Pancreatic cancer often has a poor prognosis, even when diagnosed early. Pancreatic cancer typically spreads rapidly and is seldom detected in its early stages, which is a major reason why it is a leading cause of cancer death. Signs and symptoms may not appear until pancreatic cancer is so advanced that complete surgical removal is not possible. Pancreatic cancer is one of the few cancers where survival has not improved significantly during the past 40 years. The NCI estimates that the number of new incidences of pancreatic cancer was 13.3 per 100,000 people per year based on 2015-2019 cases. Pancreatic cancer has a very high mortality rate with approximately 88% of patients dying within five years of their initial diagnosis based on the five-year relative survival rate from 2012 to 2018. The median age for diagnosis is 70 with the disease affecting males slightly more than females.

The prognosis for pancreatic cancer is extremely poor as shown by the survival rate, which indicates the need for new treatments. Chemotherapy or chemotherapy plus radiation is offered to patients whose tumors are unable to be removed surgically. Immuno-oncology agents have not demonstrated a significant improvement in treatment outcome for patients with pancreatic cancer. The limited impact of chemotherapies and immunotherapies to improve the outcome may be due to the dense stroma that is prevalent in pancreatic tumors and the tumor microenvironment. Activating mutations in KRAS represent a key initiating event in pancreatic cancer. KRAS mutations occur in up to 98% of pancreatic cancer, with KRAS G12D, G12V and G12R occurring in approximately 28%, 19% and 14% of patients, respectively. Furthermore, pancreatic cancer typically presents with high stromal density, comprised of fibroblasts and dense extracellular matrix, which is thought to limit the penetration of cytotoxic drugs and T cells into pancreatic tumors. Thus, there is a strong scientific rationale for combining avutometinib (to target mutant KRAS) and defactinib (to reduce stromal density and adaptive resistance to avutometinib) to the standard GEMZAR/ABRAXANE regimen with the objective of increasing response rate and survival. Currently, avutometinib is being evaluated in combination with defactinib + gemcitabine/nab-paclitaxel for the treatment of patients with advanced pancreatic cancer in a Phase 1b/2 clinical trial entitled RAMP 205.

Melanoma

In 2022, the NCI estimated melanoma cancer was diagnosed in approximately 99,780 patients or 21.5 cases per 100,000 people based on 2015-2019 cases. The NCI estimates the five year survival rate from 2012-2018 was approximately 94% Melanoma is a type of skin cancer that develops in melanocytes. Melanocytes are in the deep layer of the epidermis between the layer of basal cells. Melanocytes make a pigment called melanin. This gives skin its natural color. The pigment helps to protect the body from ultraviolet light (UV radiation) from the sun. Melanoma is most common at body sites that have received intense, intermittent sun/UV exposure. Melanoma is dangerous and aggressive due to its ability to spread to other organs rapidly if it is not treated at an early stage. About 30% of melanomas begin in existing moles, but the rest start in normal skin.

The five types of standard treatment for melanoma are surgery, chemotherapy, radiation therapy, immunotherapy and targeted therapy. In patients with melanoma, mutations in the MAPK pathway occur mainly in BRAF (41%), NRAS (27%), NF1 (25%) and RAF1 (CRAF) (2.6%). Although several selective BRAF inhibitors are FDA-approved alone or in combination with MEK inhibitors for melanomas with BRAF V600E/K, there is still a need for agents to improve response rate, duration of response, and tolerability. Furthermore, there are no targeted therapy options for patients with BRAF V600E melanoma following progression on BRAF + MEK inhibitor combination and immune checkpoint inhibitors. This provides rationale for the planned IST which will evaluate avutometinib in combination with the anti-PD-1 antibody pembrolizumab for patients with BRAF V600E melanoma.

OUR STRATEGY

With the combination of avutometinib and defactinib, we seek to utilize a multi-faceted approach to treat cancer by directly targeting the cancer cells, enhancing anti-tumor immunity, modulating the local tumor microenvironment, and overcoming mechanisms of adaptive resistance to MAPK pathway inhibition. Our goal is to

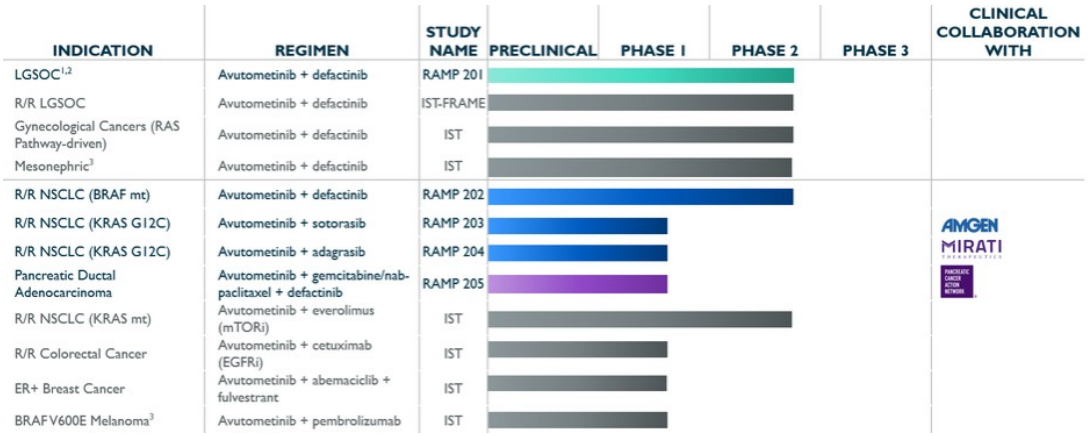
build a leading biopharmaceutical company focused on the development and commercialization of novel drugs that use a multi-faceted approach to improving outcomes for patients with cancer.

Key elements of our strategy to achieve this goal are:

- Establishing avutometinib as the backbone of therapy for MAPK pathway-driven tumors.
- Assessing synergy of avutometinib with other agents in preclinical models to prioritize for clinical development. It is becoming well established that blockade of multiple nodes in the MAPK pathway is necessary for maximal depth and duration of anti-tumor response. We are assessing combinations of avutometinib with (i) agents targeting other nodes in the MAPK pathway (e.g. KRAS G12C, KRAS G12D, anti-EGFR and SOS1 inhibitors), (ii) agents targeting parallel pathways that may mediate resistance to MAPK pathway inhibition (e.g. mTOR and CDK4/6 inhibitors), (iii) chemotherapy, and (iv) anti-PD-1. These studies may lead to discussions with other companies and clinical investigators with the objective of assessing high priority combinations in the clinic.
- Continuing to develop and explore avutometinib in combination with defactinib and execute on the registration-directed study RAMP 201. The combination of avutometinib with defactinib has been selected vs. avutometinib monotherapy as the go-forward treatment for all recurrent LGSOC regardless of KRAS status, acknowledging the demonstrated contribution of defactinib. Avutometinib is also being investigated in combination with defactinib in ISTs to assess efficacy in other gynecological cancers (e.g. high-grade and mucinous ovarian cancers, endometrial and cervical cancers) with MAPK pathway mutations.
- Expanding the indications in which avutometinib may be used alone and in combination with other agents. We have entered into clinical collaboration agreements with both Amgen and Mirati to evaluate avutometinib in patients with KRAS G12C NSCLC in combination with Amgen's G12C inhibitor LUMAKRAS (sotorasib) in a trial entitled RAMP 203 or in combination with Mirati's G12C inhibitor KRAZATI (adagrasib) in a trial entitled RAMP 204. Avutometinib is also being investigated in combination with defactinib + GEMZAR/ABRAXANE in patients with frontline pancreatic cancer in a trial entitled RAMP 205. Additionally, ISTs and preclinical studies are in progress to prioritize additional cancer indications and approaches to expand the potential clinical development of our product candidates. Avutometinib is being investigated in combination with the anti-EGFR antibody cetuximab in KRAS mutant CRC and in combination with the anti-PD-1 antibody pembrolizumab in BRAF V600E melanoma through ISTs.
- Considering the acquisition or in-licensing of rights to additional agents. We may pursue the acquisition or in-license of rights to additional agents from third parties that may supplement our internal programs and allow us to initiate clinical development of a diverse pipeline of agents more quickly.
- We may seek third-party collaborators for the eventual commercialization of our product candidates both in the U.S. and around the world.

OUR PRODUCT CANDIDATES AND PIPELINE

Our pipeline product candidates currently consist of avutometinib as a monotherapy and in combination with defactinib and other agents which continue to be evaluated in the clinic for the treatment of a variety of cancer types. The following table represents the status of our pipeline:



[1] FDA breakthrough therapy designation
[2] Registration-directed trial
[3] Imminent initiation
* Pre-clinical studies ongoing in multiple KRAS mutant tumors
RAMP 201 Study = NCT04625270
RAMP 202 Study = NCT04620330
RAMP 203 Study = NCT05074810
RAMP 204 Study = NCT05375994
RAMP 205 Study = NCT05669482
FRAME Study = NCT03875820
IST in KRAS mutant CRC = NCT05200442
IST in ER+ breast cancer = NCT05608252
IST in MAPK pathway-driven gynecological cancer = NCT05512208
IST in KRAS mutant NSCLC combining avutometinib + everolimus = NCT02407509

The status of our development programs in the table above represents the ongoing phase of development and does not correspond to the completion of a particular phase. Drug development involves a high degree of risk and investment, and the status, timing, and scope of our development programs are subject to change. Important factors that could adversely affect our drug development efforts are discussed in the "Risk Factors" section of this Annual Report on Form 10-K.

Avutometinib and defactinib

Avutometinib is an investigational oral first-in-class unique small molecule RAF/MEK clamp. In contrast to other MEK inhibitors commercially available and in development, avutometinib is a dual RAF/MEK clamp that blocks MEK kinase activity and induces the formation of dominant negative RAF-MEK complexes preventing phosphorylation of MEK by ARAF, BRAF and CRAF. MEK-only inhibitors (e.g., PD0325901) paradoxically induce MEK phosphorylation ("pMEK") by relieving extracellular-signal-regulated-kinase (ERK)-dependent feedback inhibition of RAF which may limit their efficacy. By inhibiting RAF-mediated phosphorylation of MEK, avutometinib has the advantage of not inducing pMEK. This unique mechanism of avutometinib enables more effective inhibition of ERK signaling and may confer enhanced therapeutic activity against MAPK pathway-driven cancers.

Defactinib is an oral small molecule inhibitor of FAK and PYK2 that is currently being evaluated as a potential combination therapy for various solid tumors. FAK is a non-receptor tyrosine kinase encoded by PTK-2 gene that is involved in cellular adhesion and, in cancer, metastatic capability. Defactinib targets malignant cells both directly and through modulation of the tumor microenvironment. Defactinib has received orphan drug designation in ovarian cancer in the United States, European Union, and Australia. Preclinical research by our scientists and collaborators at world-renowned research institutions has described the effect of FAK inhibition to enhance immune response by decreasing immuno-suppressive cells, increasing cytotoxic T cells, and reducing stromal density, which allows tumor-killing immune cells to enter the tumor. Furthermore, it has been shown that FAK activation in response to MAPK inhibitor therapy may bypass MAPK pathway blockade by driving tumor growth through activation of downstream pathways such as RhoA and YAP, supporting the clinical evaluation of avutometinib in combination with defactinib for treatment of cancers harboring MAPK alterations.

The combination of avutometinib and defactinib has received breakthrough designation from the FDA for the treatment of all patients with recurrent LGSOC, regardless of KRAS status after one or more prior lines of therapy, including platinum-based chemotherapy.

Avutometinib and defactinib are clinically active against MAPK pathway-driven cancers.

Phase 1/2 Study (FRAME) Investigating the Combination of avutometinib and Defactinib in Patients with KRAS Mutant Cancers and Subsequent Analyses

The FRAME study is an open-label, investigator-initiated study that is designed to assess safety, dose response and preliminary efficacy of the avutometinib/defactinib combination in patients with KRAS mutant solid tumors, including LGSOC (including KRAS mutant and KRAS wild type), KRAS mutant NSCLC, KRAS G12V NSCLC, KRAS mutant CRC, pancreatic cancer, and RAS/RAF mutant endometrial cancer. The FRAME study is being led by Dr. Udai Banerji and is being conducted in the United Kingdom. In this study, avutometinib was administered using a twice-weekly dose escalation schedule and was administered three out of every four weeks. Defactinib was administered using a twice-daily dose escalation schedule, also three out of every four weeks. Dose levels were assessed in three cohorts: cohort 1 (avutometinib 3.2mg, defactinib 200mg); cohort 2a (avutometinib 4mg, defactinib 200mg); and cohort 2b (avutometinib 3.2mg, defactinib 400mg). The recommended Phase 2 dose was determined to be avutometinib 3.2mg, defactinib 200mg.

Updated Phase 1/2 FRAME Study Results in Patients with LGSOC (September 2021)

At the September 2021 European Society of Medical Oncology Congress, updated data from the LGSOC cohort of the ongoing, investigatory sponsored Phase 1/2 FRAME study were presented. The results showed encouraging response rates and progression-free survival (“PFS”).

Among the evaluable patients with LGSOC (n=24), the ORR was 46% (11 of 24). Among the patients with KRAS mutant LGSOC (n=11), the ORR was 64% (7 of 11). Among the patients with KRAS wild type LGSOC (n=9), the ORR was 44% (4 of 9). Of the evaluable patients, 10 (42%) received previous MEK inhibitor therapy.

The estimated median PFS (“mPFS”) across all patients was 23.0 months (95% CI: 10.6- not reached). As of the April 2021 data cutoff date, 13 of 24 patients (54%) remained on study.

In the FRAME study, the most common Grade 3/4 treatment-related adverse events were creatine kinase elevation (12%), rash (8%), diarrhea (4%), mouth ulcer/mucositis/glossitis (4%), and hyperbilirubinemia (4%), with only one discontinuation due to adverse events as of the data cutoff.

This data suggests that the novel, intermittent dosing schedule used in the FRAME study continues to show encouraging clinical activity in patients with recurrent LGSOC, including in patients previously treated with a MEK inhibitor.

Phase 2 study (known as RAMP (RAF and MEK Program) 201 Study) Registration-Directed Trial of avutometinib and defactinib in Recurrent LGSOC

The RAMP 201 Study that was initiated in November 2020 is a registration-directed clinical trial of avutometinib and defactinib in patients with recurrent LGSOC.

The RAMP 201 Study is an adaptive two-part multicenter, parallel cohort, randomized, open label trial to evaluate the efficacy and safety of avutometinib alone and in combination with defactinib in patients with recurrent LGSOC. The objective of Part A (selection phase) of the RAMP 201 study was to select the go-forward regimen between avutometinib monotherapy or the combination of avutometinib and defactinib to be studied in Part B (expansion phase). In addition, the efficacy was assessed in both KRAS mutant and KRAS wild type LGSOC. Part B (expansion phase) of the study will examine efficacy and safety parameters of the regimen selected. Part A randomized eligible patients to avutometinib monotherapy (n=33) or the combination of avutometinib and defactinib (n=31). The combination of avutometinib and defactinib has been declared the go-forward treatment regimen based on a higher rate of confirmed objective responses in a planned interim analysis with prespecified criteria.

Updated Phase 2 RAMP 201 Study Results in Patients with LGSOC (January 2023)

Overall, patients on the combination arm were heavily pretreated with an average of four prior systemic regimens (up to 11), including prior platinum-based chemotherapy, endocrine therapy and bevacizumab in most patients and prior MEK inhibitor therapy in about 20% of patients.

Of the 29 patients evaluable for response by BICR in the combination arm, the initial results showed a confirmed objective response rate (ORR) of 28% in all patients and 27% vs 29% in KRAS mutant (n=15) and KRAS wild-type (n=14) LGSOC, respectively. Three additional patients with KRAS mutant LGSOC showed an unconfirmed partial response. In addition, the vast majority of patients showed tumor regression, as the overall disease control rate (stable disease plus partial response) was 93%. Most evaluable patients (62%) were still on study treatment on the combination arm at the time of the data cut with a minimum follow-up of five months.

The confirmed ORR for the monotherapy arm by BICR was 7% in evaluable patients (n=30). The overall disease control rate for the monotherapy arm by BICR was 90%.

Across both the combination and monotherapy arms, there have been no additional safety signals reported with a continued favorable safety and tolerability profile. The most common treatment-related adverse events for the combination in all treated patients were diarrhea, nausea, blood creatine phosphokinase (“CPK”) increased, vision blurred, dermatitis acneiform and rash, fatigue and peripheral edema, most of which were mild to moderate, with 9% discontinuation due to adverse events.

We intend to include mature data from RAMP 201 study and the FRAME study to potentially support filing for accelerated approval. We will continue future enrollment of RAMP 201 in the combination arm only to expand on the clinical experience in anticipation of a confirmatory study. Target enrollment for the combination arm has been achieved. We are in ongoing discussions with the FDA on the confirmatory study and plan to provide an update after agreement with the FDA. We are planning a RAMP 201 presentation at a scientific medical conference in 2023.

Phase 2 Study (known as RAMP (RAF and MEK Program) 202 Study) Registration-Directed Trial of avutometinib and defactinib in Previously Treated KRAS Mutant NSCLC

The RAMP 202 Study that was initiated in December 2020 is a registration-directed clinical trial of avutometinib and defactinib, in patients with KRAS G12V NSCLC. Additionally, and based on preclinical data, we added several exploratory cohorts to the RAMP 202 study including KRAS non-G12V NSCLC and BRAF mutant (V600E and non-V600E) NSCLC.

The RAMP 202 study is a Phase 2, adaptive two-part multicenter, parallel cohort, randomized, open-label trial to evaluate the efficacy and safety of avutometinib alone and in combination with defactinib in patients with

KRAS and BRAF mutant NSCLC, following treatment with a platinum-based regimen and immune checkpoint inhibitor. The first part of the study will determine the optimal regimen of either avutometinib monotherapy or in combination with defactinib in patients with KRAS G12V NSCLC. The second phase of the study (expansion phase) will examine efficacy and safety parameters of the most effective regimen in patients with KRAS G12V NSCLC.

In October 2022, we reported data from a planned interim analysis of Part A from the RAMP 202 trial among patients with KRAS G12V NSCLC treated with avutometinib or the combination of avutometinib and defactinib. While active, the results did not meet the pre-defined criteria to continue to the trial expansion phase. Also among patients with KRAS non G12V NSCLC, no KRAS subtype was identified for further clinical evaluation of avutometinib with defactinib in this trial. We plan to present the Part A results of RAMP 202 at an upcoming medical congress.

Phase 1/2 Trial (known as RAMP (RAF and MEK Program) 203 Study) of avutometinib in Combination with Amgen's LUMAKRAS (sotorasib) in Patients with KRAS G12C NSCLC

In September 2021, we entered into a clinical collaboration agreement with Amgen to evaluate the combination of avutometinib with Amgen's KRAS G12C inhibitor LUMAKRAS (sotorasib) in a Phase 1/2 trial entitled RAMP 203. The Phase 1/2 trial will evaluate the safety, tolerability and efficacy of avutometinib in combination with LUMAKRAS in patients with KRAS G12C NSCLC who have not been previously treated with a KRAS G12C inhibitor as well as in patients who have progressed on a KRAS G12C inhibitor. The study will investigate the potential benefits of a more complete vertical blockade of the MAPK pathway with the combination of avutometinib (RAF/MEK inhibition) with LUMAKRAS (KRAS G12C inhibition) in KRAS G12C locally advanced or metastatic NSCLC. The RAMP 203 trial has advanced to cohort 2 of 4 mg avutometinib in combination with 960 mg of LUMAKRAS.

Phase 1/2 Trial (known as RAMP (RAF and MEK Program) 204 Study) of avutometinib in Combination with Mirati's KRAZATI *(adagrasib) in Patients with KRAS G12C NSCLC*

In November 2021, we entered into a clinical collaboration agreement to evaluate the combination of avutometinib with Mirati's KRAS G12C inhibitor KRAZATI (adagrasib) in a Phase 1/2 trial entitled RAMP 204. The Phase 1/2 trial will evaluate the safety, tolerability and efficacy of avutometinib in combination with KRAZATI in patients who have progressed on a KRAS G12C inhibitor. The trial will build on preclinical data showing deeper blockade of MAPK pathway signaling resulting in enhanced anti-tumor efficacy with the combination of KRAZATI (KRAS G12C inhibition) and avutometinib (RAF/MEK inhibition) relative to either agent alone. The RAMP 204 trial is open and enrolling.

Phase 1/2 Trial (known as RAMP (RAF and MEK Program) 205 Study) of avutometinib + defactinib + gemcitabine/nab-paclitaxel

In May 2022, we received the first "Therapeutic Accelerator Award" from PanCAN for up to $3.8 million. The grant is expected to support a Phase 1b/2 clinical trial of avutometinib in combination with defactinib entitled RAMP 205. This Phase 1b/2 trial will evaluate the safety, tolerability and efficacy of GEMZAR (gemcitabine) and ABRAXANE (Nab-paclitaxel) in combination with avutometinib and defactinib in patients with previously untreated metastatic adenocarcinoma of the pancreas. The RAMP 205 trial will evaluate whether combining avutometinib (to target mutant KRAS which is mutated in more than 90% of pancreatic tumors) and defactinib (to reduce stromal density and adaptive resistance to avutometinib) to the standard GEMZAR/ABRAXANE regimen improves outcomes for patients with pancreatic cancer. We opened the RAMP 205 trial in the fourth quarter of 2022.

INTELLECTUAL PROPERTY

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the

development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of treatment and patient selection created or identified from our ongoing development of our product candidates. Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention.

Patents

Our patent portfolio includes issued and pending applications worldwide. These patent applications fall into two categories: (1) RAF/MEK inhibition program; and (2) FAK inhibition program.

RAF/MEK inhibition program

We have exclusively licensed a portfolio of four patent families owned by Chugai Pharmaceutical Co., Ltd. (“Chugai”). The first patent family has claims directed to the composition of matter of avutometinib, and includes granted patents in the United States, Australia, Brazil, Canada, China, Europe, Japan, Korea, Israel, and New Zealand that are expected to expire in February of 2027. The second patent family has claims directed to methods of making avutometinib and includes granted patents in Europe, Japan, and the United States that are expected to expire in September of 2032. The third patent family has claims directed to a dosing protocol of avutometinib, and includes a granted patent in the United States that is expected to expire in November of 2038 and pending patent applications in the United States, Australia, Brazil, Canada, China, Europe, Hong Kong, Japan, Korea, Mexico, Singapore, Taiwan, and Russia. Patents that issue in this family will have a statutory expiration date in May of 2038. The fourth patent family covers a method of using avutometinib in combination with a FAK inhibitor, such as defactinib, for treating a patient, and includes a granted patent in the United States that is expected to expire in September of 2040 and pending patent applications in Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, Indonesia, Japan, Korea, Mexico, Malaysia, New Zealand, Singapore, the United States, and Taiwan.

In addition to the issued and pending patent applications exclusively licensed from Chugai, we own eleven patent families covering methods of using a dual RAF/MEK inhibitor for treating a patient. The first and second patent families cover methods of using a dual RAF/MEK inhibitor in combination with a KRAS G12C inhibitor or an immunotherapeutic agent for treating a patient, and are pending in the United States and worldwide. The third patent family covers a method of using a dual RAF/MEK inhibitor to treat a patient with certain mutations, and is pending in the United States and worldwide. The fourth patent family covers solid forms of avutometinib, and is pending in the United States as a nonprovisional patent application. We also have six patent families covering methods of using a dual RAF/MEK inhibitor in combination with another therapeutic agent for treating a patient,

which are pending as international applications. Any U.S. patents that will issue in the ten families will have a statutory expiration date ranging from January of 2041 to January of 2043. We also have one patent family covering methods of using a MEK inhibitor to treat certain populations of patients, which is pending as a provisional patent application in the United States.

FAK inhibition program

We have exclusively licensed a portfolio of patent applications owned by Pfizer, Inc. ("Pfizer"), which are directed to FAK inhibitor compounds and methods of their use, for example in cancer. One patent family is related generally to defactinib. This patent family includes issued patents having claims covering defactinib generically and specifically. For example, US 7,928,109 covers the composition of matter of defactinib specifically, and US 8,247,411 covers the composition of matter of defactinib generically. Also included are issued and pending patent applications having claims directed to methods of treatment and methods of making defactinib. For example, US 8,440,822 and US 10,450,297 cover methods of making defactinib. Any U.S. patents that have issued or will issue in this family will have a statutory expiration date in April of 2028. Related cases are pending worldwide, including in Thailand, and granted in Australia, Europe, Brazil, Mexico, India, Hong Kong, Canada, China, Korea, Israel, New Zealand, South Africa, Singapore, Taiwan, and Japan.

In addition to the issued and pending patent applications exclusively licensed from Pfizer, we own three patent families covering defactinib. One family is directed to compositions (e.g., oral dosage forms) of defactinib and certain methods of use. Any U.S. patents that will issue in this family will have a statutory expiration date in January of 2035. Patent applications in this family are pending worldwide, including in the United States, Thailand, Brazil, and China, and granted in Australia, Canada, Europe, Hong Kong, Israel, Mexico, Japan, Korea, New Zealand, Singapore, and South Africa. The second family is directed to methods of using a FAK inhibitor, such as defactinib, in combination with a MEK inhibitor for treating a patient. Any U.S. patents that will issue in this family will have a statutory expiration date in February of 2035. Patent applications in this family are pending worldwide, including for example in Japan, and granted in the United States, Hong Kong, and Europe. The third family is directed to methods of using a FAK inhibitor, such as defactinib, in combination with an immunotherapeutic agent. Any U.S. patents that have issued or will issue in this family will have a statutory expiration date in June of 2036. Patent applications in this family are pending worldwide, including for example in Europe, New Zealand, Brazil, Korea, Israel, Canada, Japan, and Hong Kong, and granted in the United States, Australia, China, Eurasia, Mexico, Singapore, and South Africa.

Our licensed portfolio of patent applications from Pfizer also includes four families of patent applications directed to VS-6062 and related methods of use. The patent families include issued and pending patent applications having claims directed to VS-6062, methods of manufacture, and pharmaceutical salts. Patents have issued in these families in the United States that will expire in December of 2023, April of 2025, and November of 2028, respectively. Related cases have been granted worldwide, including in Australia, Canada, China, Japan, and Europe. Stanford University has an option to certain United States rights in VS-6062.

Patent Term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the U.S. Patent and Trademark Office. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a United States patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one United States patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug, and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign

jurisdictions, including Europe and Japan, have analogous patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency.

LICENSES AND COMMERCIAL AGREEMENTS

Secura

On August 10, 2020, we and Secura Bio, Inc. ("Secura") signed an Asset Purchase Agreement ("Secura APA") and on September 30, 2020, the transaction closed.

Pursuant to the Secura APA, we sold to Secura our exclusive worldwide license for the research, development, commercialization, and manufacture in oncology indications of products containing duvelisib. The sale included certain intellectual property related to duvelisib in oncology indications, certain existing duvelisib inventory, claims and rights under certain contracts pertaining to duvelisib. Pursuant to the Secura APA, Secura assumed all operational and financial responsibility for activities that were part of the duvelisib oncology program, including all commercialization efforts related to duvelisib in the United States and Europe, as well as our ongoing duvelisib clinical trials. Further, Secura assumed all obligations with existing collaboration partners developing and commercializing duvelisib, which include Yakult Honsha Co., Ltd. ("Yakult"), CSPC Pharmaceutical Group Limited ("CSPC"), and Sanofi. Additionally, Secura assumed all royalty payment obligations due under the amended and restated license agreement with Infinity Pharmaceuticals, Inc. ("Infinity").

Pursuant to the terms of the Secura APA, Secura has paid us an up-front payment of $70.0 million, and has agreed to pay us (i) regulatory milestone payments up to $45.0 million, consisting of a payment of $35.0 million upon receipt of regulatory approval of COPIKTRA in the United States for the treatment of peripheral T-cell lymphoma ("PTCL") and a payment of $10.0 million upon receipt of the first regulatory approval for the commercial sale of COPIKTRA in the European Union for the treatment of PTCL, (ii) sales milestone payments of up to $50.0 million, consisting of $10.0 million when total worldwide net sales of COPIKTRA exceed $100.0 million, $15.0 million when total worldwide net sales of COPIKTRA exceed $200.0 million and $25.0 million when total worldwide net sales of COPIKTRA exceed $300.0 million, (iii) low double-digit royalties on the annual aggregate net sales above $100.0 million in the United States, European Union, and the United Kingdom of Great Britain and Northern Ireland and (iv) 50% of all royalty, milestone and sublicense revenue payments payable to Secura under our existing license agreements with Sanofi, Yakult, and CSPC, and 50% of all royalty, and royalty payments payable to Secura under any license or sublicense agreement entered into by Secura in certain jurisdictions.

Secura's royalty obligations remain in effect on a country-by-country basis upon the last to occur (a) 10 years from the first commercial sale of product containing duvelisib in such country or (b) the expiration of all valid patent claims covering products containing duvelisib in such country.

In December 2021, Secura announced it had voluntarily withdrawn COPIKTRA (duvelisib) from the U.S. for treatment of patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies. On June 30, 2022, the FDA issued a drug safety communication warning that resulted from a clinical trial showing a possible increased risk of death with COPIKTRA compared to another medicine to treat chronic blood cancer called leukemia and lymphoma. The clinical trial also found that COPIKTRA was associated with a higher risk of serious side effects, including infections, diarrhea, inflammation of the intestines and lungs, skin reactions, and high liver enzyme levels in the blood. In September 2022, the FDA's Oncologic Drug Advisory Committee ("ODAC") voted eight to four against COPIKTRA's use in patients with relapsed or refractory chronic lymphocytic leukemia/ small lymphocytic lymphoma after at least two prior therapies citing an unfavorable risk/benefit profile. In September 2022, Secura's sublicensee, Yakult, announced it had withdrawn its NDA for duvelisib in Japan.

Chugai Pharmaceutical Co., Ltd.

On January 7, 2020, we entered into a license agreement with Chugai (the "Chugai Agreement") whereby Chugai granted us an exclusive worldwide license for the development, commercialization, and manufacture of products containing avutometinib.

Under the terms of the Chugai Agreement, we received an exclusive right to develop and commercialize products containing avutometinib at our own cost and expense. In February 2020, we paid Chugai a non-refundable payment of $3.0 million. We are further obligated to pay Chugai double-digit royalties on net sales of products containing avutometinib, subject to reduction in certain circumstances. Chugai also obtained opt back rights to develop and commercialize avutometinib (a) in the European Union, which option may be exercised through the date we submit a New Drug Application ("NDA") to the FDA for a product which contains avutometinib as the sole active pharmaceutical ingredient and (b) in Japan and Taiwan, which option may be exercised through the date we receive marketing authorization from the FDA for a product which contains avutometinib as the sole active pharmaceutical ingredient. As consideration for executing either option, Chugai would have to make a payment to us calculated on our development costs to date. Chugai has communicated their intention not to exercise their opt back rights for Japan, Taiwan, or the European Union. Chugai and we have made customary representations and warranties and have agreed to certain customary covenants, including confidentiality and indemnification.

Unless earlier terminated, the Chugai Agreement will expire upon the fulfillment of our royalty obligations to Chugai for the sale of any products containing the avutometinib, which royalty obligations expire on a product-by-product and country-by-country basis, upon the last to occur, in each specific country, of (a) expiration of valid patent claims covering such product or (b) 12 years from the first commercial sale of such product in such country.

We may terminate the Chugai Agreement upon 180 days' written notice. Subject to certain limitations, Chugai may terminate the Chugai Agreement upon written notice if we challenge any patent licensed by Chugai to us under the Chugai Agreement. Either party may terminate the license agreement in its entirety with 120 days' written notice for the other party's material breach if such party fails to cure the breach. Either party may also terminate the Chugai Agreement in its entirety upon certain insolvency events involving the other party.

Pfizer Inc.

On July 11, 2012, we entered into a license agreement (the "Pfizer Agreement") with Pfizer under which Pfizer granted us worldwide, exclusive rights to research, develop, manufacture and commercialize products containing certain of Pfizer's inhibitors of FAK, including defactinib, for all therapeutic, diagnostic and prophylactic uses in humans. We have the right to grant sublicenses under the foregoing licensed rights, subject to certain restrictions. We are solely responsible, at our own expense, for the clinical development of these products, which is to be conducted in accordance with an agreed-upon development plan. We are also responsible for all manufacturing and commercialization activities at our own expense. Pfizer provided us with an initial quantity of clinical supplies of one of the products for an agreed upon price.

Upon entering into the Pfizer Agreement, we made a one-time cash payment to Pfizer in the amount of $1.5 million and issued 192,012 shares of our common stock. Pfizer is also eligible to receive up to $2.0 million in developmental milestones and up to an additional $125.0 million based on the successful attainment of regulatory and commercial sales milestones. Pfizer is also eligible to receive high single to mid-double-digit royalties on future net sales of the products. Our royalty obligations with respect to each product in each country begin on the date of first commercial sale of the product in that country, and end on the later of 10 years after the date of first commercial sale of the product in that country or the date of expiration or abandonment of the last claim contained in any issued patent or patent application licensed by Pfizer to us that covers the product in that country.

The Pfizer Agreement will remain in effect until the expiration of all our royalty obligations to Pfizer, determined on a product-by-product and country-by-country basis. So long as we are not in breach of the Pfizer Agreement, we have the right to terminate the license agreement at will on a product-by-product and country-by-country basis, or in its entirety, upon 90 days written notice to Pfizer. Either party has the right to terminate the Pfizer Agreement in connection with an insolvency event involving the other party or a material breach of the Pfizer Agreement by the other party that remains uncured for a specified period of time. If the Pfizer Agreement is terminated by either party for any reason, worldwide rights to the research, development, manufacture and commercialization of the products revert back to Pfizer.

COMPETITION

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

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

The key competitive factors affecting the success of all our product candidates, if approved, are likely to be their efficacy, safety, side effects, convenience, price, the level of generic competition, and the availability of reimbursement from government and other third-party payors.

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 regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are many generic products currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our therapeutic product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

The most common methods of treating patients with cancer are surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, immunotherapy, and targeted drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. To the extent our product candidates are ultimately used in combination with or as an adjunct to existing drug or other therapies, our product candidates will not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed therapies, there are also a number of products in late stage clinical development to treat cancer. These products in development may provide efficacy, safety, convenience, and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

RAF/MEK inhibition program

There are other companies with approved RAF and/or MEK inhibitors with FDA approval in the market and companies working to develop RAF and/or MEK inhibitor. We believe the following companies have an approved RAF and/or MEK inhibitor:

- Novartis AG, which has received FDA approval for Taflinar® (dabrafenib), a RAF inhibitor, in combination with Mekinist® (trametinib), a MEK inhibitor, for treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, adjuvant treatment for melanoma with BRAF V600E or V600K mutations and involvement of lymph nodes following complete resection, metastatic NSCLC with BRAF V600E or V600K mutations and locally advanced or metastatic anaplastic thyroid cancer with BRAF V600E mutation;

- Pfizer, through its acquisition of Array BioPharma, Inc, has received FDA approval for Braftovi® (encorafenib), a RAF inhibitor, in combination with Mektovi® (binimetinib), a MEK inhibitor, for treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation. In addition, the FDA has granted approval for Braftovi® (encorafenib) in combination with Erbitux® (cetuximab), an anti-EGFR antibody for treatment of adult patients with metastatic CRC with a BRAF V600E mutation;

- Genentech, Inc. a member of the Roche Company, which has received FDA approval for Zelboraf® (vemurafenib), a RAF inhibitor, in combination with Cotellic® (cobimetinib), a MEK inhibitor, to treat patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation; and

- AstraZeneca and Merck & Co., Inc. has received FDA approval for Koselugo® (selumetinib), a MEK inhibitor, for the treatment of pediatric patients two years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic inoperable plexiform neurofibromas.

FAK inhibition program

There is a company, InxMed, developing a FAK small molecule inhibitor program. We believe InxMed is conducting Phase 1 and Phase 2 clinical trials of their product candidate IN10018.

MAPK Pathway Inhibitors

There are two companies with an approved drug with FDA approval targeting the MAPK pathway in the market and companies working to develop therapies to target the MAPK pathway. We believe the following companies, among others, have an approved drug, developed or in the clinical stage of development of compounds targeting the MAPK pathway:

- Amgen has received FDA approval for LUMAKRAS (sotorasib) for the treatment of adult patients with KRAS G12C locally advanced or metastatic NSCLC, who have received at least one prior systemic therapy. In addition, we believe Amgen, Inc. is conducting Phase 1, Phase 2 and Phase 3 clinical trials of LUMAKRAS (sotorasib) as monotherapy or in combination with other agents;

- Mirati has received FDA approval for KRAZTI (adagrasib) for treatment of adult patients with KRAS G12C locally advanced or metastatic NSCLC, who have received at least one prior systemic therapy. In addition, we believe Mirati is conducting Phase 2 and Phase 3 clinical trials of KRAZTI (adagrasib) as monotherapy or in combination with other agents;

- Revolution Medicines, Inc., which we believe is conducting Phase 2 clinical trial of RMC-4630 in collaboration with Sanofi and Phase 1 clinical trials of RMC-5552, RMC-6236, and RMC-6291;

- SpringWorks Therapeutics, Inc., which we believe is conducting Phase 1 and Phase 2 clinical trials of mirdametinib;

- Recursion Pharmaceuticals, Inc., which we believe is conducting Phase 2 and Phase 1 clinical trials of REC-4881;
- Fochon Pharmaceutical Ltd. which we believe is conducting Phase 2 and Phase 1 clinical trials of FCN-159;
- Eisai Co., Ltd., which we believe is conducting Phase 1 clinical trials of E-6201;
- Binjang Pharma, Inc. which we believe is conducting Phase 2 and Phase 1 clinical trials of HL-085;
- Jiangsu Hengrui Medicine Co., Ltd., which we believe is conducting Phase 1 clinical trials of SHR-7390;
- Mapkure, LLC, together with BeiGene Ltd. and SpringWorks Therapeutics, Inc., which we believe is conducting a Phase 2 clinical trial of BGB-3245;
- BeiGene Ltd., which we believe is conducting Phase 2 clinical trials of lifrafenib;
- Fore Biotherapeutics, Inc., which we believe is conducting a Phase 2 clinical trial of FORE-8394 (previously PLX-8394);
- Day One Biopharmaceuticals, Inc., which we believe is conducting Phase 2 and Phase 1 clinical trials of DAY-101 (tovorafenib);
- Erasca, Inc. which we believe is conducting Phase 1 and Phase 2 clinical trials of naporafenib (ERAS-254) and ERAS-007, and Phase 1 clinical trials of ERAS-601;
- Genentech Inc., which we believe is conducting a Phase 1 clinical trial of belvarafenib;
- Relay Therapeutics, Inc., which we believe is conducting Phase 1 clinical trials of RLY-1971;
- Kinnate Biopharma, Inc., which we believe is conducting Phase 1 clinical trials of exarafenib (KIN-2787);
- Boehringer Ingelheim, which we believe is conducting Phase 1 clinical trials of BI 1701963 and BI 3011441; and
- Moderna, Inc., which we believe is conducting a Phase 1 clinical trial of mRNA-5671.

Oncology

In addition to companies that have inhibitors addressing our targets of interest, our competition also includes hundreds of private and publicly traded companies that operate in the area of oncology but have therapeutics with different mechanisms of action. The oncology market in general is highly competitive, with over 1,000 molecules currently in clinical development.

MANUFACTURING

We contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials, and we intend to continue to do so in the future. We currently work with one contract manufacturing organization ("CMO") for the manufacture of avutometinib drug product, one CMO for the production of avutometinib drug substance, and one CMO for avutometinib drug packaging/labeling. For defactinib, we currently have one CMO for the manufacture of drug product, one CMO for the production of drug substance, and one CMO for drug packaging /labeling. We have development agreements in place with these CMOs and we obtain drug

substance, drug product and packaging/labeling services from these CMOs on a purchase order basis. We may elect to pursue relationships with other CMOs for manufacturing of drug product, drug substance, and packaging/labeling for later-stage clinical trials, commercialization or for risk management. We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We have personnel with pharmaceutical development and manufacturing experience who are responsible for the relationships with our CMOs.

All of our drug candidates are organic compounds of low molecular weight, generally called small molecules. We select compounds not only on the basis of their potential efficacy and safety, but also for their ease of synthesis and the reasonable cost of their starting materials. We expect to continue to develop drug candidates that can be produced cost-effectively at third-party CMOs.

APPLICABLE LAWS AND GOVERNMENT REGULATION

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical products, such as those we are developing.

United States drug approval process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal penalties.

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

- completion of preclinical laboratory tests, animal studies, and formulation studies in compliance with the FDA's good laboratory practice ("GLP") regulations and applicable requirements for the humane use of laboratory animals or other applicable requirements;
- submission to the FDA of an investigational new drug ("IND") application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB") at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCP") and other clinical-trial related regulations to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of an NDA and payment of user fees for FDA review of NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices

("cGMP") requirements and to assure that the facilities, methods, and controls are adequate to preserve the drug's identity, strength, quality and purity; and

- FDA review and approval of the NDA.

Preclinical studies

Before testing any product candidate in humans, the product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective thirty days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

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

- *Phase 1:* The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- *Phase 2:* The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3:* The drug is administered to an expanded patient population in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and are commonly intended to generate additional safety data regarding use of the product in a

clinical setting. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of a NDA or, in certain circumstances, post-approval.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, scheduled in 2023 to exceed $3.2 million, and the sponsor of an approved NDA is also subject to annual program fees, based on the number of approved products. These fees are typically adjusted annually. User fee statutory authority expires every five years. The Prescription Drug User Fee Act was re-authorized for an additional five years in 2022 until 2027. Fee waivers are available in certain circumstances, including a waiver of the application fee for an orphan drug application.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review of NDAs. Under these goals, the FDA has committed to review most such applications for non-priority products within 10 months after accepting the application for filing, and most applications for priority review products, that is, drugs that the FDA determines represent a significant improvement over existing therapy, within six months after accepting the application for filing. The review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drugs or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Under the Pediatric Research Equity Act of 2003, as amended and reauthorized by the Food and Drug Administration Amendments Act of 2007 ("FDAAA"), an NDA or supplement to an NDA must contain data that are adequate 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 product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan drug designation.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The testing and approval process requires substantial time, effort and financial resources, and each may take many years to complete. Data obtained from clinical activities are not always conclusive and may be

susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products.

After the FDA's evaluation of the NDA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If the FDA issues a complete response letter, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application If and 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. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and refuse to approve the NDA.

Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Expedited Development and Review Programs

The FDA has various programs, including fast track designation, breakthrough therapy designation, priority review and accelerated approval, which are designed to expedite or facilitate the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs and biologics to patients earlier than under standard FDA review procedures.

Fast Track Designation. To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that the product is intended for the treatment of a serious or life-threatening condition for which there is no effective treatment, and demonstrates the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

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

Breakthrough Designation. A drug may be designated as a breakthrough therapy if the drug is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The breakthrough therapy designation provides all the benefits of the fast track program, including the eligibility for rolling review. The FDA may take certain administrative actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process, providing timely advice to the product

sponsor regarding development and approval, involving more senior staff in the review process, assigning a cross-disciplinary project lead for the review team and taking other steps to aid sponsors in designing the clinical trials. Although breakthrough designation does not affect the regulatory standards for approval, the frequent interactions with the FDA may facilitate a more efficient development program. In addition, the breakthrough designation may be withdrawn by the FDA if the FDA believes that the drug no longer meets the conditions for qualification.

Priority Review. Under FDA policies, a product candidate may be eligible for priority review, or review within a six-month time frame, compared to the ten-month time frame for a standard review, from the time a complete application is accepted for filing. Products regulated by the FDA's Center for Drug Evaluation and Research (CDER) are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease.

Accelerated Approval. Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of one or more Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. The Food and Drug Omnibus Reform Act of 2022 ("FDORA") signed by President Biden on December 29, 2022 as part of the Consolidated Appropriations Act, 2023 (H.R. 2617) includes numerous reforms to the accelerated approval process for drugs and biologics and enables FDA to require, as appropriate, that a post-approval study be underway prior to granting accelerated approval. FDORA also expands the expedited withdrawal procedures available to FDA to allow the agency to use expedited procedures if a sponsor fails to conduct any required post-approval study of the product with due diligence." FDORA also adds the failure of a sponsor of a product approved under accelerated approval to conduct with due diligence any required post-approval study with respect to such product or to submit timely reports with respect to such product to the list of prohibited acts in the Food, Drug, and Cosmetic Act. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. The FDA has historically taken the position that the scope of orphan exclusivity aligns with the approved indication or use of a product, rather than the disease or condition for which the product received orphan designation. However, on September 30, 2021, the U.S. Court of Appeals for the 11th Circuit issued a decision in *Catalyst Pharms., Inc. v. Becerra* holding that the scope of orphan drug exclusivity must align with the disease or condition for which the product received orphan designation, even if the product's approval was for a narrower use or indication. It remains to be seen how this decision affects orphan drug exclusivity going forward. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

The Hatch-Waxman Act

Abbreviated New Drug Applications

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated New Drug Application (ANDA). Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths, dosage form and route of administration as the listed drug and has been shown to be bioequivalent through *in vitro* or *in vivo* testing or otherwise to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

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 after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the NDA or patent holder's receipt of the Paragraph IV certification, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA also will not be approved until any applicable non-patent exclusivity period, such as exclusivity for obtaining approval of a new chemical entity, for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active moiety during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an ANDA for the conditions of use covered by the exclusivity, but FDA requires as a condition of approval new clinical trials conducted by or for the sponsor. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Under the Best Pharmaceuticals for Children Act, federal law also provides that periods of patent and non-patent marketing exclusivity listed in the Orange Book for a drug may be extended by six months if the NDA sponsor conducts pediatric studies identified by the FDA in a written request. For written requests issued

by the FDA after September 27, 2007, the date of enactment of the FDAAA, the FDA must grant pediatric exclusivity no later than nine months prior to the date of expiration of patent or non-patent exclusivity in order for the six-month pediatric extension to apply to that exclusivity period.

Combination Therapy

Combination therapy is a treatment modality that involves the use of two or more drugs to be used in combination to treat a disease or condition. If those drugs are combined in one dosage form, such as one pill, that is known as a fixed dose combination product and it is reviewed pursuant to the FDA's Combination Rule at 21 CFR 300.50. The Rule provides that two or more drugs may be combined in a single dosage form when each component contributes to the claimed effects and the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective for a significant patient population requiring such concurrent therapy as defined in the labeling for the drug.

But not all combination therapy falls under the category of a fixed dose combination. For example, the FDA recognizes that two drugs in separate dosage forms and in separate packaging, that otherwise might be administered as monotherapy for an indication, also may be used in combination for the same indication. In 2013, the FDA issued guidance to assist sponsors that were developing the range of combination therapies that fall outside the category of fixed dose combinations. That guidance provides recommendations and advice on such topics as: (1) assessment at the outset whether two or more therapies are appropriate for use in combination; (2) guiding principles for nonclinical and clinical development of the combination; (3) options for regulatory pathways to seek marketing approval of the combination; and (4) post-marketing safety monitoring and reporting obligations. Given the wide range of potential combination therapy variations, the FDA indicated it intends to assess each potential combination on a case-by case basis and encouraged sponsors to engage in early and regular consultation with the relevant review division at the agency throughout the development process for its proposed combination.

Combination products

The FDA regulates combinations of products that cross FDA centers, such as drug, biologic or medical device components that are physically, chemically or otherwise combined into a single entity, as a combination product. The FDA center with primary jurisdiction for the combination product will take the lead in the premarket review of the product, with the other center consulting or collaborating with the lead center.

The FDA's Office of Combination Products ("OCP") determines which center will have primary jurisdiction for the combination product based on the combination product's "primary mode of action." A mode of action is the means by which a product achieves an intended therapeutic effect or action. The primary mode of action is the mode of action that provides the most important therapeutic action of the combination product, or the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

Often it is difficult for the OCP to determine with reasonable certainty the most important therapeutic action of the combination product. In those difficult cases, the OCP will consider consistency with other combination products raising similar types of safety and effectiveness questions, or which center has the most expertise to evaluate the most significant safety and effectiveness questions raised by the combination product.

A sponsor may use a voluntary formal process, known as a Request for Designation, when the product classification is unclear or in dispute, to obtain a binding decision as to which center will regulate the combination product. If the sponsor objects to that decision, it may request that the agency reconsider that decision.

Other regulatory requirements

Any drug manufactured or distributed by us pursuant to FDA approvals would be subject to extensive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with

the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

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 product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks or imposition of distribution or other restrictions under a Risk Evaluation and Mitigation Strategy 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 holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- consent decrees, corporate integrity agreements, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability.

Additional provisions

Physician drug samples

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act ("PDMA") imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations.

Foreign regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Regardless of our current FDA approval or any future FDA approvals we may obtain for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Pharmaceutical coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of new drug products. Sales of product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, we 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. We may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may not be considered medically necessary or cost-effective. Even if covered, third party payors may seek to control utilization of our products through various managed care mechanisms (e.g., requiring a prescriber to obtain prior authorization from a health plan before the product will be covered by the health plan or establishing patient copays and deductibles that encourage use of other products over our products). A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for drug products can differ significantly from payor to payor. One third-party payor's decision to cover a particular drug product or service does not ensure that other payors will also provide coverage for the drug product, or will provide coverage at an adequate reimbursement rate.

Within the United States, FDA-approved drugs could potentially be covered by various government health benefit programs as well as purchased by government agencies. The participation in such programs or the sale of products to such agencies is subject to regulation. The marketability of any of our approved products may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement.

Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. Under the Medicaid Drug Rebate Program, participating manufacturers are required to pay a rebate for each unit of product reimbursed by the state Medicaid programs. The amount of the rebate for each product is set by law and may be subject to an additional discount if certain pricing increases more than inflation.

Medicare is a federal program that is administered by the federal government that covers individuals aged 65 and over as well as those with certain disabilities. Oral drugs may be covered under Medicare Part D. Medicare Part D provides coverage to enrolled Medicare patients for self-administered drugs (i.e., drugs that do not need to be injected or otherwise administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time-to-time. The prescription drug plans negotiate pricing with manufacturers and may condition formulary placement on the availability of manufacturer discounts. Under the Medicare Coverage Gap Discount Program, manufacturers with marketed brand

name drugs are currently required to provide a 70% discount on the negotiated price for brand name prescription drugs utilized by Medicare Part D beneficiaries when those beneficiaries reach the coverage gap in their drug benefits.

Drug products are subject to discounted pricing when purchased by federal agencies via the Federal Supply Schedule ("FSS"). FSS participation is required for a drug product to be covered and reimbursed by certain federal agencies and for coverage under Medicaid, Medicare Part B and the Public Health Service (PHS) pharmaceutical pricing program. FSS pricing is negotiated periodically with the Department of Veterans Affairs. FSS pricing is intended not to exceed the price that a manufacturer charges its most-favored non-federal customer for its product. In addition, prices for drugs purchased by the Veterans Administration, Department of Defense (including drugs purchased by military personnel and dependents through the TRICARE retail pharmacy program), Coast Guard, and PHS are subject to a cap on pricing (known as the "federal ceiling price") and may be subject to an additional discount if pricing increases more than the rate of inflation.

To maintain coverage of drugs under the Medicaid Drug Rebate Program, manufacturers are required to extend discounts to certain purchasers under the PHS pharmaceutical pricing program. Purchasers eligible for discounts include hospitals that serve a disproportionate share of financially needy patients, community health clinics and other entities that receive health services grants from the PHS.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available 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 at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of existing controls and measures, could limit payments for pharmaceuticals such as the drug candidates that we are developing and could adversely affect our net revenue and results.

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 a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or 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 company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

The marketability of products for which we may receive regulatory approval for commercial sale may suffer if the government and private third-party payors fail to provide adequate coverage and reimbursement, seek to control utilization, or create pressure to provide price concessions, coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. Even if favorable coverage and reimbursement status is attained for a product, less favorable coverage policies and reimbursement rates may be implemented in the future.

New legislation and regulations

From time to time, legislation is drafted, introduced and passed in the United States Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of

pharmaceutical products. For example, in December 2016, Congress enacted and President Obama signed into law the 21st Century Cures Act that amends a number of sections of the FDCA. Additionally, in December 2022, President Biden signed into law the Consolidated Appropriations Act, 2023 (H.R. 2617) that contains important reforms relevant to the FDA, including the Food and Drug Omnibus Reform Act of 2022 ("FDORA") and the Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act (the "PREVENT Pandemics Act"). In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations changed or what the effect of such changes, if any, may be.

In the United States, federal and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, healthcare, which include initiatives to reduce the cost of healthcare generally and drugs specifically. For example, in March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act, or the Healthcare Reform Act, which expanded healthcare coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under government healthcare programs as well as the imposition of annual fees on manufacturers of branded pharmaceuticals. There have been ongoing efforts to modify or repeal all or certain provisions of the Healthcare Reform Act. For example, tax reform legislation was enacted at the end of 2017 that eliminated the tax penalty for individuals who do not maintain mandated health insurance coverage beginning in 2019. The Healthcare Reform Act has also been subject to judicial challenge. In 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the Healthcare Reform Act brought by several states without specifically ruling on the constitutionality of the Healthcare Reform Act.

Beyond the Healthcare Reform Act, there have been ongoing health care reform efforts. Some recent healthcare reform efforts have sought to address certain issues related to the COVID-19 pandemic, including an expansion of telehealth coverage under Medicare and accelerated or advanced Medicare payments to healthcare providers. Other reform efforts affect pricing or payment for drug products. Drug pricing and payment reform was a focus of the Trump Administration and has been a focus of the Biden Administration. For example, in 2022, the Inflation Reduction Act (IRA) of 2022 contains numerous drug pricing and payment reforms. Among other provisions, the IRA imposes a yearly cap ($2,000 in 2025) on out-of-pocket prescription drug costs in Medicare Part D, implements a new Medicare Part D manufacturer discount drug program in 2025; requires manufacturers to pay a rebate to the federal government if prices for single-source drugs and biologicals covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation and, starting in 2026, creates a drug price negotiation program under which the prices for certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be limited by a cap that is defined by reference to, among other things, a specified non-federal average manufacturer price.

Healthcare reform efforts have been and may continue to be subject to scrutiny and legal challenge. For example, revisions to regulations under the federal anti-kickback statute would remove protection for traditional Medicare Part D discounts offered by pharmaceutical manufacturers to pharmacy benefit managers and health plans. Pursuant to court order, the removal was delayed and recent legislation imposed a moratorium on implementation of the rule until January 1, 2032.

Recently, there has been considerable public and government scrutiny of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been efforts at the federal level to implement measures to regulate drug pricing or payment for pharmaceutical products, including legislation on drug importation. There have also been recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices. As another example, legislation passed in 2019 revised how certain prices reported by manufacturers under the Medicaid Drug Rebate Program are calculated and legislation enacted in 2021 eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates if approved for sale. We cannot predict the ultimate content, timing or effect of any changes to the Health

Care Reform Act or other federal and state reform efforts. There is no assurance that federal or state healthcare reform will not adversely affect our future business and financial results.

HUMAN CAPITAL RESOURCES

We believe our employees are among the most important assets to our company and are key to achieving our goals and expectations. Accordingly, we focus significant attention on attracting and retaining talented individuals. To support these objectives, our human resources programs reflect our commitment to our core values (Purposeful, Unwavering, Influential, Insightful and Symbiotic) and are designed to prioritize our employees' well-being, support their career goals, offer competitive wages and benefits, and enhance our culture through efforts aimed at making the workplace more satisfying, engaging and inclusive.

In order to attract qualified applicants to Verastem and retain such employees, we offer a total rewards package consisting of base salary and cash target bonus, a comprehensive benefit package and equity compensation for every employee. Bonus opportunity and equity compensation increase as a percentage of total compensation based on level of responsibility. Actual bonus payout is based on our achievement of corporate goals and individual performance. In addition, many of our employees are stockholders of the company through participation in our Employee Stock Purchase Plan, which aligns the interests of our employees with our stockholders by providing stock ownership on a tax-deferred basis. We also provide for employer matching contributions equal to 100% of employee deferral contributions up to a deferral rate of 6% of eligible compensation to our Section 401(k) retirement savings plan.

As of December 31, 2022, we had 57 full-time equivalent employees, including a total of nine employees with M.D. or Ph.D. degrees, and four part-time employees. Of the full-time equivalent employees, 31 employees are engaged in research and development activities. We consider the intellectual capital of our employees to be an essential driver of our business and key to our success.

None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

BUSINESS—EXECUTIVE OFFICERS OF THE REGISTRANT

The following table sets forth the name, age and position of each of our executive officers as of February 28, 2023.

Name	Age	Position
Executive Officers:		
Brian Stuglik	63	Chief Executive Officer
Daniel Paterson	61	President, Chief Operating Officer
Significant Employees:		
Daniel Calkins	35	Vice President, Finance

Brian Stuglik, age 63, has served as our Chief Executive Officer since July 2019 and as a member of our Board of Directors since September 2017. Mr. Stuglik founded Proventus Health Solutions in January 2016 and has over three decades of experience in U.S. and international pharmaceutical development, product strategy, and commercialization. Prior to founding Proventus Health Solutions, Mr. Stuglik served as the Vice President and Chief Marketing Officer for the oncology division of Eli Lilly and Company, from 2009 to December 2015. Mr. Stuglik received a Bachelor of Science in Pharmacy from Purdue University and holds memberships in the American Society of Clinical Oncology, the American Association of Cancer Research, and the International Association for the Study of Lung Cancer.

Daniel Paterson, age 61, has served as our President since June 2019 in addition to serving as our Chief Operating Officer since December 2014, our Chief Business Officer from July 2013 to December 2014 and as our Vice President, Head of Corporate Development and Diagnostics from March 2012 until July 2013. Prior to joining

us in March 2012, Mr. Paterson was a consultant in 2011. From 2009 through 2010, Mr. Paterson was the Chief Operating Officer of On-Q-ity. Mr. Paterson was the President and Chief Executive Officer of The DNA Repair Company from 2006 until 2009, when it was acquired by On-Q-ity. Previously, he held senior level positions at IMS Health, CareTools, OnCare, and Axion. Mr. Paterson holds a B.A. in Biology from Boston University, and attended the Northeastern University Graduate Pharmacology program.

Daniel Calkins, age 35, has served as our Vice President, Finance since September 2022 in addition to serving as our Corporate Controller since March 2020, our Assistant Controller from May 2019 to March 2020, and our Associate Director, SEC Reporting and Technical Accounting from December 2018 to May 2019. Prior to joining us in December 2018, Mr. Calkins held various positions of increasing responsibility at CFGI from May 2013 to December 2018. Prior to CFGI, Mr. Calkins began his career at PwC LLP in the assurance practice. Mr. Calkins holds a B.S. in Accounting from Bryant University and M.S. in Accounting from Northeastern University.

OUR CORPORATE INFORMATION

We were incorporated under the laws of the State of Delaware in August 2010. Our principal executive offices are located at 117 Kendrick Street, Suite 500, Needham, Massachusetts 02494 and our telephone number is (781) 292-4200.

ADDITIONAL INFORMATION

We maintain a website at www.verastem.com. We make available, free of charge on our website, 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 filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act) as soon as reasonably practicable after we electronically file those reports with, or furnish them to, the SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

ITEM 1A. Risk Factors

Investment in our Common Stock involves a high degree of risk. You should carefully consider the risks that are summarized below and discussed in greater detail in the following pages before making an investment decision. If any of the following risks and uncertainties actually occur, our business, financial condition, and results of operations could be negatively impacted, and you could lose all or part of your investment.

Summary of Risk Factors

- The approval of our product candidates as single agents or part of a combination therapy for the treatment of certain cancers may be more costly than our prior clinical trials, may take longer to achieve regulatory approval, may be associated with new, more severe or serious and unanticipated adverse events, and may have a smaller market opportunity.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for our product candidates, we will not be able to commercialize such candidates, and our ability to generate revenue will be materially impaired.
- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- If serious adverse or unexpected side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- Our approach to the treatment of cancer through cell death, inhibition of tumor growth, and the disruption of the tumor microenvironment is relatively unproven, and we do not know whether we will be able to develop any products of significant commercial value.
- We may need additional funding. If we are unable to raise capital if needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts, including for avutometinib.
- Raising additional capital or entering into certain licensing arrangements may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our product candidates.
- Preclinical testing and clinical trials of our product candidates may not be successful. If we are unable to obtain marketing approval for or successfully commercialize any of our product candidates, or if we experience significant delays in doing so, our business will be materially harmed.
- A pandemic, epidemic or outbreak of an infectious disease, such as COVID-19, has, and may in the future, adversely affect our business.
- We face substantial competition, which may result in others developing or commercializing products before or more successfully than we do.
- We rely in part on third parties to conduct our clinical trials and preclinical testing, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for and commercialize any of our other product candidates.
- We rely on third parties to conduct investigator sponsored clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates.
- We contract with third parties for the manufacture of our product candidates and for compound formulation research, and these third parties may not perform satisfactorily.
- We may not be successful in obtaining necessary rights to compounds and product candidates for our development pipeline through acquisitions and in-licenses.
- If we are unable to obtain and maintain patent protection for our products, or if our licensors are unable to obtain and maintain patent protection for the products that we license from them, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and

commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.

- We depend on Secura for the achievement and payment of the contingent consideration under the asset purchase agreement between us and Secura pursuant to which we sold the COPIKTRA assets to Secura. If Secura is unsuccessful in developing and commercializing COPIKTRA, we may not receive such payments or otherwise capitalize on the market potential of COPIKTRA.
- Our ability to receive future contingent consideration, including milestone payments and royalties, from the sale of our rights, title, and interest in COPIKTRA to Secura may be adversely affected by lower than expected COPIKTRA sales and Secura's ability to achieve other developmental and regulatory milestones.
- We have incurred significant losses since our inception. We may incur losses for the foreseeable future and may never achieve or maintain profitability.
- Our common stock may be at risk for delisting from the Nasdaq Global Market in the future. Delisting could adversely affect the liquidity of our common stock, the market price of our common stock could decrease, and other unfavorable impacts.

Risk Factors

Risks Related to the Development of Our Product Candidates.

We may not be successful in obtaining necessary rights to compounds and product candidates for our development pipeline through acquisitions and in-licenses.

We may seek to acquire new compounds and product candidates from other pharmaceutical and biotechnology companies, academic scientists and other researchers, such as our exclusive in-license from Pfizer, and Chugai to research, develop, commercialize, and manufacture products in oncology indications containing defactinib and avutometinib, respectively. The success of this strategy depends partly upon our ability to identify, select, discover and acquire promising pharmaceutical product candidates and products. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing, and sales resources, may compete with us for the license or acquisition of product candidates and approved products. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We also may be unable to license or acquire the relevant compound or product candidate on terms that would allow us to make an appropriate return on our investment. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including manufacturing, pre-clinical testing, extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development.

In addition, future product or business acquisitions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products, product candidates, or technologies;
- higher than expected acquisition and integration costs;
- increased amortization expenses; and
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions.

Future business acquisitions may also entail certain additional risks, such as:

- difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to motivate key employees of any acquired businesses.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, a further review and analysis of this data may change the conclusions drawn from this unaudited data indicating less promising results than we currently anticipate.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols, and the rate of dropout among clinical trial participants. There also may be significant variability in the safety results obtained through the long-term follow-up of patients from ongoing studies. We do not know whether any clinical trial we may conduct or follow-up data we collect will demonstrate consistent or adequate efficacy and/or safety sufficient to obtain regulatory approval to market our product candidates.

In addition, the design of a clinical trial may determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. 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.

A failure of one or more clinical trials could indicate a higher likelihood that subsequent clinical trials of the same product candidate in the same or other indications or subsequent clinical trials of other related product candidates will be unsuccessful for the same reasons as the unsuccessful clinical trials.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or our participants may drop out of these clinical trials at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks; or
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, 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 or not obtain marketing approval for our product candidates;
- 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 including imposition of a Risk Evaluation and Mitigation Strategy (REMS), or safety warnings, including boxed warnings;
- be subject to additional post marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

The FDA and foreign regulatory authorities may determine that the results from our ongoing and future trials do not support regulatory approval and may require us to conduct an additional clinical trial or trials. If these agencies take such a position, the costs of development of our product candidates could increase materially and their potential market introduction could be delayed. The regulatory agencies could also require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will consider an NDA. Our product development costs will also increase if we experience delays in clinical testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In addition, there are a number of ongoing clinical trials being conducted by other companies for product candidates treating cancer. Patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates, particularly if they view such treatments to be more conventional and established.

Patient enrollment is affected by other factors including:

- the size and nature of the patient population;
- severity of the disease under investigation;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study in relation to other available treatments including any new treatments that may be approved for the indications we are investigating;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;

- proximity and availability of clinical trial sites for prospective patients; and
- constraints on the healthcare system such as COVID-19.

Furthermore, enrolled patients may drop out of a clinical trial, which could impair the validity or statistical significance of the clinical trial. A number of factors can influence the patient discontinuation rate, including, but not limited to:

- the inclusion of a placebo arm in a trial;
- possible inactivity or low activity of the product candidate being tested at one or more of the dose levels being tested;
- the occurrence of adverse side effects, whether or not related to the product candidate; and
- the availability of numerous alternative treatment options, including clinical trials evaluating competing product candidates, that may induce patients to discontinue their participation in the trial.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Preclinical studies and preliminary and interim data from clinical trials of our product candidates are not necessarily predictive of the results or success of ongoing or later clinical trials of our product candidates. If we cannot replicate the results from our preclinical studies and clinical trials of our product candidates, we may be unable to successfully develop, obtain regulatory approval for, and commercialize our product candidates.

Preclinical studies and any positive preliminary and interim data from our clinical trials of our product candidates may not necessarily be predictive of the results of ongoing or later clinical trials. Even if we are able to complete our planned clinical trials of our product candidates according to our current development timeline, the positive results from clinical trials of our product candidates may not be replicated in subsequent clinical trial results. Also, our later stage clinical trials could differ in significant ways from earlier stage clinical trials, which could cause the outcome of the later stage trials to differ from our earlier stage clinical trials. For example, these differences may include changes to inclusion and exclusion criteria, efficacy endpoints and statistical design. Many companies in the pharmaceutical and biotechnology industries, including us, have suffered significant setbacks in late stage clinical trials after achieving positive results in an earlier stage of development. If we fail to produce positive results in our planned clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Our approach to the treatment of cancer through cell death, inhibition of tumor growth, and disruption of the tumor microenvironment is relatively unproven, and we do not know whether we will be able to develop any products of significant commercial value.

We are developing product candidates to treat cancer by using targeted agents to cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment, and thereby thwart the growth and proliferation of cancer cells.

Research on the use of small molecules to cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment is an emerging field and, consequently, there is still uncertainty about whether defactinib and avutometinib are effective in improving outcomes for patients with cancer.

Any products that we develop may not effectively cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment. While we are currently conducting clinical trials for product candidates that we believe will cause cell death, inhibition of tumor growth, and disruption of the tumor microenvironment, we may not ultimately be successful in demonstrating their efficacy, alone or in combination with other treatments.

The approval of our product candidates as single agents or part of a combination therapy for the treatment of certain cancers may be more costly than our prior clinical trials, may take longer to achieve regulatory approval, may be associated with new, more severe or serious and unanticipated adverse events, and may have a smaller market opportunity.

Part of our current business model involves conducting clinical trials to study the effects of combining our product candidates with other approved and investigational targeted therapies, chemotherapies, and immunotherapies to treat patients with cancer. Regulatory approval for a combination treatment generally requires clinical trials to evaluate the activity of each component of the combination treatment. As a result, it may be more difficult and costly to obtain regulatory approval of our product candidates for use as part of a combination treatment than obtaining regulatory approval of our product candidates alone. In addition, we also risk losing the supply of any approved or investigational product being combined with our product candidate in these clinical trials. Furthermore, the potential market opportunity for our product candidates is difficult to estimate precisely. For instance, if one of our product candidates receives regulatory approval from a combination study, it may be approved solely for use in combination with the approved or investigational product in a particular indication and the market opportunity our product candidate would be dependent upon the continued use and availability of the approved or investigational product. In addition, because physicians, patients, and third-party payors may be sensitive to the addition of the cost of our product candidates to the cost of treatment with the other products, we may experience downward pressure on the price that we can charge for our product candidates if they receive regulatory approval. Further, we cannot be sure that physicians will view our product candidates, if approved as part of a combination treatment, as sufficiently superior to a treatment regimen consisting of only the approved or investigational product. Additionally, the adverse side effects of our product candidates may be enhanced when combined with other products. If such adverse side effects are experienced, we could be required to conduct additional pre-clinical and clinical studies, and if such adverse side effects are severe, we may not be able to continue the clinical trials of the combination therapy because the risks may outweigh the therapeutic benefit of the combination.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates, including Novartis AG, Pfizer, Genentech, Inc., AstraZeneca PLC, Mirati, Amgen, Revolution Medicines, Inc., Relay Therapeutics, Inc., Boehringer Ingelheim, Moderna, Inc. and others. 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.

We are developing our product candidates for the treatment of cancer. There are a variety of available therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that our product candidates, if approved, will be priced at a significant premium over competitive generic products.

Many of our competitors 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 approved products. 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 other 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.

In addition, to the extent that products or product candidates of our competitors demonstrate serious adverse side effects or are determined to be ineffective in clinical trials, the commercialization and the development of our product candidates could be negatively impacted.

If we fail to obtain regulatory approval in jurisdictions outside the United States, we will not be able to market our products in those jurisdictions.

We intend to seek regulatory approval for our product candidates in countries outside of the United States and expect that these countries will be important markets for our products, if approved. Marketing our products in these countries will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The regulations that apply to the conduct of clinical trials and approval procedures vary from country to country and may require additional testing. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a drug must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Failure to obtain regulatory approval in one country may have a negative effect on the regulatory approval process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any foreign market.

Preclinical testing and clinical trials of our product candidates may not be successful. If we are unable to obtain marketing approval for or successfully commercialize any of our product candidates, or if we experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the research and development of our product candidates. Our ability to generate product revenues will depend heavily on the successful commercialization and development of our product candidates. The success of our product candidates will depend on several factors, including the following:

- initiation and successful enrollment and completion of our clinical trials;
- receipt of marketing approvals from the FDA and other regulatory authorities for our future product candidates, including pricing approvals where required;
- establishing and maintaining commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- establishing and maintaining commercial capabilities, including hiring and training a sales force, and launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community, and third-party payors;
- securing and maintaining coverage and adequate reimbursement for our products from third party payors;
- effectively competing with other therapies; and
- a continued acceptable safety and efficacy profile of the products following approval.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If we do not achieve one or more of these factors in a timely manner or at all, we could experience

significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

If serious adverse or unexpected side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

Our product candidates are in various stages of clinical development, and their risk of failure is high. It is impossible to predict when or if our other product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk benefit perspective. Patients in our clinical trials have experienced serious adverse events, deemed by us and the clinical investigator to be related to our product candidates. Serious adverse events generally refer to adverse events, that result in death, are life threatening, require hospitalization or prolonging of hospitalization, or cause a significant and permanent disruption of normal life functions, congenital anomalies or birth defects, or require intervention to prevent such outcomes.

Avutometinib and defactinib are being administered and studied in our Phase 1 and Phase 2 clinical trials, and the development program continues to progress. For both avutometinib and defactinib, the toxicities reported to date have been predictable and manageable.

As a result of adverse events observed to date, or further safety or toxicity issues that we may experience in our clinical trials in the future, we may not receive approval to market any product candidates, which could prevent us from ever generating revenue from the sale of products or achieving profitability. Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our products candidates for any or all targeted indications. Many compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound. In addition, while we and our clinical trial investigators currently determine if serious adverse or unacceptable side effects are drug related, the FDA or other non-U.S. regulatory authorities may disagree with our or our clinical trial investigators' interpretation of data from clinical trials and the conclusion that a serious adverse effect or unacceptable side effect was not drug related.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications 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 research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

Any future product candidates that we commercialize may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

In both domestic and foreign markets, any product candidates that may receive marketing approval in the future will depend, in part, on favorable pricing as well as the availability of coverage and amount of reimbursement by third party payors, including governments and private health plans. Substantial uncertainty exists regarding coverage and reimbursement by third party payors of newly approved health care products.

Outside the United States, some countries require approval of the sale price of a drug before the product can be marketed. In many such countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing

governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in product candidates, even if those product candidates obtain marketing approval.

Cost containment is a key trend in the United States and elsewhere. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize the product candidates for which we may obtain marketing approval.

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

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

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we commercialize any future product candidates or if we initiate additional clinical trials in the United States and around the world. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

A pandemic, epidemic, or outbreak of an infectious disease, such as COVID-19, has and may in the future adversely affect our business.

Broad-based business or economic disruptions could adversely affect our ongoing or planned research and development activities, our financial condition and our results of operations. For example, United States residents and businesses in major urban centers have been hit especially hard by the global spread of COVID-19, which has resulted in certain disruptions to our business and may in the future result in additional disruptions to our business. Examples of both include:

- Shortages of personnel at clinical trial sites and delay in startup activities. Shortages in personnel in clinics and hospitals have cause some United States sites to institute limits on new clinical trials which could impact our ability to open new sites for our clinical trials. Clinics in Europe and United States continue to have delays in startup activities due to the ongoing pandemic and the increase in COVID-19 variant infections. In addition, participant dosing, study monitoring and data analysis may be paused or delayed due to changes in hospital or academic institution policies, federal, state, or local

regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the COVID-19 pandemic.

- Accessibility limitations on our contract research organizations ("CROs"). The ability of principal investigators and site staff to perform their functions, who, as healthcare providers, may have heightened exposure to COVID-19, could be disrupted and cause elongation or de-prioritization of our clinical trials, increase the costs related to such development, and materially adversely impact our clinical trial operations.
- Capital markets volatility. Equity and debt markets have experienced significant volatility since the spread of COVID-19 into the United States, which makes it more difficult to raise capital at a reasonable valuation or at all.
- Limitations on third-party manufacturers and distributors. We currently utilize third parties to, among other things, supply raw materials, produce drug substance, drug product, and drug packaging. Some of our third party manufacturers and distributors may in the future be limited and, at times, precluded from delivering us raw materials, drug substance, drug product, and drug packaging on a timely basis, for a variety of reasons, including without limitation to an evolving understanding of how international, federal, and/or state authorities define "essential business", their inability to remain open due to lost business in other parts of their portfolios, or because of international, federal, and/or state prioritization orders requiring our manufacturers to produce for and our distributors to distribute to governmental entities, competitors and/or other companies before they produce for us.
- Health risks for our employees. The health and wellbeing of our employees, including the employees of our third parties is at risk – if a significant number of our personnel were to be diagnosed with COVID-19, placed in quarantine due to potential exposure to COVID-19, or need to care for family members diagnosed with COVID-19, it may result in significant business disruption.
- Work-from-home limitations. We have adopted a hybrid work program allowing our employees the option to primarily work from home, which could impact our ability to effectively plan, execute, communicate, and maintain our corporate culture. The remote working environment could increase our cyber security risk, create data accessibility concerns, and make us more susceptible to communication disruptions.
- Regulatory disruption. There may be interruptions or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines.
- Business interruptions or disruptions. There may be interruptions or disruptions that directly or indirectly adversely affect our or our current or potential collaboration partners' organizations, which may delay or disrupt our business plans or impact a collaboration partner's ability to fully perform under our agreements with them.

Each of these factors could have a material adverse effect on our business and results of operations. The extent to which COVID-19 impacts our results will depend on many factors and future developments, including new information about COVID-19 and any new government regulations which may emerge to contain the virus, among others.

Risks Related to Our Commercial Agreements

We depend on Secura for the achievement and payment of the contingent consideration under the asset purchase agreement between us and Secura pursuant to which we sold the COPIKTRA assets to Secura. If Secura is unsuccessful in developing and commercializing COPIKTRA, we may not receive such payments or otherwise capitalize on the market potential of COPIKTRA.

On September 30, 2020, we completed the disposition of our rights, title, and interest in and to COPIKTRA to Secura. Under the terms of the asset purchase agreement with Secura, we are entitled to contingent consideration, including milestone payments and royalties, dependent upon the further development and commercial success of COPIKTRA. Accordingly, our ability to receive the contingent consideration will depend on Secura's ability to successfully develop and commercialize COPIKTRA.

Secura's ability to develop and commercialize COPIKTRA is subject to a number of risks and uncertainties, including the following:

- Secura has significant discretion in determining how to develop further and commercialize COPIKTRA, including through potential collaborators and partners;
- Secura may not commit sufficient resources to development, marketing or distribution of COPIKTRA;
- even if diligently pursued, Secura's efforts to develop and commercialize COPIKTRA may not be successful;
- Secura may not properly maintain or defend its intellectual property rights or may use its proprietary information in such a way as to invite litigation that could jeopardize or invalidate the intellectual property of COPIKTRA;
- Secura may fail to maintain compliance with ongoing FDA labeling, packaging, storage, advertising, promotion, recordkeeping, safety and other post-market requirements;
- Secura may not be able to obtain regulatory approval in United States for certain oncology indications or obtain approval in jurisdictions outside of the United States and as a result, will not be able to market COPIKTRA for those indications or in those jurisdictions; and
- disputes may arise between Secura and us that result in the delay of payments or in costly litigation that diverts management attention and resources.

Our ability to receive future contingent consideration, including milestone payments and royalties, from the sale of our rights, title, and interest in COPIKTRA to Secura may be adversely affected by lower than expected COPIKTRA sales and Secura's ability to achieve other developmental and regulatory milestones.

On June 30, 2022, the FDA issued a drug safety communication warning that resulted from a clinical trial showing a possible increased risk of death with COPIKTRA compared to another medicine to treat chronic blood cancer called leukemia and lymphoma. The aforementioned clinical trial also found that COPIKTRA was associated with a higher risk of serious side effects, including infections, diarrhea, inflammation of the intestines and lungs, skin reactions, and high liver enzyme levels in the blood. In September 2022, the FDA's Oncologic Drug Advisory Committee ("ODAC") voted eight to four against COPIKTRA's use in patients with relapsed or refractory chronic lymphocytic leukemia/ small lymphocytic lymphoma after at least two prior therapies citing an unfavorable risk/benefit profile. The FDA drug safety communication warning, the FDA's ODAC vote, future actions by the FDA, and any safety concerns associated with COPIKTRA, perceived or real, may materially and adversely affect Secura's development and commercialization success of COPIKTRA and, consequently, our ability to receive future contingent consideration from our sale of our right, title, and interest in COPIKTRA to Secura.

If we do not realize the anticipated benefits of our license agreements with Pfizer for the FAK program and Chugai for the dual RAF/MEK candidate program, our business could be adversely affected.

Our license agreements with Pfizer for defactinib and Chugai for avutometinib may fail to further our business strategy as anticipated or to achieve anticipated benefits and success. We may make or have made assumptions relating to the impact of the acquisition of defactinib and avutometinib on our financial results relating to numerous matters, including:

- the cost of development and commercialization of defactinib and avutometinib; and
- other financial and strategic risks related to the license agreements with Pfizer and Chugai.

Further, we may incur higher than expected operating and transaction costs, and we may encounter general economic and business conditions that adversely affect us relating to our license agreements with Pfizer and Chugai. If one or more of these assumptions are incorrect, it could have an adverse effect on our business and operating results, and the benefits from our license agreements with Pfizer for defactinib and Chugai for avutometinib may not be realized or be of the magnitude expected.

Risks Related to Our Financial Position and Need for Additional Capital

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

Since inception, we have incurred significant operating losses. As of December 31, 2022, we had an accumulated deficit of $737.5 million. To date, we have generated minimal product revenues and have financed our operations primarily through public and private offerings of our common stock and preferred stock, sales of our common stock pursuant to our at-the-market equity offering programs, our loan and security agreement (the "Loan Agreement") with Oxford Finance LLC ("Oxford"), our loan and security agreement, as amended, with Hercules Capital Inc. ("Hercules"), the issuance of our 5.00% Convertible Senior Notes due 2048 ("2018 Notes"), upfront payments under our license and collaboration agreements with Yakult, CSPC, and Sanofi, and the upfront payment under the Secura APA. We have devoted substantially all of our efforts to research and development. We expect to continue to incur significant expenses and may incur operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our ongoing clinical trials with our product candidates, including with defactinib and avutometinib;
- initiate additional clinical trials for our product candidates;
- maintain, expand, and protect our intellectual property portfolio;
- acquire or in-license other products and technologies;
- hire additional clinical, development, and scientific personnel; and
- establish and maintain a sales, marketing and distribution infrastructure to commercialize any products for which we obtain marketing approval.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, and manufacturing, marketing, and selling those products for which we may obtain marketing approval. 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 research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We may need additional funding. If we are unable to raise capital if needed, we would be forced to delay, reduce, or eliminate our product development programs or commercialization efforts, including for avutometinib.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical development of our product candidates. We expect our existing cash resources at December 31, 2022 will be sufficient to fund our current operating plan and capital expenditure requirements through at least next twelve months from the issuance date of these financial statements. This estimate does not reflect the possibility that we may not be able to access a portion of our existing cash, cash equivalents and investments due to market conditions. For example, on March 10, 2023, the Federal Deposit Insurance Corporation (the "FDIC"), took control and was appointed receiver of Silicon Valley Bank ("SVB"). On March 12, 2023, the Department of the Treasury, the Federal Reserve, and the FDIC announced that all depositors of SVB will be fully protected and have access to all their money starting March 13, 2023. As of March 13, 2023, we had approximately $2 million on deposit at SVB. If other banks and financial institutions enter receivership or become insolvent in the future in response to financial conditions affecting the banking system and financial markets, our ability to access our existing cash, cash equivalents and investments may be threatened and could have a material adverse effect on our business and financial condition.

We may need to obtain additional funding in connection with our continuing operations, including for our clinical development programs. Our future capital requirements will depend on many factors, including:

- the scope, progress, and results of our ongoing and potential future clinical trials;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs, timing, and outcome of regulatory review of our product candidates (including our efforts to seek approval and fund the preparation and filing of regulatory submissions);
- revenue received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending intellectual property related claims; and
- our ability to establish collaborations or partnerships on favorable terms, if at all.

Conducting clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval of any of our product candidates. Our commercial revenues will be derived from sales of products. Even if our product candidates gain approval, it may take several years to achieve a significant level of sales, and as a result we may need to continue to rely on additional financing to further our clinical development objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Unfavorable economic conditions could have a material adverse effect on our business, financial condition, results of operations, or cash flows.

Unfavorable macroeconomic conditions and other adverse macroeconomic factors have resulted, among other matters, in tightening in the debt and equity markets, and high levels of inflation. For example, tightening of the equity markets, makes it more difficult to raise capital at a reasonable valuation or at all. In addition, the U.S. Bureau of Labor Statistics has reported for the period from June 2021 to June 2022, the Consumer Price Index for All Urban Consumers rose 9.1 percent, which is the largest increase since the 12 month period ended November 1981. The U.S. Bureau of Labor Statistics reported for the period from December 2021 to December 2022, the Consumer Price Index for All Urban Consumers increased 6.5 percent. If the inflationary pressure continues for a prolonged period, it may continue to result in increased costs of labor, cost of clinical trials, and costs of manufacturing which could adversely affect our results of operations.

Our ability to use our net operating loss carryforwards may be limited.

As of December 31, 2022, we had U.S. federal and state net operating loss ("NOL") carryforwards of approximately $436.6 million and $203.3 million, respectively. As of December 31, 2022, we also had federal and state tax credits of $5.6 million and $1.9 million, respectively, which may be used to offset future tax liabilities. The NOL and tax credit carryforwards will expire at various dates through 2042, except for $240.9 million of federal NOL carryforwards which may be carried forward indefinitely. Sections 382 and 383 of the Internal Revenue Code and similar provisions under state law limits the annual use of NOL carry-forwards and tax credit carryforwards, respectively, following an ownership change pursuant to section 382 of the Internal Revenue Code and similar state provisions. In general, an ownership change occurs for purposes of Section 382 if there are certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%.

Based on our analysis under Section 382, we believe that our federal NOL carryforwards, state NOL carryforwards, research and development credits, and orphan drug credits are limited by Section 382 and similar provisions under state law as of December 31, 2022. The portion of federal NOL carryforwards, state NOL carryforwards, research and development credits, and orphan drug credits that were determined to be limited by Section 382 and similar provisions under state law have been written off as of December 31, 2022. Future changes in our stock ownership, some of which are outside of our control, could result in ownership changes in the future. We may not be able to use some or all of our NOL and tax credit carryforwards, even if we attain profitability.

Risks Related to Our Indebtedness

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.

In March 2022, we entered into a Loan Agreement with Oxford, as collateral agent and a lender, and Oxford Finance Credit Fund III LP, as a lender ("OFCF III" and together with Oxford, the "Lenders"), pursuant to which the Lenders have agreed to lend us up to an aggregate principal amount of $150.0 million in a series of term loans (the "Term Loans"). As of December 31, 2022, there was $25.0 million outstanding under the Loan Agreement. In connection with the Loan Agreement, we granted Oxford a security interest in all of our personal property now owned or hereafter acquired, excluding intellectual property (but including the right to payments and proceeds of intellectual property), and a negative pledge on 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 other important negative consequences, including 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 research and development efforts and other general corporate activities.

To the extent additional debt is added to our current debt levels, the risks described above could increase.

We may not have cash available in an amount sufficient to enable us to make interest or principal payments on our indebtedness when due.

Failure to satisfy our current and future debt obligations under the Loan Agreement or breaching any covenants under the Loan Agreement, subject to specified cure periods with respect to certain breaches, could result in an event of default and, as a result, could accelerate all of the amounts due. In the event of an acceleration of amounts due under the Loan Agreement, we may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time of such acceleration. In that case, we may be required to delay, limit, reduce or terminate our product candidate development or grant to others the rights to develop and market our product candidates that we would otherwise prefer to develop and market internally. Oxford could also exercise its rights as collateral agent to take possession and dispose of the collateral securing the term loans for its benefit, which collateral includes substantially all of our property other than our intellectual property. Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events.

Risks Related to Our Dependence on Third Parties

We rely in part on third parties to conduct our clinical trials and preclinical testing, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for and commercialize any of our other product candidates.

We rely on third parties, such as CROs, clinical data management organizations, medical institutions, and clinical investigators, to conduct, provide monitors for, and manage data from all of our clinical trials. We compete with many other companies for the resources of these third parties.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and ultimately the commercialization of our product candidates.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA and other regulatory agencies require us to comply with standards, commonly referred to as Good Clinical Practices ("GCP") for conducting, recording, and reporting the results of clinical trials to assure

that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. We also are required to register ongoing clinical trials and post the results of completed clinical trials on government-sponsored databases, such as ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity, and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for some of our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We rely on third parties to conduct investigator-sponsored clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates.

We rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to our product candidates. We will not control the design or conduct of the investigator sponsored trials, and it is possible that the FDA or non-U.S. regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results.

Such arrangements will provide us certain information rights with respect to the investigator sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator-sponsored trials, nor do we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

Additionally, the FDA or non-U.S. regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing, or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing, or clinical data from these investigator-sponsored trials. If so, the FDA or other non-U.S. regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and/or may not accept such additional data as adequate to initiate our planned trials.

We contract with third parties for the manufacture of our product candidates and for compound formulation research, and these third parties may not perform satisfactorily.

We do not have any manufacturing facilities or personnel. We currently obtain all of our supply of our product candidates for clinical development from third-party manufacturers or third-party collaborators, and we expect to continue to rely on third parties for the manufacture of clinical quantities of our product candidates. In addition, we currently rely on third parties for the development of various formulations of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost or quality, which could delay, prevent, or impair our development or commercialization efforts.

We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance or drug product. Even though we have supply agreements in place with our 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, including the misappropriation of our proprietary information, trade secrets, and know-how;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- disruptions to the operations of our manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and harm our business and results of operations.

Any products that we may develop may compete with other product candidates and products 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 interruption of the development or operation of the manufacturing facilities due to, among other reasons, events such as order delays for equipment or materials, equipment malfunction, quality control, and quality assurance issues, regulatory delays and possible negative effects of such delays on supply chains and expected timelines for product availability, production yield issues, shortages of qualified personnel, discontinuation of a facility or business, failure, or damage to a facility by natural disasters or public health crises, such as the COVID-19 pandemic, could result in the cancellation of shipments, loss of product in the manufacturing process, or a shortfall in available product candidates or materials.

If our current contract manufacturers cannot perform as agreed or these parties cease to provide quality manufacturing and related services to us, we may be required to replace that manufacturer. If we are not able to engage appropriate replacements in a timely manner, our ability to manufacture our product candidates in sufficient quality and quantity required for planned pre-clinical testing, clinical trials and potential commercial use of our product candidates would be adversely affected. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement, as well as producing the drug product and obtaining regulatory approvals for the new manufacturer. In addition, we have to enter into technical transfer agreements and share our know-how with the third-party manufacturers, which can be time consuming and may result in delays. In light of the lead time needed to manufacture our product candidates, and the availability of underlying materials, we may not be able to, in a timely manner or at all, establish or maintain sufficient commercial manufacturing arrangements on commercially reasonable terms necessary to provide adequate supply of our product candidates to meet demands that exceed our clinical assumptions. Furthermore, we may not be able to obtain the significant financial capital that may be required in connection with such arrangements. Even after successfully engaging third parties to execute the manufacturing process for our product candidates, such parties may not comply with the terms and timelines they have agreed to for various reasons, some of which may be out of their or our control, which could impact our ability to execute our business plans on expected or required timelines in connection with the commercialization of and the continued development of our product candidates. We may also be required to enter into long-term manufacturing agreements that contain exclusivity provisions and/or substantial termination penalties, which could have a material adverse effect on our business prior to and after commercialization.

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

If we are not able to establish collaborations, we may have to alter our development and commercialization plans.

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

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, and the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. 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 certain product candidates, reduce or delay our development programs, delay potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We may depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates.

We may seek third-party collaborators for the development and commercialization of our product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, and biotechnology companies. If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product

candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

Our operations in foreign jurisdictions, and those of third parties for which we rely on, may be impacted by economic, political and social conditions in such jurisdictions.

Tensions between the Ukraine and Russia have escalated in recent months, culminating in Russia's recent invasion of the Ukraine. While we do not currently have clinical trials in Ukraine or Russia, we have clinical trial sites in Europe. We also source clinical supply for our product candidates from third party contract manufacturing organizations in Europe. Furthermore, Secura's sublicensee, Sanofi, has exclusive rights to develop and commercialize products containing duvelisib in Russia, the Commonwealth of Independent States ("CIS") including Ukraine, Turkey, the Middle East and Africa (collectively the "Sanofi Territory") for which we are entitled to receive future milestones and royalties pursuant to the Secura APA. The invasion of Ukraine and the retaliatory measures taken or that may be taken by the United States, North Atlantic Treaty Organization ("NATO") and others create global security concerns, including the possibility of expanded regional or global conflict, and are likely to have short-term and likely longer-term negative impacts on regional and global economies, any or all of which could disrupt our supply chain, adversely affect our ability to conduct ongoing and future clinical trials of our product candidates, and the recognition of future milestones and royalties pursuant to the Secura APA in the Sanofi Territory.

Risks Related to Our Intellectual Property

If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements with third parties, including Pfizer and Chugai, and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance, and other obligations on us. For example, under our license agreements with Pfizer and Chugai, we are required to use diligent or commercially reasonable efforts to develop and commercialize licensed products under the agreement and to satisfy other specified obligations. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or to convert the exclusive licenses to non-exclusive licenses, which could materially adversely affect the value of the product candidate being developed under these license agreements. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, which may not be possible. If Pfizer were to terminate its license agreement with us for any reason, we would lose our rights to defactinib. If Chugai were to terminate its license agreement with us for any reason, we could lose our rights to avutometinib.

If we are unable to obtain and maintain patent protection for our products, or if our licensors are unable to obtain and maintain patent protection for the products that we license from them, or if the scope of the patent

protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent protection in the United States and other countries with respect to our products. We and our licensors seek to protect our proprietary position by filing patent applications in the United States and abroad related to our products that are important to our business. We cannot be certain that any patents will issue with claims that cover our product candidates.

The patent prosecution process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering products that we license from third parties and are reliant on our licensors. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

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. As a result, the issuance, scope, validity, enforceability, and commercial value of our and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our products or which effectively prevent others from commercializing competitive 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.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. 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, at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, in the United States, for patents that have an effective filing date prior to March 15, 2013, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. In March 2013, the United States transitioned to a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter parties review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding, or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our owned and licensed 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 abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical products, or limit the duration of the patent protection of our 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.

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

Competitors may infringe our patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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, our licensors may have rights to file and prosecute such claims, and we are reliant on them.

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.

Our commercial success depends upon our ability and the ability of our collaborators to commercialize, develop, manufacture, market, and sell our product candidates without infringing the proprietary rights of third parties. We have yet to conduct comprehensive freedom to operate searches to determine whether our use of certain of the patent rights owned by or licensed to us would infringe patents issued to third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products, including interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products. 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 product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

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 we or these employees 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. If we fail in 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 defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we 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 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 also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive, and time consuming, and the outcome is unpredictable. In addition, some courts 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 from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Achieving Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

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

Obtaining approval of an NDA can be a lengthy, expensive, and uncertain process. The activities associated with a product candidate's development and commercialization, including its design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for product candidates will prevent us from commercializing such product candidates. We have not received approval to market any of our current product candidates from regulatory authorities in any jurisdiction in the United States. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish the product candidate's safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. A product candidate may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, 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. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical, or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing

could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be subject to more limited indications than those we propose or subject to restrictions or post approval commitments that render the approved product not commercially viable.

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

We have received orphan drug designation for certain of our product candidates, but there can be no assurance that we will be able to prevent third parties from developing and commercializing products that are competitive to these product candidates.

We received orphan drug designation in the United States and European Union for the use of defactinib in ovarian cancer, and in the United States, the European Union, and Australia for the use of defactinib in mesothelioma. Orphan drug exclusivity grants seven years of marketing exclusivity under the Federal Food, Drug and Cosmetic Act ("FDCA"), up to ten years of marketing exclusivity in Europe, and five years of marketing exclusivity in Australia. Other companies have received orphan drug designations for compounds other than defactinib for the same indications for which we may have received orphan drug designation in corresponding territories. While orphan drug exclusivity for defactinib provides market exclusivity against the same active ingredient for the same indication, we would not be able to exclude other companies from manufacturing and/or selling drugs using the same active ingredient for the same indication beyond that timeframe on the basis of orphan drug exclusivity. Furthermore, the marketing exclusivity in Europe can be reduced from ten years to six years if the orphan designation criteria are no longer met or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Even if we are the first to obtain marketing authorization for an orphan drug indication, there are circumstances under which the FDA may approve a competing product for the same indication during the seven-year period of marketing exclusivity, such as if the later product is the same compound as our product but is shown to be clinically superior to our product, or if the later product is a different drug than our product candidate. Further, the seven-year marketing exclusivity would not prevent competitors from obtaining approval of the same compound for other indications or of another compound for the same use as the orphan drug. A decision in 2021 by the U.S. Court of Appeals for the Eleventh Circuit in *Catalyst Pharmaceuticals, Inc. vs. Becerra* regarding interpretation of the Orphan Drug Act's exclusivity provisions as applied to drugs and biologics approved for orphan indications narrower than the product's orphan designation has the potential to significantly broaden the scope of orphan exclusivity for such products. FDA announced on January 24, 2023 that despite the *Catalyst* decision, it will continue to apply its longstanding regulations, which tie the scope of orphan exclusivity to the uses or indications for which the drug is approved, rather than to the designation. FDA's application of its orphan drug regulations post-*Catalyst* could be the subject of future legislation or to further challenges in court, which could impact our ability to obtain or seek to work around orphan exclusivity, and might affect our ability to retain orphan exclusivity that the FDA previously has recognized for our products.

We may seek fast track designation for one or more of our product candidates, but we might not receive such designation, and even if we do, such designation may not actually lead to a faster development or regulatory review or approval process, and it does not ensure that we will receive marketing approval.

Any sponsor may seek fast track designation for a drug if it is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for FDA fast track designation. If we seek fast track designation for a product candidate, we may not receive it from the FDA. However, even if we receive fast track designation, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

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

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance, and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post marketing testing and surveillance to monitor the safety or efficacy of the product, including the imposition of a REMS.

The FDA closely regulates the post approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off label marketing.

In addition, later discovery of previously unknown 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 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 revenue;
- 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.

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 candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may fail to obtain any marketing approvals, lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Our business operations, including our relationships with healthcare providers, third-party payors, and patients, 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.

Healthcare providers, including physicians, and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, third-party payors, patients and other parties within the healthcare industry may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell, and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare and regulatory laws and regulations within the United States include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in

kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the anti-kickback statute or specific intent to violate it in order to have committed a violation;

- the federal False Claims Act ("FCA"), which imposes criminal and civil penalties on individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government and actions under the FCA may be brought by private whistleblowers as well as the government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the FCA;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also establishes requirements related to the privacy, security, and transmission of individually identifiable health information which apply to many healthcare providers, physicians, and third-party payors with whom we interact;
- the federal false statements statute prohibits 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;
- the federal anti-kickback prohibition known as Eliminating Kickbacks in Recovery Act, or EKRA, which prohibits certain payments related to referrals of patients to certain providers (recovery homes, clinical treatment facilities, and laboratories) and applies to services reimbursed by private health plans as well as government health care programs;
- the FDCA, which, among other things, strictly regulates drug product and medical device marketing, prohibits manufacturers from marketing such products for off-label use and regulates the distribution of samples;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under governmental healthcare programs;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the so-called federal "sunshine law" or Open Payments which requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to teaching hospitals, physicians, and other healthcare practitioners, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and state laws which regulate interactions between pharmaceutical companies and healthcare providers, require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, require pharmaceutical companies to report information on transfers of value to other healthcare providers, marketing expenditures or pricing information and/or require licensing of sales representatives. State laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Similar healthcare and data privacy laws and regulations exist in the European Union and other foreign jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of certain protected information. For example, in May 2018, a new privacy regime, the General Data Protection Regulation ("GDPR"), took effect enhancing our obligations with respect to operations in the European Economic Area ("EEA"), and increasing the scrutiny applied to transfers of personal data from the EEA (including health data from our clinical sites in the EEA) to countries that are considered by the European Commission to lack an adequate level of data protection, such as the United States. The compliance obligations imposed by the GDPR have required us to revise our operations and increased our cost of doing business. In addition, the GDPR imposes substantial fines for breaches of data protection requirements, and it confers a private right of action on data subjects for breaches of data protection requirements. In connection with the separation from the European Union, the United Kingdom adopted similar legislation.

The number and complexity of both federal and state laws continues to increase; the laws contain ambiguous requirements or require administrative guidance for implementation; government interpretations of the laws continue to evolve; and additional governmental resources are being used to enforce these laws and to prosecute companies and individuals who are believed to be violating them. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Governmental authorities may potentially conclude that our business practices, including arrangements we may have with physicians and other healthcare providers, or patient assistance programs, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs. Further, defending against any such actions can be costly, time-consuming and may require significant 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.

Our employees, independent contractors, principal investigators, CROs, consultants, and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraud or other misconduct, including intentional failures to: comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could,

among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post approval activities, and affect our ability to profitably sell any of our product candidates for which we obtain marketing approval.

The U.S. healthcare industry generally and U.S. government healthcare programs in particular are highly regulated and subject to frequent and substantial changes. The U.S. government and individual states have been aggressively pursuing healthcare reform. For example, the Healthcare Reform Act, enacted in March 2010, was intended to broaden access to health insurance through a Medicaid expansion and the implementation of the individual mandate for health insurance coverage, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry, and impose additional health policy reforms. The law, for example, increased drug rebates under state Medicaid programs for brand name prescription drugs and extended those rebates to Medicaid managed care and assessed a fee on manufacturers and importers of brand name prescription drugs reimbursed under certain government programs, including Medicare and Medicaid.

There have been ongoing efforts to modify or repeal certain provisions of the Healthcare Reform Act For example, tax reform legislation was enacted at the end of 2017 that eliminated the tax penalty for individuals who do not maintain mandated health insurance coverage beginning in 2019. The Healthcare Reform Act has also been subject to judicial challenge. In 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the Healthcare Reform Act brought by several states without specifically ruling on the constitutionality of the Healthcare Reform Act.

Beyond the Healthcare Reform Act, there have been ongoing health care reform efforts, some of which affect pricing or payment for drug products. For example, legislation enacted in 2018 increased the discount that manufacturers of Medicare Part D brand name drugs must provide to Medicare Part D beneficiaries during the coverage gap from 50% to 70% starting in 2019. The Biden Administration has focused on increasing access to health care coverage as well as drug pricing and payment reform. As an example, legislation enacted in 2021 eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. As another example, in 2022, the Inflation Reduction Act (IRA) of 2022 contains numerous drug pricing and payment reforms. Among other provisions, the IRA imposes a yearly cap ($2,000 in 2025) on out-of-pocket prescription drug costs in Medicare Part D, implements a new Medicare Part D manufacturer discount drug program in 2025; requires manufacturers to pay a rebate to the federal government if prices for single-source drugs and biologicals covered under Medicare Part B and nearly all covered drugs under Part D increase faster than the rate of inflation and, starting in 2026, creates a drug price negotiation program under which the prices for certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be limited by a cap that is defined by reference to, among other things, a specified non-federal average manufacturer price. We continue to evaluate federal and state health care reform efforts and the effect that such efforts may have on our business. Healthcare reform measures that may be adopted in the future could have a material adverse effect on our industry generally and on our ability to successfully commercialize our products and product candidates.

In addition, other broader legislative changes have been adopted that could have an adverse effect upon, and could prevent, our products' commercial success. For example, the Budget Control Act of 2011, as amended, resulted in the imposition of reductions in Medicare (but not Medicaid) payments to providers in 2013 and remains in effect through 2031 (except May 1, 2020 to March 31, 2022) unless additional Congressional action is taken. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price constraints, restrictions on copayment assistance by pharmaceutical manufacturers, marketing cost disclosure and transparency measures, and, in some cases, measures designed to encourage importation from other countries and bulk purchasing.

We cannot be sure whether additional legislative changes will be enacted, or whether the regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals 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 testing and other requirements.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Brian Stuglik, Chief Executive Officer and Daniel Paterson, our President and Chief Operating Officer. Although we have formal employment agreements with Brian Stuglik and Daniel Paterson, these agreements do not prevent them from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing, and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, universities, and research institutions for similar personnel. Although we have implemented a retention plan for certain key employees, our retention plan may not be successful in incentivizing these employees to continue their employment with us. 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, including our scientific co-founders, 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.

We may expand our development, regulatory and future sales and marketing capabilities over time, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We may experience significant growth over time in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs, and sales and marketing. To manage our anticipated future growth, we may continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel when we expand. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our business and operations may be materially adversely affected in the event of computer system breaches or failures.

Despite our effort to implement security measures, our internal computer systems, and those of our contract research organizations and other third parties, including software providers, on which we rely, are vulnerable to damage from computer viruses, ransomware, unauthorized access, natural disasters, fire, terrorism, war, and telecommunication and electrical failures. Cybersecurity breaches may be the result of negligent or unauthorized activity by our employees and contractors, as well as by third parties who use cyberattack techniques involving malware, ransomware, hacking and phishing, among others. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our key business processes and clinical development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory 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 inappropriate disclosure of confidential or proprietary information, we could be exposed to liability, which could have a material adverse effect on our operating results and financial condition, affect our reputation, undermine market and

commercial confidence, erode goodwill, and possibly delay the further development and commercialization of our product candidates.

Risks Related to Our Capital Stock

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, 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 corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition, or other change in control of us 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. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- 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 the board;
- 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 affected 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 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

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.

The market price of our common stock has been, and may continue to be, highly volatile.

Our stock price has been volatile. Since January 27, 2012, when we became a public company, the price for one share of our common stock has reached a high of $18.82 and a low of $0.30 through December 31, 2022. We cannot predict whether the price of our common stock will rise or fall. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;

- the results of our efforts to discover, develop, acquire, or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market in general and the market for small pharmaceutical companies and biotechnology companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of particular companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

Our common stock may be at risk for delisting from the Nasdaq Global Market in the future. Delisting could adversely affect the liquidity of our common stock, the market price of our common stock could decrease, and other unfavorable impacts.

Our common stock is currently listed on the Nasdaq Global Market. The Nasdaq Stock Market LLC ("Nasdaq") has minimum requirements that a company must meet in order to remain listed on the Nasdaq Global Market, including a requirement that we maintain a minimum closing bid price of $1.00 per share. On November 4, 2022 we received a letter from the listing qualifications department (the "Staff") of Nasdaq notifying us that for the last 30 consecutive business days the bid price of our common stock had closed below $1.00 per share minimum bid price requirement for continued inclusion on the Nasdaq Global Market pursuant to Nasdaq Listing Rule 5450(a)(1) (the "Bid Price Requirement").

In accordance with Nasdaq Listing Rule 5810(c)(3)(A) (the "Compliance Period Rule"), we have been provided a period of 180 calendar days, or until May 3, 2023 (the "Compliance Date"), to regain compliance with the Bid Price Requirement. If, at any time before the Compliance Date, the bid price for the common stock closes at $1.00 or more for a minimum of 10 consecutive business days, as required under the Compliance Period Rule, the Staff will provide written notification to us that it has regained compliance with the Bid Price Requirement.

If we do not regain compliance with the Bid Price Requirement by the Compliance Date, we may be eligible for an additional 180 calendar day compliance period. To qualify, we will be required to meet the continued listing requirement for market value of its publicly held shares and all other initial listing standards for The Nasdaq Global Market, with the exception of the Bid Price Requirement, and will need to provide written notice of our intention to cure the deficiency during the second 180 calendar day compliance period, by effecting a reverse stock split, if necessary.

If we do not regain compliance with the Bid Price Requirement by the Compliance Date and are not eligible for an additional compliance period at that time, or the Staff concludes that we will not be able to cure the deficiency during the additional compliance period, the Staff will provide written notification to us that our common stock will be subject to delisting. At that time, we may appeal the Staff's delisting determination to a Nasdaq hearings panel. However, there can be no assurance that, if we receive a delisting notice and appeals the delisting determination by the listing qualifications department of Nasdaq to the Nasdaq hearings panel, such appeal would be successful.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the Bid Price Requirement, which could include seeking to effect a reverse stock split. However, there can be no assurance that we will be able to regain compliance with the Bid Price Requirement.

The delisting of our common stock would significantly affect the ability of investors to trade our common stock and negatively impact the liquidity and price of our common stock. In addition, the delisting of our common stock could materially adversely impact our ability to raise capital on acceptable terms or at all. Delisting from Nasdaq could also have other negative results, including the potential loss of confidence by our current or prospective third-party providers and collaboration partners, the loss of institutional investor interest, the triggering of a default under the Loan Agreement with Oxford, which in turn could cause our borrowings to become immediately due, and fewer licensing and partnering opportunities.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings to finance the growth and development of our business. In addition, the terms of any current or 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.

We can issue and have issued shares of preferred stock, which may adversely affect the rights of holders of our common stock.

We have in the past issued, and we may at any time in the future issue, shares of preferred stock, and as of February 28, 2023 we have 1,000,000 shares of our Series A convertible preferred stock, par value $0.0001 per share (the "Series A Preferred Stock") and 1,200,000 shares of our Series B convertible preferred stock, par value $0.0001 per share (the "Series B Preferred Stock" and together with the Series A Preferred Stock, the "Preferred Stock") outstanding. Our amended and restated certificate of incorporation authorizes us to issue up to 5,000,000 shares of preferred stock with designations, rights and preferences determined from time-to-time by our board of directors. Accordingly, our board of directors is empowered, without stockholder approval, to issue preferred stock with dividend, liquidation, conversion, voting or other rights superior to those of holders of our common stock. For example, our Series B Preferred Stock ranks senior to our common stock, and the holders of our Series B Preferred Stock are entitled to a liquidation preference of $1.00 per share of Series B Preferred Stock in the event of our liquidation, dissolution or winding up, which could limit or eliminate any payments that the holders of our common stock could expect to receive upon our liquidation. Additionally, holders of our Preferred Stock are entitled to receive, on an as converted basis, dividends and consideration in the event of certain transactions equivalent to the dividends and consideration received by the holders of our common stock, which would make paying dividends and engaging in certain transactions more expensive. We also may not make any changes to our amended and restated certificate of incorporation that would limit the rights of the holders of our either series of our preferred stock without the affirmative vote of a majority of such series of preferred stock, which may make it more difficult to take certain corporate actions in the future.

Our stockholders will experience substantial dilution if shares of our Series B Preferred Stock are converted into common stock.

As of February 28, 2023, there were 1,200,000 shares of our Series B Preferred Stock outstanding, which are convertible without payment of additional consideration into 50,838,840 shares of our common stock, subject to certain ownership limitations. The conversion of the outstanding shares of our Series B Preferred Stock into common stock would be substantially dilutive to existing stockholders. Any dilatation or potential dilution may cause our stockholders to sell their shares, which may contribute to a downward movement in the stock price of our common stock.

Raising additional capital or entering into certain licensing arrangements may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, grants and government funding, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. To the

extent that we enter into certain licensing arrangements, the ownership interest of our existing stockholders may be diluted if we elect to make certain payments in shares of our common stock. 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 additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish future revenue streams or valuable rights to product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings 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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We occupy approximately 27,810 square feet of office space in Needham, Massachusetts under a lease that expires in June 2025. We believe that our facility is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings

From time to time, we are subject to various legal proceedings and claims that arise in the ordinary course of our business activities. We do not believe we are currently party to any pending legal action, the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business or operating results.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

MARKET INFORMATION

Our common stock is publicly traded on The Nasdaq Global Market under the symbol "VSTM."

HOLDERS

As of February 28, 2023 there were 7 holders of record of our common stock and the closing price of our common stock on The Nasdaq Global Market as of that date was $0.52. The number of holders of record does not include beneficial owners whose shares are held by nominees in street name.

DIVIDENDS

We have never declared or paid cash dividends on our common stock, and we do not expect to pay any cash dividends on our common stock in the foreseeable future.

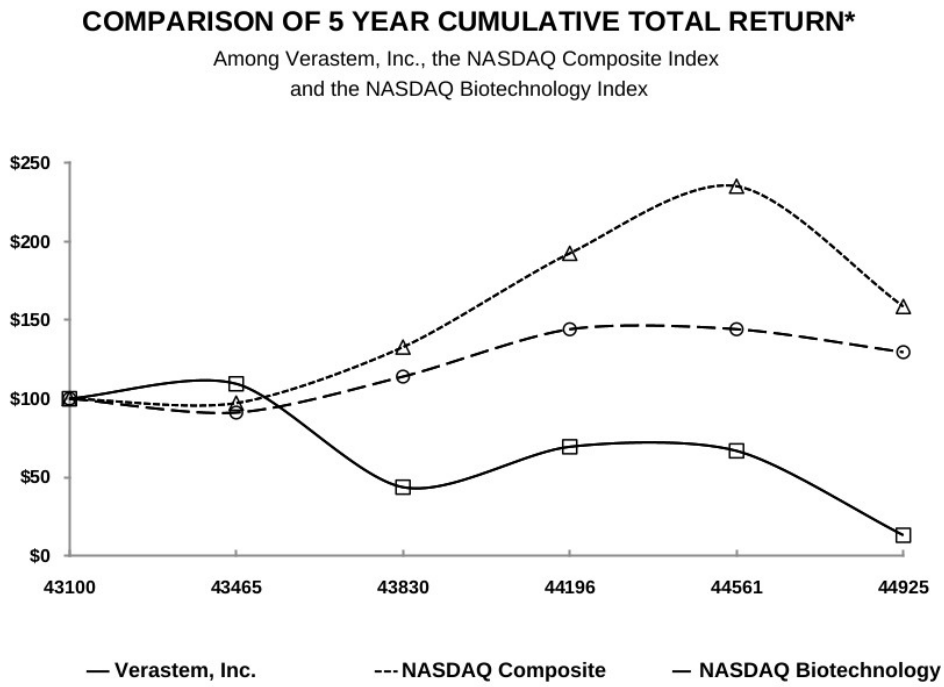
SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS

The information required by this Item 5 of Form 10-K regarding equity compensation plans will be included in our 2023 Proxy Statement and is incorporated herein by reference.

PERFORMANCE GRAPH

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933, as amended, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our common stock to the Nasdaq Composite Index and to the Nasdaq Biotechnology Index from December 31, 2017 through December 31, 2022. The comparison assumes $100 was invested after the market closed on December 31, 2017 in our common stock and in each of the foregoing indices, and it assumes reinvestment of dividends, if any.



Cumulative Total Return Comparison

	December 31,					
	2017	2018	2019	2020	2021	2022
Verastem, Inc.	100.00	109.45	43.65	69.38	66.78	13.11
NASDAQ Composite	100.00	97.16	132.81	192.47	235.15	158.65
NASDAQ Biotechnology	100.00	91.14	114.03	144.15	144.18	129.59

PURCHASE OF EQUITY SECURITIES

We did not purchase any of our equity securities during the period covered by this Annual Report on Form 10-K.

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 consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results and the timing of certain events could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including those discussed below and as set forth under "Risk Factors." Please also refer to the section under the heading "Forward-Looking Statements."

OVERVIEW

We are a late-stage development biopharmaceutical company, with an ongoing registration directed trial, committed to advancing new medicines for patients battling cancer. Our pipeline is focused on novel anticancer agents that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, particularly RAF/MEK inhibition and FAK inhibition.

Our most advanced product candidates, avutometinib (VS-6766) and defactinib, are being investigated in both preclinical and clinical studies for the treatment of various solid tumors, including, but not limited to low-grade serous ovarian cancer ("LGSOC"), non-small cell lung cancer ("NSCLC"), colorectal cancer ("CRC"), pancreatic cancer, and melanoma. We believe that avutometinib may be beneficial as a therapeutic as a single agent or when used together in combination with defactinib, other agents, other pathway inhibitors or other current and emerging standard of care treatments in cancers that do not adequately respond to currently available therapies.

On August 10, 2020, we and Secura Bio, Inc. ("Secura") signed an Asset Purchase Agreement ("Secura APA") and on September 30, 2020, the transaction closed. Pursuant to the Secura APA, we sold our exclusive worldwide license for the research, development, commercialization, and manufacture in oncology indications of products containing duvelisib. Refer to *Note 13. License, collaboration and commercial agreements* in our consolidated financial statements located in this Annual Report on Form 10-K for a detailed description of the terms and conditions of the Secura APA. With the transition of the duvelisib program to Secura, we are focusing our efforts on our lead product candidates, avutometinib and defactinib.

Our operations to date have been organizing and staffing our company, business planning, raising capital, identifying and acquiring potential product candidates, undertaking preclinical studies and clinical trials for our product candidates and initiating U.S. commercial operations following the approval of COPIKTRA through our ownership period ending in September 2020. We have financed our operations to date primarily through public offerings of our common stock, sales of common stock under our at-the-market equity offering programs, our loan and security agreement executed with Hercules Capital, Inc. ("Hercules") in March 2017, as amended, the upfront payments and milestone payments under our license and collaboration agreements with Sanofi, CSPC Pharmaceutical Group Limited ("CSPC"), and Yakult Honsha Co., Ltd. ("Yakult"), the upfront payment and milestone payments received under the Secura APA, the issuance of the 2018 Notes (defined herein) in October 2018, the proceeds in connection with the private investment in public equity (the "PIPE"), and our loan and security agreement executed with Oxford Finance LLC ("Oxford") in March 2022. Additionally, from our U.S. commercial launch of COPIKTRA on September 24, 2018, through our ownership period ending in September 2020, we financed a portion of our operations through product revenue.

As of December 31, 2022, we had an accumulated deficit of $737.5 million. Our net loss was $73.8 million, $71.2 million, and $67.7 million, for the years ended December 31, 2022, 2021, and 2020, respectively. We expect to incur significant expenses and may continue to incur operating losses for the foreseeable future as a result of the continued research and development of avutometinib and defactinib. As of December 31, 2022, we had cash, cash equivalents, and investments of $87.9 million. We expect our existing cash resources, $30.0 million gross proceeds from our Series B Preferred Stock issuance in January 2023, and expected $15.0 million debt drawdown through our loan and security agreement with Oxford expected in March 2023 will be sufficient to fund our planned operations through at least 12 months from the date of issuance of these consolidated financial statements. See *Note*

16. Subsequent events located in this Annual Report on Form 10-K for further discussion of the Series B Preferred Stock issuance.

We expect to finance the future development costs of our clinical product portfolio with our existing cash, cash equivalents and investments, through future milestones and royalties received pursuant to the Secura APA, through our loan and security agreement with Oxford, or through other strategic financing opportunities that could include, but are not limited to, collaboration agreements, future offerings of our equity, or the incurrence of debt. However, there is no guarantee that any of these strategic or financing opportunities will be executed or executed on favorable terms, and some could be dilutive to existing stockholders. If we fail to obtain additional future capital, we may be unable to complete our planned preclinical studies and clinical trials and obtain approval of certain investigational product candidates from the FDA or foreign regulatory authorities.

COVID-19 pandemic

The current COVID-19 pandemic has presented a substantial public health and economic challenge around the world and is affecting our employees, patients, communities and business operations, as well as the U.S. economy and financial markets. We have been carefully monitoring the COVID-19 pandemic and its impact on our operations. Our corporate headquarters remains open and we have adopted a hybrid work program allowing our employees the option to primarily work from home. Shortages in personnel in clinics and hospitals have caused some United States sites to institute limits on new clinical trials which could impact our ability to open new sites for our clinical trials. In addition, clinics in Europe and the United States continue to have delays in startup activities due to the ongoing pandemic and the increase in COVID-19 variant infections. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, new variants, the actions taken to contain it or treat its impact and the economic impact on local, regional, national, and international markets.

For additional information on the various risks posed by the COVID-19 pandemic, please read Item *1A. Risk Factors* included within.

FINANCIAL OPERATIONS OVERVIEW

Revenue

From our U.S. commercial launch of COPIKTRA on September 24, 2018 through our ownership period ending in September 2020 product revenue, net represented the gross sales of COPIKTRA in the United States less provisions for product sales allowances and accruals. These provisions included trade allowances, rebates, chargebacks and discounts, product returns and other incentives. We sold COPIKTRA to a limited number of specialty pharmacies and specialty distributors. The provisions for product sales and allowances fluctuated based on the mix of sales to either specialty pharmacy or specialty distributor customers. See "Critical Accounting Policies and Significant Judgements and Estimates" below and *Note 2. Significant Accounting Policies* located within the notes to the financial statements included within for more information on the components of net U.S. product sales of COPIKTRA.

License and collaboration revenue to date has been generated through our license and collaboration agreements for the development and commercialization of duvelisib with Sanofi in the Sanofi Territory, CSPC in China, and Yakult in Japan. The terms of these agreements contain multiple deliverables which may include (i) licenses, (ii) research and development activities, and (iii) the manufacture of finished drug product, active pharmaceutical ingredient ("API"), or development materials for a partner, which are reimbursed at a contractually determined rate. Payments to us may include (i) up-front license fees, (ii) payments for research and development activities, (iii) payments for the manufacture of finished drug product, API or development materials, (iv) payments based upon the achievement of certain milestones, and (v) royalties on product sales.

Sale of licenses and related assets revenue to date have been generated through our sale of our duvelisib license and related assets to Secura. The sale included intellectual property related to duvelisib in oncology indications, certain existing duvelisib inventory, certain manufacturing equipment and, claims and rights under certain contracts pertaining to duvelisib including net contract prepaid balances.

Costs of sales - product

Cost of sales - product consisted of costs of COPIKTRA on which product revenue was recognized, royalties owed to Healthcare Royalty Partners ("HCR") and Infinity we incurred as a result of such sales of COPIKTRA, and certain period costs. Certain of the costs of COPIKTRA units recognized as revenue during 2020 were expensed prior to the September 2018 FDA marketing approval and, therefore, are not included in cost of sales during 2020. There were no cost of sales – product in 2022 and 2021.

Costs of sales - sale of COPIKTRA license and related assets

Cost of sales - sale of COPIKTRA license and related assets represent assets delivered to Secura as part of the sale pursuant to the Secura APA. This included our intangible assets, certain duvelisib inventory, net duvelisib contract prepaid balances, and manufacturing equipment. There were no cost of sales –sale of COPIKTRA license and related assets in 2022 and 2021.

Research and development expenses

Research and development expenses consist of costs associated with our research activities, including the development of our product candidates. Research and development expenses include product/ product candidate and/or project-specific costs, as well as unallocated costs. We allocate the expenses related to external research and development services, such as contract research organizations ("CROs"), clinical sites, manufacturing organizations and consultants, by project and/or product candidate. We use our employee and infrastructure resources in a cross-functional manner across multiple research and development projects. Our project costing methodology does not allocate personnel, infrastructure and other indirect costs to specific clinical programs or projects.

Product/ product candidate/ project specific costs include:

- direct third-party costs, which include expenses incurred under agreements with CROs, the cost of consultants who assist with the development of our product candidates on a program-specific basis, clinical site costs, and any other third-party expenses directly attributable to the development of the product candidates;
- costs related to contract manufacturing operations including manufacturing costs in connection with producing product candidates for use in conducting preclinical and clinical studies. Costs associated with manufacturing avutometinib are included in "Avutometinib manufacturing and non-clinical trial specific" category below as these costs relate to both the "Avutometinib + defactinib" and "Avutometinib + other combinations" categories and are not specifically allocated to any particular project. Costs to produce defactinib are included in "Avutometinib + defactinib" below; and
- license fees.

Unallocated costs include:

- research and development employee-related expenses, including salaries, benefits, travel, and stock-based compensation expense;
- cost of consultants, including our scientific advisory board, who assist with our research and development but are not allocated to a specific program; and
- facilities, depreciation, and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, and laboratory supplies.

The table below summarizes our direct research and development expenses for our product/ product candidates/ projects and our unallocated research and development costs for the years ended December 31, 2022, 2021, and 2020:

	Year ended December 31,		
	2022 (in thousands)	2021 (in thousands)	2020 (in thousands)
Product/ product candidate / project specific costs			
Avutometinib + defactinib	$ 22,374	$ 17,025	$ 6,199
Avutometinib + other combinations	2,373	416	—
Avutometinib manufacturing and non-clinical trial specific	8,204	5,441	5,874
COPIKTRA	183	1,194	13,454
Unallocated costs			
Personnel costs, excluding stock-based compensation	10,848	9,953	8,937
Stock-based compensation expense	1,766	2,099	1,935
Other unallocated expenses	4,810	3,219	4,977
Total research and development expense	$ 50,558	$ 39,347	$ 41,376

Costs for certain development activities, such as clinical trial expenses, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, and information provided us by our vendors on their actual costs incurred or level of effort expended. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as prepaid expenses and other current assets or accrued expenses.

Our research and development expenses may increase significantly in future periods as we undertake costlier development activities for our existing and future product candidates, including larger and later-stage clinical trials.

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete

development of our product candidates or the period, if any, in which material net cash inflows from our product candidates may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- clinical trial results;
- the scope, rate of progress, and expense of our research and development activities, including preclinical research and clinical trials;
- the potential benefits of our product candidates over other therapies;
- our ability to market, commercialize, and achieve market acceptance for any of our product candidates that we receive regulatory approval for;
- the terms and timing of regulatory approvals; and
- the expense of filing, prosecuting, defending, and enforcing patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or other regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Selling, general, and administrative expenses

Selling, general, and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation expense, in our executive, finance, legal, information technology, commercial, communication, human resources, and business development functions. Other selling, general, and administrative expenses include allocated facility costs, commercial costs, professional fees for legal, patent, investor and public relations, consulting, insurance premiums, audit, tax, and other public company costs.

Other income, other expense, interest income and interest expense

Other income for the year ended December 31, 2022 was comprised of a gain on the sale of fixed assets and changes in foreign currency exchange rates. There was no other income or other expense for the year ended December 31, 2021. Other expense for the year ended December 31, 2020, consists entirely of the mark-to-market adjustment of the bifurcated make-whole interest provision derivative liability related to the 2019 Notes.

Interest income reflects interest earned on our cash, cash equivalents and available-for-sale securities.

Interest expense reflects interest expense due on our Loan Agreement with Oxford, our term loan facility executed with Hercules and the Notes, as well as non-cash interest related to the amortization of debt discount and issuance costs.

CRITICAL ACCOUNTING POLICIES AND SIGNIFICANT JUDGMENTS AND ESTIMATES

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles ("GAAP"). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of certain assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued and prepaid research and development expenses, leases, stock-based compensation, revenue recognition, and collaborative agreements, described in greater detail below. We base our estimates on our limited historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. However, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue recognition

We recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services in accordance with Accounting Standards Codification ("ASC") Topic 606 *Revenue from Contracts with Customers* (ASC 606).

Product revenue, net

Product Revenue, Net – From September 24, 2018 (the date of our U.S. commercial launch of COPIKTRA) through September 30, 2020 (the date we sold COPIKTRA to Secura), we sold COPIKTRA to a limited number of specialty pharmacies and specialty distributors in the United States. We recognized revenue on sales of COPIKTRA when a customer obtains control of the product, which occurs at a point in time (typically upon delivery). Product revenues are recorded at the wholesale acquisition costs, net of applicable reserves for variable consideration. Components of variable consideration include trade discounts and allowances, Third-Party Payer chargebacks and discounts, government rebates, other incentives, such as voluntary co-pay assistance, product returns, and other allowances that are offered within contracts between us and customers, payors, and other indirect customers relating to our sale of COPIKTRA. These reserves, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable or a current liability. These estimates take into consideration a range of possible outcomes based upon relevant factors such as customer contract terms, information received from third parties regarding the anticipated payor mix for COPIKTRA, known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which it is entitled with respect to sales made.

The amount of variable consideration which is included in the transaction price 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 under contracts will not occur in a future period. Our analyses contemplate the application of the constraint in accordance with ASC 606. For the year ended December 31, 2020, we determined a material reversal of revenue would not occur in a future period for variable consideration, and the transaction price was not reduced further. There was not any product revenue, net recorded for the years ended December 31, 2022 and 2021. Actual amounts of consideration ultimately received could differ from our estimates. However, as of December 31, 2022, we do not have any reserve balances associated with product revenue, net.

Licenses and sales of intellectual property

Licenses of Intellectual Property - We may enter into collaboration and licensing arrangements for research and development, manufacturing, and commercialization activities with collaboration partners for the development and commercialization of our product candidates, which have components within the scope of ASC 606. The arrangements generally contain multiple elements or deliverables, which may include (i) licenses, or options to obtain licenses, to our intellectual property or sale of our license, (ii) research and development activities performed for the collaboration partner, (iii) participation on joint steering committees, and (iv) the manufacturing of commercial, clinical or preclinical material. Payments pursuant to these arrangements typically include non-refundable, upfront payments, milestone payments upon the achievement of significant development events, research and development reimbursements, sales milestones, and royalties on product sales. The amount of variable consideration is constrained until it is probable that the revenue is not at a significant risk of reversal in a future period. The contracts into which we enter generally do not include significant financing components.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our collaboration and license agreements, we perform the following steps: (i) identification of the promised goods or services in the contract within the scope of ASC 606; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the

transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for these arrangements, we must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above; and d) the measure of progress in step (v) above. We use judgment to determine whether milestones or other variable consideration, except for royalties on license arrangements, should be included in the transaction price.

For sales of license and intellectual property, that include sale-based royalties, including milestone payments based on a level of sales, we evaluate whether the royalties and sales-based milestones are considered probable of being achieved and estimate the amount of royalties to include over the contractual term using the expected value method and estimate the sales-based milestones using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated royalty and milestone value is included in the transaction price. Royalties and sales-based milestones for territories for which there is not regulatory approval are not considered probable until such regulatory approval is achieved. We evaluate factors such as whether consideration is outside of our control, timeline for when the uncertainty will be resolved and historical sales of COPIKTRA if applicable. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, we reevaluate the probability of achievement of all milestones subject to constraint and amount of royalty revenue to be received and, if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. At December 31, 2022, we determined $0.1 million of future potential royalties, we expect to receive pursuant to the Secura APA, were not constrained and have been recorded in the transaction price. As the consideration for future royalties is conditional, we recorded a corresponding contract asset for the expected future royalties. Portions of the contract asset are reclassified to accounts receivable when the right to consideration becomes unconditional.

Refer to *Note 2. Significant Accounting Policies*, *Note 6. Product revenue reserves and allowances* and *Note 13. License, collaboration and commercial agreements* to our consolidated financial statements located in this Annual Report on Form 10-K for further discussion of revenue.

Collaborative Arrangements

Collaborative Arrangements: Contracts are considered to be collaborative arrangements pursuant to GAAP when they satisfy the following criteria defined in ASC Topic 808, *Collaborative Arrangements* (ASC 808): (i) the parties to the contract must actively participate in the joint operating activity and (ii) the joint operating activity must expose the parties to the possibility of significant risk and rewards, based on whether or not the activity is successful. Payments received from or made to a partner that are the result of a collaborative relationship with a partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction or increase to research and development expense, respectively.

Accrued and prepaid research and development expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses. This process involves reviewing contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include fees paid to CROs in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services

provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Refer to *Note 2. Significant Accounting Policies*, and *Note 4. Accrued expenses* to our consolidated financial statements located in this Annual Report on Form 10-K for further discussion of accrued research and development expenses.

Stock-based compensation

For service-based awards, we recognize stock-based compensation expense for stock options, and restricted stock units ("RSUs") issued to employees, directors and consultants based on the grant date fair value of the awards on a straight-line basis over the requisite service period. In addition, we issue shares under our employee stock purchase plan ("ESPP") to employees. The fair value of our stock options and ESPP grants is estimated at the date of grant using the Black-Scholes option pricing model.

We have also granted performance-based RSUs and stock options with terms that allow the recipients to vest in a specific number of shares based upon the achievement of performance-based milestones as specified in the grants. Stock-based compensation expense associated with these performance-based RSUs and stock options is recognized if the performance condition is considered probable of achievement using management's best estimates of the time to vesting for the achievement of the performance-based milestones. If the actual achievement of the performance-based milestones varies from our estimates, stock-based compensation expense could be materially different than what is recorded in the period. The cumulative effect on current and prior periods of a change in the estimated time to vesting for performance-based RSUs and stock options will be recognized as compensation cost in the period of the revision, and recorded as a change in estimate.

While the assumptions used to calculate and account for stock-based compensation awards represent management's best estimates, these estimates involve inherent uncertainties and the application of management's judgment. As a result, if revisions are made to our underlying assumptions and estimates, our stock-based compensation expense could vary significantly from period to period.

During the year ended December 31, 2022, we recorded $6.0 million of stock-based compensation expense. As of December 31, 2022, there was approximately $6.6 million of unrecognized stock-based compensation related to stock options, which are expected to be recognized over a weighted-average period of 2.6 years. As of December 31, 2022, there was approximately $4.3 million of unrecognized stock-based compensation related to RSUs, which are expected to be recognized over a weighted-average period of 2.8 years. See *Note 2. Significant accounting policies* and *Note 8. Stock-based compensation* to our consolidated financial statements located in this Annual Report on Form 10-K for further discussion of stock-based compensation.

Leases

Leases are accounted for in accordance with *ASC Topic 842, Leases* ("*ASC 842*"). This standard requires lessees to recognize in the statement of financial position a liability to make lease payments and a right-of-use asset representing its right to use the underlying asset for the lease term for both finance and operating leases.

At the inception of an arrangement, we determine whether the arrangement is or contains a lease based on the unique facts and circumstances within the arrangement. A lease is identified where an arrangement conveys the right to control the use of identified property, plant, and equipment for a period of time in exchange for consideration. Leases which are identified within the scope of ASC 842 and which have a term greater than one year are recognized on our consolidated balance sheets as right-of-use assets, lease liabilities and, if applicable, long-term

lease liabilities. We have elected not to recognize leases with terms of one year or less on our consolidated balance sheets. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. However, certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, we utilize our incremental borrowing rates to calculate the present value of lease payments. Incremental borrowing rates are the rates we incur to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. As of December 31, 2022, we have a right-of-use asset of $1.8 million and lease liability of $2.3 million which reflected on the consolidated balance sheets. See *Note 2. Significant accounting policies* and *Note 6. Leases* to our consolidated financial statements located in this Annual Report on Form 10-K for further discussion of leases.

RESULTS OF OPERATIONS

All financial information presented has been consolidated and includes the accounts of our wholly-owned subsidiaries, Verastem Securities Company and Verastem Europe GmbH. All intercompany balances and transactions have been eliminated in consolidation.

	Year Ended December 31,		
	2022	2021	2020
Revenue:			
Product revenue, net	—	—	15,232
License and collaboration revenue	—	—	2,912
Sale of COPIKTRA license and related assets	2,596	1,447	70,000
Transition services revenue	—	606	372
Total revenue	2,596	2,053	88,516
Operating expenses:			
Cost of sales - product	—	—	1,765
Cost of sales - intangible amortization	—	—	793
Cost of sales - sale of COPIKTRA license and related assets	—	—	31,187
Research and development	50,558	39,347	41,376
Selling, general and administrative	24,975	24,115	62,755
Total operating expenses	75,533	63,462	137,876
Loss from operations	(72,937)	(61,409)	(49,360)
Other income (expense)	47	—	(1,313)
Interest income	1,215	181	515
Interest expense	(2,137)	(9,972)	(15,794)
Loss on debt extinguishment	—	—	(1,580)
Net loss before income taxes	(73,812)	(71,200)	(67,532)
Income tax expense	—	—	(194)
Net loss	$ (73,812)	$ (71,200)	$ (67,726)

Comparison of the Year Ended December 31, 2022 to the Year Ended December 31, 2021

Sale of COPIKTRA license and related assets revenue. Sale of COPIKTRA license and related assets revenue for the year ended December 31, 2022 (the "2022 Period") was $2.6 million compared to $1.4 million for the year ended December 31, 2021 (the "2021 Period"). Sale of COPIKTRA license and related assets revenue for the 2022 Period was comprised of one regulatory milestone for $2.5 million achieved by Secura's sublicensee, CSPC, and $0.1 million related to royalties on COPIKTRA sales in the 2022 Period and future royalties expected to be received pursuant to the Secura APA that are not constrained. Sale of COPIKTRA license and related assets revenue for the 2021 Period primarily related to two regulatory milestones for $1.3 million achieved by Secura's sublicensee and $0.2 million related to royalties we received and expected to be received pursuant to the Secura APA.

Transition services revenue. Transition services revenue for the 2022 Period was $0.0 million compared to $0.6 million for the 2021 Period. Transition services revenue was comprised of the revenue recognized for us providing certain support functions to Secura pursuant to the transition services agreement, which was entered into

in connection with the Secura APA ("Secura TSA"). The services were provided at a mutually agreed upon rate. The services were substantially completed in 2021 and there will not be revenue recorded in the future pursuant to the Secura TSA.

Research and development expense. Research and development expense for the 2022 Period was $50.6 million compared to $39.3 million for the 2021 Period. The $11.3 million increase from the 2021 Period to the 2022 Period was primarily related to an increase of $4.1 million in drug substance and drug product costs, an increase of $4.1 million in CRO costs, an increase of $1.5 million in consulting costs, an increase of $0.9 million in investigator fees, an increase of $0.5 million in personnel related costs, including non-cash stock-based compensation, an increase of $0.4 million in clinical supply costs and an increase of $0.8 million in other costs. The increase was partially offset by a decrease of $1.0 million in investigator sponsored trial costs.

Selling, general and administrative expense. Selling, general and administrative expense for the 2022 Period was $25.0 million compared to $24.1 million for the 2021 Period. The increase of $0.9 million from the 2021 Period to the 2022 Period primarily resulted from an increase of $1.1 million of commercial operations costs, an increase of $0.4 million in personnel related costs, including non-cash stock-based compensation and an increase of $0.4 million of other costs. The increase was partially offset by a decrease of $1.0 million of consulting and professional fees.

Other Income. Other income for the 2022 Period was less than $0.1 million compared to $0.0 million in the 2021 Period. Other income for the 2022 Period was comprised of a gain on the sale of fixed assets and changes in foreign currency exchange rates.

Interest income. Interest income for the 2022 Period was $1.2 million compared to $0.2 million for the 2021 Period. The increase of $1.0 million in interest income was primarily driven by an increase in interest rates on debt securities.

Interest expense. Interest expense for the 2022 Period was $2.1 million compared to $10.0 million for the 2021 Period. The decrease of $7.9 million from the 2021 Period to the 2022 Period was primarily driven by $7.8 million of non-cash interest expense recorded in the 2021 Period upon conversion of the 2020 Notes into common stock in July 2021. In addition, as a result of the conversion, there were no interest charges recorded for the 2020 Notes in the 2022 Period. The decrease is partially offset by the interest expense recorded pursuant to the Loan Agreement entered into with Oxford.

LIQUIDITY AND CAPITAL RESOURCES

Sources of liquidity

We have financed our operations to date primarily through public and private offerings of our common stock, sales of common stock under our at-the-market equity offering programs, our loan and security agreement executed with Hercules in March 2017, as amended, the upfront payments under our license and collaboration agreements with Sanofi, Yakult, and CSPC, the upfront payment under the Secura APA, the issuance of 2018 Notes in October 2018, the proceeds in connection with the PIPE, the Loan Agreement with Oxford, and issuance of our Series B Preferred Stock in January 2023. With the commercial launch of COPIKTRA in the United States in September 2018 through our ownership period ending in September 2020, we financed a portion of our operations through product revenue. As of September 30, 2020, we have sold our COPIKTRA license and no longer sell COPIKTRA in the United States. We expect to finance a portion of our business through potential future milestones and royalties received pursuant to the Secura APA.

As of December 31, 2022, we had $87.9 million in cash, cash equivalents, and investments. We primarily invest our cash, cash equivalents and investments in U.S. Government money market funds, government bonds, corporate bonds and commercial paper of publicly traded companies.

On March 10, 2023, SVB was closed by the California Department of Financial Protection and Innovation, which appointed the FDIC as receiver. On March 12, 2023, the Department of the Treasury, the Federal Reserve,

and the FDIC announced that all depositors of SVB will be fully protected and have access to all their money starting March 13, 2023. As of March 13, 2023, our deposit balance at SVB was approximately $2 million. We are continually monitoring developments related to the recovery of uninsured funds at SVB.

Risks and uncertainties include those identified under Item 1A. *Risk Factors,* in this Annual Report on Form 10-K.

Cash flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below (in thousands):

	Year ended December 31,		
	2022	2021	2020
Net cash (used in) provided by:			
Operating activities	$ (63,673)	$ (53,502)	$ (33,506)
Investing activities	66,185	87	(47,363)
Financing activities	51,784	6,885	69,630
Increase (decrease) in cash, cash equivalents and restricted cash	**$** 54,296	$ (46,530)	(11,239)

Operating activities. The use of cash in operating activities in the 2022 Period and 2021 Period resulted primarily from our net losses adjusted for non-cash charges and changes in the components of working capital. Our cash outflow from net losses adjusted for non-cash charges was $67.6 million and $54.1 million for the 2022 Period and 2021 Period, respectively. Non-cash charges were primarily related to stock-based compensation expense in the 2022 Period and stock-based compensation expense and non-cash interest, net in the 2021 Period. Our cash inflow from operating activities due to changes in operating assets and liabilities was $3.9 million and $0.6 million for the 2022 Period and 2021 Period, respectively. Cash inflow due to changes in operating assets and liabilities for the 2022 Period was primarily driven by an increase of $2.6 million in accounts payable, an increase of $0.7 million in deferred liabilities, a decrease of $0.7 million of prepaid expenses, other current assets and other assets, and a decrease of $0.5 million in accounts receivable. The decrease in prepaid expenses, other current assets, and other assets is exclusive of the cash received from PanCAN. Cash inflow due to changes in operating assets and liabilities for the 2021 Period was primarily driven by an increase of $1.8 million in accrued expenses, an increase of $0.6 million in accounts payable, partially offset by an increase in $1.6 million in prepaid expenses, other current assets, and other assets. Cash used in operating activities was $63.7 million and $53.5 million for the 2022 Period and 2021 Period, respectively.

Investing activities. The cash provided by investing activities for the 2022 Period primarily relates to the net maturities of investments of $66.2 million. The cash provided by investing activities for the 2021 Period primarily relates to the net maturities of investments of $0.3 million, partially offset by purchases of fixed assets of $0.2 million.

Financing activities. The cash provided by financing activities for the 2022 Period primarily represents $27.4 million of net proceeds received under our at-the market equity offering program, $24.1 million of net proceeds received from the Loan Agreement with Oxford, and $0.3 million of proceeds received related to exercise of stock options and employee stock purchase plan. The cash provided by financing activities for the 2021 Period primarily represents $6.7 million in net proceeds received under our at-the-market equity offering program, and $1.1 million of proceeds received related to exercise of stock options and employee stock purchase plan. This is partially offset by $0.9 million of payments for settlement of restricted stock for tax withholdings.

On March 25, 2022 (the “Closing Date”) we entered into a loan and security agreement (the “Loan Agreement”), with Oxford as collateral agent and a lender, and Oxford Finance Credit Fund III LP, as a lender (“OFCF III” and together with Oxford, the “Lenders”) pursuant to which the Lenders have agreed to lend us up to an aggregate principal amount of $150.0 million in a series of term loans (the “Term Loans”). The initial Term Loan of $25.0 million was funded at the Closing Date of the Loan Agreement, an additional $75.0 million will be available at our option upon achievement of certain milestones as outlined in *Note 5. Debt* to our consolidated financial statements included in this Annual Report on Form 10-K, and $50.0 million is subject to the Lenders’ sole

discretion. In January 2023, we met the Term B Milestone as outlined in *Note 5. Debt* to our consolidated financial statements included in this Annual Report on Form 10-K and we expect to draw down an additional $15.0 million Term Loan in March 2023.

The Term Loans bear interest at a floating rate equal to (a) the greater of (i) the one-month CME Secured Overnight Financing Rate and (ii) 0.13% plus (b) 7.37%, which is subject to an overall floor and cap. Interest is payable monthly in arrears on the first calendar day of each calendar month. Beginning (i) April 1, 2024, if the Term B Loan (as defined in *Note 5. Debt* to our consolidated financial statements included in this Annual Report on Form 10-K) is not made, (ii) April 1, 2025, if the Term B Loan is made, or (iii) April 1, 2026, if the Term B Loan is made and either (A) avutometinib has received FDA approval for the treatment of LGSOC or (B) COPIKTRA has received FDA approval for the treatment of peripheral T-cell lymphoma ("PTCL"), we shall repay the Term Loans in consecutive equal monthly payments of principal, together with applicable interest, in arrears. All unpaid principal and accrued and unpaid interest with respect to each Term Loan is due and payable in full on March 1, 2027. As we have drawn the Term B Milestone, principal repayments will not be required to commence until at least April 1, 2025.

We are required to make a final payment of 5.0% of the original principal amount of the Term Loans that were drawn, payable at maturity or upon any earlier acceleration or prepayment of the Term Loans. We may prepay all, but not less than all, of the Term Loans, subject to a prepayment fee equal to (i) 3.0% of the principal amount of the applicable Term Loan if prepaid on or before the first anniversary date of the funding date of such Term Loan, (ii) 2.0% of the principal amount of the applicable Term Loan if prepaid after the first anniversary and on or before the second anniversary of the funding date of such Term Loan, and (iii) 1.0% of the principal amount of the applicable Term Loan if prepaid after the second anniversary of the applicable funding date of such Term Loan. All Term Loans are subject to a facility fee of 0.5% of the principal amount.

The Loan Agreement contains no financial covenants. The Loan Agreement includes customary events of default, including, among others, payment defaults, breach of representations and warrants, covenant defaults, judgment defaults, insolvency and bankruptcy defaults, and a material adverse change. The occurrence of an event of default could result in the acceleration of the obligations under the Loan Agreement, termination of the Term Loan commitments and the right to foreclose on the collateral securing the obligations. During the existence of an event of default, the Term Loans will accrue interest at a rate per annum equal to 5.0% above the otherwise applicable interest rate.

In connection with the Loan Agreement, we granted Oxford a security interest in all of our personal property now owned or hereafter acquired, excluding intellectual property (but including the right to payments and proceeds of intellectual property), and a negative pledge on intellectual property.

In August 2021, we entered into a sales agreement with Cantor Fitzgerald & Co. ("Cantor") pursuant to which we can offer and sell up to $100.0 million of our common stock at the current market prices from time to time through Cantor as sales agent ("August 2021 ATM"). During the 2022 Period and 2021 Period, we sold 23,573,403 shares and 2,930,585 shares, respectively, under the August 2021 ATM for net proceeds of approximately $27.4 million, and $6.8 million, respectively (after deducting commissions and other offering expenses). As of December 31, 2022, we can issue an aggregate amount of $65.1 million of common stock under this program.

On October 17, 2018, we closed a registered direct public offering of $150.0 million aggregate principal amount of our 2018 issued 5.00% Convertible Senior Notes due 2048 (the "2018 Notes"), for net proceeds of approximately $145.3 million. The 2018 Notes are governed by the terms of a base indenture for senior debt securities (the "Base Indenture"), as supplemented by the first supplemental indenture thereto (the "2018 Notes Supplemental Indenture" and together with the Base Indenture, the "2018 Indenture"), each dated October 17, 2018, by and between us and Wilmington Trust, National Association ("Wilmington"), as trustee. The 2018 Notes are senior unsecured obligations of us and bear interest at a rate of 5.00% per annum, payable semi-annually in arrears on May 1 and November 1 of each year. The 2018 Notes will mature on November 1, 2048, unless earlier repurchased, redeemed or converted in accordance with their terms.

The 2018 Notes are convertible into shares of our common stock, par value $0.0001 per share, together, if applicable, with cash in lieu of any fractional share, at an initial conversion rate of 139.5771 shares of common

stock per $1,000 principal amount of the 2018 Notes, which corresponds to an initial conversion price of approximately $7.16 per share of common stock. Upon conversion, converting noteholders will be entitled to receive accrued interest on their converted 2018 Notes.

We will have the right, exercisable at our option, to cause all 2018 Notes then outstanding to be converted automatically if the "Daily VWAP" (as defined in the 2018 Indenture) per share of our common stock equals or exceeds 130% of the conversion price, which equates to approximately $9.31 per share, on each of at least 20 "VWAP Trading Days" (as defined in the 2018 Indenture), whether or not consecutive, during any 30 consecutive VWAP Trading Day period commencing on or after the date we first issued the 2018 Notes.

In the fourth quarter of 2019, we entered into privately negotiated agreements to exchange approximately $121.7 million aggregate principal amount of the 2018 Notes for (i) approximately $66.9 million aggregate principal amount of 5.00% Convertible Senior Second Lien Notes due 2048 (the "2019 Notes"), (ii) an aggregate of approximately $12.1 million in 2018 Notes principal repayment and (iii) accrued interest on the 2018 Notes through the exchange date. As of March 31, 2020, all 2019 Notes have converted into shares of common stock and are no longer outstanding.

On November 6, 2020, we entered into a privately negotiated agreement with an investor who is a holder of our 2018 Notes to exchange approximately $28.0 million aggregate principal amount of 2018 Notes for approximately $28.0 million aggregate principal amount of newly issued 5.00% Convertible Senior Notes due 2048 (the "2020 Notes"). The issuance of the 2020 Notes closed on November 13, 2020. The 2020 Notes were governed pursuant to the Base Indenture between us and Wilmington dated as of October 17, 2018 as supplemented by the second supplemental indenture thereto dated as of November 13, 2020 (the "2020 Notes Supplemental Indenture" and together with the Base Indenture, the "2020 Indenture").

We had the right, exercisable at our option, to cause all 2020 Notes then outstanding to be converted automatically if the "Daily VWAP" (as defined in the 2020 Indenture) per share of our common stock equals or exceeds 123.08% of the conversion price on each of at least 20 "VWAP Trading Days" (as defined in the 2020 Indenture), whether or not consecutive, during any 30 consecutive VWAP Trading Day period commencing on or after the date we first issued the 2020 Notes ("2020 Notes Mandatory Conversion Option").

On July 1, 2021, we exercised our 2020 Notes Mandatory Conversion Option for the aggregate principal amount of $28.0 million of the 2020 Notes. On July 16, 2021, the aggregate principal of $28.0 million of 2020 Notes was converted into 8,615,384 shares of common stock. Upon conversion of the 2020 Notes, holders received a cash payment equal to the accrued and unpaid interest on the converted 2020 Notes. As a result, as of September 30, 2021, all 2020 Notes have converted into shares of common stock.

As of December 31, 2022 and 2021 there was $0.3 million aggregate principal amount outstanding of 2018 Notes.

Funding requirements

We expect to continue to incur significant expenses and may continue to incur operating losses. Refer to risk factor titled *We have incurred significant losses since our inception. We may incur losses for the foreseeable future and may never achieve or maintain profitability* within section Item *1A. Risk Factors* for detailed activities which may drive our continued operating losses and expenses in future periods.

Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, and the extent to which we may enter into collaborations with third parties for development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the development of our current product candidates. Our future capital requirements will depend on many factors, including:

- the costs and timing of commercialization activities for our product candidates for which we expect to receive marketing approval;

- the scope, progress, and results of our ongoing and potential future clinical trials;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs, timing, and outcome of regulatory review of our product candidates (including our efforts to seek approval and fund the preparation and filing of regulatory submissions);
- revenue received from commercial sales our product candidates, should any of our other product candidates receive marketing approval;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending intellectual property related claims;
- our ability to establish collaborations or partnerships on favorable terms, if at all; and
- receipt of milestone payments and royalties pursuant to the Secura APA including timing of such receipt.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements, and through future milestones and royalties received pursuant to the Secura APA. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. 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 additional funds through 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 grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

On April 15, 2014, we entered into a lease agreement for approximately 15,197 square feet of office and laboratory space in Needham, Massachusetts. The lease term commenced on April 15, 2014, and it was scheduled to expire on September 30, 2019. Effective February 15, 2018, we amended the lease agreement to relocate within the facility to another location consisting of 27,810 square feet of office space (the "Amended Lease Agreement"). The Amended Lease Agreement extends the expiration date of the lease from September 2019 through June 2025. Pursuant to the Amended Lease Agreement, the initial annual base rent amount is approximately $0.7 million, which increases during the lease term to $1.1 million for the last twelve-month period. As of December 31, 2022, the total future minimum lease payments under the agreement are $2.7 million through June 2025.

As discussed in *Note 13. License, collaboration and commercial agreements* to the consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we are party to several agreements to license intellectual property. The license agreements may require us to pay upfront license fees, ongoing annual license maintenance fees, milestone payments, minimum royalty payments, as well as reimbursement of certain patent costs incurred by the licensors, as applicable. As of December 31, 2022, we do not have any minimum contractual obligations in relation to these agreements because: there were no upfront license fees payable in future periods; no annual license maintenance fees; we cannot estimate if milestone and/or royalty payments will occur in future periods; and patent cost reimbursement costs are perpetual and the agreements are cancelable by us at any time upon prior written notice to the licensor.

TAX LOSS CARRYFORWARDS

As of December 31, 2022, we had federal and state net operating loss ("NOL") carryforwards of $436.6 million and $203.3 million, respectively, which are available to reduce future taxable income. We also had federal and state tax credits of $5.6 million and $1.9 million, respectively, which may be used to offset future tax liabilities. The net operating loss and tax credit carryforwards will expire at various dates through 2042, except for $240.9 million of federal net operating loss carryforwards which may be carried forward indefinitely. Net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax

authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of our company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. At December 31, 2022, we recorded a 100% valuation allowance against our NOL and tax credit carryforwards of $133.9 million, as we believe it is more likely than not that the tax benefits will not be fully realized. In the future, if we determine that a portion or all of the tax benefits associated with our tax carryforwards will be realized, net income would increase in the period of determination.

Based on our analysis under Section 382 of the Internal Revenue Code and similar provisions under state law, we believe that our federal net operating loss carryforwards, our state net operating loss carryforwards, our Research and Development ("R&D") credits and our Orphan Drug ("OD") credits will be limited as of December 31, 2022. The portion of federal NOL, state NOL, R&D credits and OD credits that were determined to be limited by Section 382 have been written off as of December 31, 2022. The remaining unused carryforwards remain available for future periods. Due to our full valuation allowance the write off of NOLs, R&D credits, and OD credits did not have any impact to the statements of operation and comprehensive loss for the 2022 Period and 2021 Period.

RECENTLY ADOPTED ACCOUNTING STANDARDS

Refer to *Note 2. Significant Accounting Policies* to our consolidated financial statements located in this Annual Report on Form 10-K for recently adopted accounting standards.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents, and investments of $87.9 million and $100.3 million as of December 31, 2022 and 2021, respectively, consisting of cash, U.S. Government money market funds, government bonds, corporate bonds and commercial paper of publicly traded companies. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because most of our investments are interest bearing. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of most of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We contract with CROs and contract manufacturers globally, which may be denominated in foreign currencies. We may be subject to fluctuations in foreign currency rates in connection with these agreements. Transactions denominated in currencies other than the functional currency are recorded based on exchange rates at the time such transactions arise. As of December 31, 2022, an immaterial amount of our total liabilities was denominated in currencies other than the functional currency.

As of December 31, 2022, we have borrowed $25.0 million under the Loan Agreement. The Loan Agreement bears interest at a floating rate equal to (a) the greater of (i) the one-month CME Secured Overnight Financing Rate and (ii) 0.13% plus (b) 7.37%, which is subject to an overall floor and cap. Changes in interest rates can cause interest charges to fluctuate under the Loan Agreement. A 10% increase in current interest rates would have resulted in an immaterial increase in the amount of cash interest expense for the year ended December 31, 2022 due to the overall interest rate floor and cap.

Item 8. Consolidated Financial Statements and Supplementary Data

Our consolidated financial statements, together with the report of our independent registered public accounting firm (e.g., Report of Independent Registered Public Accounting Firm (PCAOB ID: 42)), appear on pages F-1 through F-42 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures and internal control over financial reporting, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures and internal control over financial reporting must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our Chief Executive Officer and our Vice President, Finance evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of the end of the period covered by this report. Based on that evaluation, our Chief Executive Officer and our Vice President, Finance concluded that our disclosure controls and procedures as of the end of the period covered by this report were effective.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act as the process designed by, or under the supervision of, our Chief Executive Officer and our Vice President of Finance and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of our financial statements for external purposes in accordance with U.S. generally accepted accounting principles ("GAAP"), and includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of assets;
(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that receipts and expenditures are being made only in accordance with the authorizations of management and directors; and
(3) provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and our Vice President, Finance, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework provided in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework). Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by the Company's independent registered public accounting firm, as allowed by the SEC.

Changes in Internal Control Over Financial Reporting

There has been no change in our internal control over financial reporting during the fiscal quarter ended December 31, 2022, that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS, AND CORPORATE GOVERNANCE

Information regarding our directors, including the audit committee and audit committee financial experts, and executive officers and compliance with Section 16(a) of the Exchange Act will be included in our 2023 Proxy Statement and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics for all of our directors, officers, and employees as required by Nasdaq governance rules and as defined by applicable SEC rules. Stockholders may locate a copy of our Code of Business Conduct and Ethics on our website at www.verastem.com or request a copy without charge from:

Verastem, Inc.
Attention: Investor Relations
117 Kendrick St., Suite 500
Needham, MA 02494

We will post to our website any amendments to the Code of Business Conduct and Ethics and any waivers that are required to be disclosed by the rules of either the SEC or Nasdaq.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 of Form 10-K regarding executive compensation will be included in our 2023 Proxy Statement and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item 12 of Form 10-K regarding security ownership of certain beneficial owners and management will be included in our 2023 Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item 13 of Form 10-K regarding certain relationships and related transactions and director independence will be included in our 2023 Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item 14 of Form 10-K regarding principal accountant fees and services will be included in our 2023 Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this Annual Report on Form 10-K:

(1) Consolidated Financial Statements

See Part II, Item 8 for the Financial Statements required to be included in this Annual Report on Form 10-K.

(2) Consolidated Financial Statement Schedules

All financial statement schedules are omitted because they are not applicable or the required information is included in the consolidated financial statements or notes thereto.

(3) Exhibits

Those exhibits required to be filed by Item 601 of Regulation S-K are listed in the Exhibit Index immediately preceding the exhibits hereto and such listing is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

EXHIBIT INDEX

Exhibit number	Description of exhibit
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Annual Report on Form 10-K filed by the Registrant on March 12, 2019)
3.2	Certificate of Amendment to the Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.2 to the Annual Report on Form 10-K filed by the Registrant on March 12, 2019)
3.3	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.4 to Amendment No. 3 to the Registration Statement on Form S-1 (File No. 333-177677) filed by the Registrant on January 13, 2012)
3.4	Certificate of Amendment to the Restated Certificate of Incorporation of Verastem, Inc. (incorporated by reference to Exhibit 3.1 to the Form 8-K filed by the Registrant with the Securities and Exchange Commission on May 21, 2020)
3.5	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Form 8-K filed by the Registrant with the Securities and Exchange Commission on November 7, 2022)
3.6	Certificate of Designation of Preferences, Rights and Limitations of Series B Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Form 8-K filed by the Registrant with the Securities and Exchange Commission on January 25, 2023)
4.1	Specimen certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to Amendment No. 3 to the Registration Statement on Form S-1 (File No. 333-177677) filed by the Registrant on January 13, 2012)
4.2	Indenture, dated as of October 17, 2018, by and between the Registrant and Wilmington Trust, National Association (incorporated by reference to Exhibit 4.1 to Form 8-K filed by the Registrant on October 17, 2018)
4.3	First Supplemental Indenture, dated as of October 17, 2018, by and between the Registrant and Wilmington Trust, National Association (incorporated by reference to Exhibit 4.2 to Form 8-K filed by the Registrant on October 17, 2018)
4.4	Form of 5.00% Convertible Note due 2048 (2018 Notes) (included in Exhibit 4.3)
4.5*	Description of Securities
10.1#	2010 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-1 (File No. 333-177677) filed by the Registrant on November 3, 2011)
10.2#	Amended and Restated 2012 Incentive Plan (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K filed by the Registrant on December 20, 2018)
10.3#	Form of Incentive Stock Option Agreement under 2012 Incentive Plan (incorporated by reference to Exhibit 10.3 to Amendment No. 3 to the Registration Statement on Form S-1 (File No. 333-177677) filed by the Registrant on January 13, 2012)
10.4#	Form of Incentive Stock Option Agreement under Amended and Restated 2012 Incentive Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Annual Report on Form 10-K filed by the Registrant on March 13, 2018)

10.5#	Form of Nonstatutory Stock Option Agreement under 2012 Incentive Plan (incorporated by reference to Exhibit 10.4 to Amendment No. 3 to the Registration Statement on Form S-1 (File No. 333-177677) filed by the Registrant on January 13, 2012)
10.6#	Form of Nonstatutory Stock Option Agreement under Amended and Restated 2012 Incentive Plan (incorporated by reference to Exhibit 10.6 of the Registrant's Annual Report on Form 10-K filed by the Registrant on March 13, 2018)
10.7#	Form of Restricted Stock Unit Agreement under 2012 Incentive Plan (incorporated by reference to Exhibit 10.16 to Amendment No. 3 to the Registration Statement on Form S-1 (File No. 333-177677) filed by the Registrant on January 13, 2012)
10.8#	Amendment to Form of Restricted Stock Unit Agreement under 2012 Incentive Plan (incorporated by reference to Exhibit 10.25 to the Annual Report on Form 10-K filed by the Registrant on March 26, 2013)
10.9#	Form of Restricted Stock Unit Agreement under Amended and Restated 2012 Incentive Plan (incorporated by reference to Exhibit 10.9 of the Registrant's Annual Report on Form 10-K filed by the Registrant on March 13, 2018)
10.10#	Form of Inducement Award Nonstatutory Stock Option Agreement (incorporated by reference to Exhibit 4.4 to the Registration Statement on Form S-8 filed by the Registrant with the Securities and Exchange Commission on December 19, 2014)
10.11#	Form of Inducement Award Nonstatutory Stock Option Agreement (incorporated by reference to Exhibit 10.11 of the Registrant's Annual Report on Form 10-K filed by the Registrant on March 13, 2018)
10.12#	Form of Inducement Award Restricted Stock Unit Agreement (incorporated by reference to Exhibit 4.3 of the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, filed by the Registrant with the Securities and Exchange Commission on November 7, 2018)
10.13#	2018 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.2 of the Registrant's Current Report on Form 8-K filed by the Registrant on December 20, 2018)
10.14#	Form of Indemnification Agreement between the Registrant and each director and executive officer (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on August 8, 2017)
10.15	Lease Agreement, dated April 15, 2014, between the Registrant and Intercontinental Fund III 117 Kendrick Street LLC (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed by the Registrant on April 18, 2014)
10.16	First Amendment of Lease Agreement, dated February 15, 2018, between the Registrant and 117 Kendrick DE, LLC, as successor-in-interest to Intercontinental Fund III 117 Kendrick Street, LLC (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on May 3, 2018)
10.17#	Employment Agreement, dated March 1, 2012, between the Registrant and Daniel Paterson (incorporated by reference to Exhibit 10.18 to the Annual Report on Form 10-K filed by the Registrant on March 26, 2013)
10.18†	License Agreement, dated July 11, 2012, by and between the Registrant and Pfizer Inc. (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on August 13, 2012)
10.19†	Letter Agreement, dated December 7, 2012, by and between the Registrant and Pfizer Inc. (incorporated by reference to Exhibit 10.31 to the Annual Report on Form 10-K filed by the Registrant on March 6, 2014)

10.20	Employment Agreement between the Registrant and Brian Stuglik, dated July 29, 2019 (incorporated by reference to Exhibit 10.1 to Current Report on Form 8-K filed by the Registrant on August 1, 2019)
10.21†	License Agreement for CKI27, dated January 7, 2020, between Verastem, Inc. and Chugai Pharmaceutical Co., Ltd. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on May 7, 2020)
10.22#	Form of Restricted Stock Unit Agreement under the 2012 Incentive Plan (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on May 7, 2020)
10.23#	Form of Inducement Restricted Stock Unit Agreement (incorporated by reference to Exhibit 10.3 to the Quarterly Report on Form 10-Q filed by the Registrant on May 7, 2020)
10.24#	Form of Incentive Stock Option Agreement under the 2012 Incentive Plan (Form of Restricted Stock Unit Agreement under the 2012 Incentive Plan (incorporated by reference to Exhibit 10.4 to the Quarterly Report on Form 10-Q filed by the Registrant on May 7, 2020)
10.25#	Form of Nonstatutory Stock Option Agreement under the 2012 Incentive Plan (incorporated by reference to Exhibit 10.5 to the Quarterly Report on Form 10-Q filed by the Registrant on May 7, 2020)
10.26#	Form of Inducement Nonstatutory Stock Option Agreement (incorporated by reference to Exhibit 10.6 to the Quarterly Report on Form 10-Q filed by the Registrant on May 7, 2020)
10.27#	Amended and Restated 2012 Incentive Plan (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K, filed by the Registrant with the Securities and Exchange Commission on May 21, 2020)
10.28#	2021 Equity Incentive Plan (incorporated by reference to Appendix A of the Registrant's Proxy Statement, filed by the Registrant with the Securities and Exchange Commission on April 8, 2021)
10.29#	Form of Incentive Stock Option Agreement under the 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on August 2, 2021)
10.30#	Form of Nonstatutory Stock Option Agreement (Employees) under the 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Quarterly Report on Form 10-Q filed by the Registrant on August 2, 2021)
10.31#	Form of Nonstatutory Stock Option Agreement (Non-Employees) under the 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 to the Quarterly Report on Form 10-Q filed by the Registrant on August 2, 2021)
10.32#	Form of Restricted Stock Unit Agreement under the 2021 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Quarterly Report on Form 10-Q filed by the Registrant on August 2, 2021)
10.33#	Form of Inducement Nonstatutory Stock Option Agreement (incorporated by reference to Exhibit 10.6 to the Quarterly Report on Form 10-Q filed by the Registrant on August 2, 2021)
10.34#	Form of Inducement Restricted Stock Unit Agreement (incorporated by reference to Exhibit 10.7 to the Quarterly Report on Form 10-Q filed by the Registrant on August 2, 2021)
10.35†	Asset Purchase Agreement by and between Secura Bio, Inc. and Verastem, Inc. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed by the Registrant on November 9, 2020)
10.36	Exchange Agreement by and between Verastem, Inc. and Highbridge Tactical Credit Master Fund, L.P., dated November 6, 2020 (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed by the Registrant on November 9, 2020)

10.37	Loan and Security Agreement, dated as of March 25, 2022, among Verastem, Inc., as borrower, Oxford Finance LLC, as collateral agent and a lender, and Oxford Finance Credit Fund III LP, as a lender (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K, filed by the Registrant with the Securities and Exchange Commission on March 27, 2022)
10.38	Section 203 Agreement entered into as of March 28, 2022 by and between Baker Bros. Advisors LP and Verastem, Inc. (incorporated by reference to Exhibit 10.1 to the Form 8-K filed by the Registrant with the Securities and Exchange Commission on March 30, 2022).
10.39	Exchange Agreement, dated November 4, 2022, by and among Verastem, Inc. and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS LP and MSI BVF SPV, LLC (incorporated by reference to Exhibit 10.1 to for the form 8-K filed by the Registrant with the Securities and Exchange Commission on November 7, 2022)
10.40	Securities Purchase Agreement, dated January 24, 2023, by and among Verastem, Inc. and each purchaser party thereto (incorporated by reference to Exhibit 10.1 to the form 8-K filed by the Registrant with the Securities and Exchange Commission on January 25, 2023)
21.1*	Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young LLP
31.1*	Certification of the Chief Executive Officer pursuant to Exchange Act Rule 13a-14(a)
31.2*	Certification of the Vice President, Finance pursuant to Exchange Act Rule 13a-14(a)
32.1*	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2*	Certification of the Vice President, Finance pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
99.1*	Press Release issued by Verastem, Inc. on March 14, 2023 (furnished herewith).
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)

* Filed herewith.

† Certain confidential information contained in this exhibit has been omitted because it (i) is not material and (ii) would be competitively harmful if publicly disclosed. Confidential materials omitted will be filed separately with the SEC upon request.

Management contract or compensatory plan, contract or agreement.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on this 14th day of March 2023.

VERASTEM, INC.
By: /s/ BRIAN M. STUGLIK
Brian M. Stuglik
Chief Executive Officer

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

Signature	Title	Date
/s/ BRIAN M. STUGLIK R.PH Brian M. Stuglik	Chief Executive Officer and Director (Principal Executive Officer)	March 14, 2023
/s/ DANIEL CALKINS Daniel Calkins	Vice President, Finance (Principal Financial and Accounting officer)	March 14, 2023
/s/ PAUL BUNN, M.D. Paul Bunn, M.D.	Director	March 14, 2023
/s/ ROBERT GAGNON Robert Gagnon	Director	March 14, 2023
/s/ ANIL KAPUR Anil Kapur	Director	March 14, 2023
/s/ MICHAEL KAUFFMAN, M.D.,PH.D. Michael Kauffman, M.D., PH.D.	Director	March 14, 2023
/s/ JOHN JOHNSON John Johnson	Director	March 14, 2023
/s/ MICHELLE ROBERTSON Michelle Robertson	Director	March 14, 2023
/s/ ERIC ROWINSKY, M.D. Eric Rowinsky, M.D.	Director	March 14, 2023
/s/ LESLEY SOLOMON Lesley Solomon	Director	March 14, 2023

Verastem, Inc.

CONSOLIDATED FINANCIAL STATEMENTS

CONTENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Verastem, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Verastem, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated 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 and Prepaid Clinical Trial Expense

Description of the Matter	As summarized in Note 4 to the consolidated financial statements, the Company's accrued research and development expenses were $8.5 million at December 31, 2022, which included the estimated obligation for clinical trial expenses incurred as of December 31, 2022 but not paid as of that date. In addition, the Company's total prepaid expenses and other current assets were $4.9 million, which included amounts that were paid in advance of services incurred pursuant to clinical trials. As discussed in Note 2 to the consolidated financial statements, the Company records research and development expenses as incurred. The Company's determination of costs incurred to conduct research, such as the discovery and development of the Company's product candidates as well as the related accrued expenses at each reporting period incorporates

judgment and utilizes various assumptions, including an evaluation of the information provided to the Company by third parties on actual cost incurred but not yet billed, estimated time period over which services will be performed, and the level of effort to be expended in each period. Payments for these activities are based on the terms of the individual arrangements, which often differ from the pattern of costs incurred.

Auditing the Company's accrued and prepaid clinical trial expenses was especially challenging due to the large volume of information received from multiple vendors that perform services on the Company's behalf. While the Company's estimates of accrued and prepaid clinical trial expenses are primarily based on information received from its vendors for each study, the Company may need to make an estimate for additional costs incurred. Additionally, due to the long duration of clinical trials and the timing of vendor invoices, the actual amounts incurred are not typically known at the time the financial statements are issued.

How We Addressed the Matter in Our Audit

To evaluate the Company's estimate of services incurred as of period end pursuant to its accrued and prepaid clinical trials expenses, our audit procedures included, among others, assessing the accuracy and completeness of the underlying third-party and internally generated data used in determining the accrued and prepaid clinical trial expenses and evaluating the assumptions/estimates used by management. For example, to assess the nature and extent of the services incurred, we corroborated the progress of clinical trials with the Company's research and development personnel that oversee the clinical trials and confirmed cost incurred and payments made to date directly with the Company's primary clinical research organization. To evaluate the completeness/existence and valuation of the recorded balances, we also tested subsequent payments and invoices received and inspected the Company's contracts with vendors and any pending change orders to assess the impact. We also performed analytical reviews over fluctuations in accruals by study throughout the period subject to audit.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2011.

Boston, Massachusetts

March 14, 2023

Verastem, Inc.
CONSOLIDATED BALANCE SHEETS
(in thousands, except per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 74,933	$ 21,252
Short-term investments	12,961	79,004
Accounts receivable, net	31	516
Prepaid expenses and other current assets	4,945	4,968
Total current assets	92,870	105,740
Property and equipment, net	92	210
Right-of-use asset, net	1,789	2,302
Restricted cash	241	241
Other assets	58	169
Total assets	$ 95,050	$ 108,662
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 4,901	$ 2,302
Accrued expenses	14,983	15,621
Deferred liabilities	710	—
Lease liability, short-term	794	667
Convertible senior notes	275	—
Total current liabilities	21,663	18,590
Non-current liabilities:		
Convertible senior notes	—	249
Long-term debt	24,526	—
Lease liability, long-term	1,470	2,264
Total liabilities	47,659	21,103
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000 shares authorized, 1,000 and 0 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	—	—
Common stock, $0.0001 par value; 300,000 shares authorized, 200,541 and 185,286 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	20	19
Additional paid-in capital	784,894	751,217
Accumulated other comprehensive income/(loss)	—	34
Accumulated deficit	(737,523)	(663,711)
Total stockholders' equity	47,391	87,559
Total liabilities and stockholders' equity	$ 95,050	$ 108,662

See accompanying notes to the consolidated financial statements.

Verastem, Inc.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except per share amounts)

	Year Ended December 31,		
	2022	2021	2020
Revenue:			
Product revenue, net	—	—	15,232
License and collaboration revenue	—	—	2,912
Sale of COPIKTRA license and related assets	2,596	1,447	70,000
Transition services revenue	—	606	372
Total revenue	2,596	2,053	88,516
Operating expenses:			
Cost of sales - product	—	—	1,765
Cost of sales - intangible amortization	—	—	793
Cost of sales - sale of COPIKTRA license and related assets	—	—	31,187
Research and development	50,558	39,347	41,376
Selling, general and administrative	24,975	24,115	62,755
Total operating expenses	75,533	63,462	137,876
Loss from operations	(72,937)	(61,409)	(49,360)
Other income (expense)	47	—	(1,313)
Interest income	1,215	181	515
Interest expense	(2,137)	(9,972)	(15,794)
Loss on debt extinguishment	—	—	(1,580)
Net loss before income taxes	(73,812)	(71,200)	(67,532)
Income tax expense	—	—	(194)
Net loss	$ (73,812)	$ (71,200)	$ (67,726)
Net loss per share—basic and diluted	(0.38)	(0.41)	(0.44)
Weighted average common shares outstanding used in computing net loss per share—basic and diluted	193,654	174,406	153,330
Net loss	$ (73,812)	$ (71,200)	$ (67,726)
Unrealized gain (loss) on available-for-sale securities	(34)	(19)	39
Comprehensive loss	$ (73,846)	$ (71,219)	$ (67,687)

See accompanying notes to the consolidated financial statements.

Verastem, Inc.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share data)

	Series A Preferred Stock		Common stock		Additional paid-in capital	Accumulated other comprehensive (loss) income	Accumulated deficit	Total stockholders' equity
	Shares	Amount	Shares	Amount				
Balance at December 31, 2019	—	$ —	80,117,531	$ 8	$ 531,937	$ 14	$ (524,785)	$ 7,174
Net loss	—	—	—	—	—	—	(67,726)	(67,726)
Unrealized gain on available-for-sale marketable securities	—	—	—	—	—	39	—	39
Conversion of Notes into common stock	—	—	34,796,350	3	57,411	—	—	57,414
Change in fair value of conversion option of Notes on exchange	—	—	—	—	2,331	—	—	2,331
Issuance of common stock under Employee Stock Purchase Plan	—	—	358,193	—	407	—	—	407
Issuance of common stock resulting from vesting of restricted stock units	—	—	421,695	—	(1,120)	—	—	(1,120)
Issuance of common stock resulting from exercise of stock options	—	—	1,481,223	—	2,578	—	—	2,578
Issuance of common stock resulting from at-the-market transactions, net of issuance costs of $55	—	—	6,769,559	1	12,229	—	—	12,230
Issuance of common stock resulting from private investment in public equity offering, net of issuance costs of $6,171	—	—	46,511,628	5	93,824	—	—	93,829
Stock-based compensation expense	—	—	—	—	8,118	—	—	8,118
Balance at December 31, 2020	—	$ —	170,456,179	$ 17	$ 707,715	$ 53	$ (592,511)	$ 115,274
Net loss	—	—	—	—	—	—	(71,200)	(71,200)
Unrealized loss on available-for-sale marketable securities	—	—	—	—	—	(19)	—	(19)
Conversion of Notes into common stock	—	—	8,615,384	1	27,999	—	—	28,000
Issuance of common stock under Employee Stock Purchase Plan	—	—	110,060	—	182	—	—	182
Issuance of common stock resulting from vesting of restricted stock units	—	—	2,585,054	—	(90)	—	—	(90)
Issuance of common stock resulting from exercise of stock options	—	—	589,218	—	905	—	—	905
Issuance of common stock resulting from at-the-market transactions, net	—	—	2,930,585	1	6,795	—	—	6,796
Stock-based compensation expense	—	—	—	—	7,711	—	—	7,711
Balance at December 31, 2021	—	$ —	185,286,480	$ 19	$ 751,217	$ 34	$ (663,711)	$ 87,559
Net loss	—	—	—	—	—	—	(73,812)	(73,812)
Unrealized loss on available-for-sale marketable securities	—	—	—	—	—	(34)	—	(34)
Issuance of Series A Preferred Stock in exchange for common stock	1,000,000	—	(10,000,000)	(1)	1	—	—	—
Issuance of common stock under Employee Stock Purchase Plan	—	—	122,332	—	164	—	—	164
Issuance of common stock resulting from vesting of restricted stock units	—	—	1,460,555	—	—	—	—	—
Issuance of common stock resulting from exercise of stock options	—	—	98,176	—	118	—	—	118
Issuance of common stock resulting from at-the-market transactions, net	—	—	23,573,403	2	27,347	—	—	27,349
Stock-based compensation expense	—	—	—	—	6,047	—	—	6,047
Balance at December 31, 2022	1,000,000	$ —	200,540,946	$ 20	$ 784,894	$ —	$ (737,523)	$ 47,391

See accompanying notes to the consolidated financial statements.

Verastem, Inc.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2022	2021	2020
Operating activities			
Net loss	$ (73,812)	$ (71,200)	$ (67,726)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	118	206	531
Amortization of acquired intangible asset	—	—	793
Amortization of right-of-use asset and lease liability	(154)	(134)	(69)
Stock-based compensation expense	6,047	7,711	8,118
Loss on debt extinguishment	—	—	1,580
Amortization of deferred financing costs, debt discounts and premiums and discounts on available-for-sale marketable securities	228	9,331	10,319
Change in fair value of interest make whole provision for 2019 Notes	—	—	1,313
Changes in operating assets and liabilities:			
Accounts receivable, net	485	(277)	2,285
Inventory	—	—	3,096
Prepaid expenses, other current assets and other assets	744	(1,558)	634
Accounts payable	2,599	623	(7,976)
Accrued expenses and other liabilities	(638)	1,796	(4,999)
Deferred liabilities	710	—	—
Other long-term liabilities	—	—	(870)
Intangible assets & property, plant and equipment	—	—	19,465
Net cash used in operating activities	(63,673)	(53,502)	(33,506)
Investing activities			
Purchases of property and equipment	—	(196)	(33)
Purchases of investments	(17,815)	(86,442)	(79,380)
Maturities of investments	84,000	86,725	32,050
Net cash provided by (used in) investing activities	66,185	87	(47,363)
Financing activities			
Proceeds from long-term debt, net	24,148	—	—
Repayment of long-term debt, net	—	—	(37,366)
Interest make-whole payments on the 2019 Notes	—	—	(1,763)
Proceeds from the exercise of stock options and employee stock purchase program	282	1,087	2,985
Settlement of restricted stock for tax withholdings	—	(925)	(285)
Proceeds from the issuance of common stock, net	27,354	6,723	106,059
Net cash provided by financing activities	51,784	6,885	69,630
Increase (decrease) in cash, cash equivalents and restricted cash	54,296	(46,530)	(11,239)
Cash, cash equivalents and restricted cash at beginning of period	21,493	68,023	79,262
Cash, cash equivalents and restricted cash at end of period	$ 75,789	$ 21,493	$ 68,023
Supplemental disclosure			
Cash paid for interest	$ 1,536	$ 1,007	$ 5,126
Supplemental disclosure of non-cash investing and financing activities			
Common stock issuance costs included in accounts payable and accrued expenses	$ —	$ —	$ 15
Conversion of 2019 Notes into common stock	$ —	$ —	$ 57,414
Conversion of 2020 Notes into common stock	$ —	$ 28,000	$ —
Purchases of property and equipment including in accounts payable and accrued expenses	$ —	$ —	$ 217
Change in fair value of conversion option of 2020 Notes on exchange	$ —	$ —	$ 2,331
Settlement of restricted stock for tax withholdings included in accrued expenses	$ —	$ —	$ 835

See accompanying notes to the consolidated financial statements.

1. Nature of business

Verastem, Inc. (the "Company") is a late-stage development biopharmaceutical company, with an ongoing registration directed trial, committed to advancing new medicines for patients battling cancer. The Company's pipeline is focused on novel anticancer agents that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, particularly RAF/MEK inhibition and FAK inhibition.

The Company's most advanced product candidates, avutometinib (VS-6766) and defactinib, are being investigated in both preclinical and clinical studies for the treatment of various solid tumors, including, low-grade serous ovarian cancer ("LGSOC"), non-small cell lung cancer ("NSCLC"), colorectal cancer ("CRC"), pancreatic cancer, and melanoma. The Company believes that avutometinib may be beneficial as a therapeutic as a single agent or when used together in combination with defactinib, other agents, other pathway inhibitors or other current and emerging standard of care treatments in cancers that do not adequately respond to currently available therapies.

On September 24, 2018, the Company's first commercial product, COPIKTRA® (duvelisib), was approved by the U.S. Food and Drug Administration (the "FDA") for the treatment of adult patients with certain hematologic cancers including relapsed or refractory chronic lymphocytic leukemia/ small lymphocytic lymphoma after at least two prior therapies and relapsed or refractory follicular lymphoma after at least two prior systemic therapies. On August 10, 2020, the Company and Secura Bio, Inc. ("Secura") entered into an asset purchase agreement ("Secura APA"). Pursuant to the Secura APA, the Company sold to Secura its exclusive worldwide license, including certain related assets for the research, development, commercialization, and manufacture in oncology indications of products containing COPIKTRA (duvelisib). The transaction closed on September 30, 2020. Refer to *Note 13. License, collaboration and commercial agreements* for a detailed discussion of the Secura APA.

The consolidated financial statements include the accounts of Verastem Securities Company and Verastem Europe GmbH, wholly-owned subsidiaries of the Company. All financial information presented has been consolidated and includes the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

The Company is subject to the risks associated with other life science companies, including, but not limited to, possible failure of preclinical testing or clinical trials, competitors developing new technological innovations, inability to obtain marketing approval of the Company's product candidates, avutometinib and defactinib, market acceptance and commercial success of the Company's product candidates, avutometinib and defactinib, following receipt of regulatory approval, and, protection of proprietary technology and the continued ability to obtain adequate financing to fund the Company's future operations. If the Company does not obtain marketing approval and successfully commercialize its product candidates, avutometinib and defactinib, following regulatory approval, it will be unable to generate product revenue or achieve profitability and may need to raise additional capital.

The Company has historical losses from operations and anticipates that it may continue to incur operating losses as it continues the research and development of its product candidates. As of December 31, 2022, the Company had cash, cash equivalents, and investments of $87.9 million, and an accumulated deficit of $737.5 million. The Company expects its existing cash resources along with $30.0 million of gross proceeds raised through the Series B Preferred Stock issuance in January 2023, and expected $15.0 million debt drawdown through its loan and security agreement with Oxford Finance LLC ("Oxford") expected in March 2023 will be sufficient to fund its planned operations through at least 12 months from the date of issuance of these consolidated financial statements. See *Note 16. Subsequent events* for detailed description of the Series B Preferred Stock issuance.

The Company expects to finance the future development costs of its clinical product portfolio with its existing cash, cash equivalents and investments, through potential future milestones and royalties received pursuant to the Secura APA, through the loan and security agreement with Oxford, or through other strategic financing opportunities that could include, but are not limited to collaboration agreements, future offerings of its equity, or the incurrence of debt. However, there is no guarantee that any of these strategic or financing opportunities will be executed or executed on favorable terms, and some could be dilutive to existing stockholders. If the Company fails to obtain additional future capital, it may be unable to complete its planned preclinical studies and clinical trials and obtain approval of certain investigational product candidates from the FDA or foreign regulatory authorities.

2. Significant accounting policies

Basis of presentation

The accompanying financial statements of the Company have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP") under the assumption that the Company will continue as a going concern for the next twelve months. Accordingly, they do not include any adjustments that might result from the uncertainty related to the Company's ability to continue as a going concern.

Use of estimates

The preparation of the Company's financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, management evaluates its estimates, including estimates related to revenue recognition, including returns, rebates, and other pricing adjustments, accrued and prepaid clinical trial expense and other general accruals and stock-based compensation expense. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable. Actual results could differ from such estimates.

Segment and geographic information

Operating segments are defined as components of an enterprise about which separate discrete information is available and regularly reviewed by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing drugs for the treatment of cancer. All material long-lived assets of the Company reside in the United States.

Proceeds from grants

During the year ended December 31, 2022, the Company was awarded the "Therapeutic Accelerator Award" grant from Pancreatic Cancer Network ("PanCAN") for up to $3.8 million (the "PanCAN Grant"). In August 2022, PanCAN agreed to provide the Company with an additional $0.5 million for the collection and analysis of patient samples. The grant is expected to support a Phase 1b/2 clinical trial of GEMZAR (gemcitabine) and ABRAXANE (Nab-paclitaxel) in combination with avutometinib and defactinib entitled RAMP 205. The RAMP 205 trial will evaluate whether combining avutometinib (to target mutant KRAS which is mutated in more than 90% of pancreatic tumors) and defactinib (to reduce stromal density and adaptive resistance to avutometinib) to the standard GEMZAR/ABRAXANE regimen improves outcomes for patients with pancreatic cancer. The Company received $1.0 million of cash proceeds in July 2022 which was initially recorded as deferred liabilities on the balance sheet. The Company recognizes grants as contra research and development expense in the consolidated statement of operations and comprehensive loss on a systematic basis over the periods in which the entity recognizes as expenses the related costs for which the grants are intended to compensate. The Company recorded $0.3 million of the proceeds as a reduction of research and development expense during the year ended December 31, 2022. As of December 31, 2022, the Company recorded $0.7 million as deferred liabilities in the consolidated balance sheet related to the PanCAN Grant.

Cash, cash equivalents and restricted cash

The Company considers all highly liquid investments with an original or remaining maturity of three months or less at the date of purchase to be cash equivalents. Cash equivalents consist of a U.S. Government money market funds and corporate bonds and commercial paper of publicly traded companies. Cash equivalents are reported at fair value.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statements of cash flows (in thousands):

	December 31, 2022	December 31, 2021
Cash and cash equivalents	$ 74,933	$ 21,252
Restricted cash	856	241
Total cash, cash equivalents and restricted cash	**$ 75,789**	**$ 21,493**

Amounts included in restricted cash as of December 31, 2022 represent (i) cash received pursuant to the PanCAN Grant restricted for future expenditures for specific research and development activities and (ii) cash held to collateralize outstanding letters of credit provided as a security deposit for the Company's office space located in Needham, Massachusetts in the amounts of $0.6 million and $0.2 million, respectively. Amounts included in restricted cash as of December 31, 2021 represent cash held to collateralize outstanding letters of credit provided as a security deposit for the Company's office space located in Needham, Massachusetts in the amount of $0.2 million. Cash received pursuant to the PanCAN Grant is included in prepaid expenses and other current assets on the consolidated balance sheet as of December 31, 2022. The letters of credit are included in non-current restricted cash on the consolidated balance sheets as of December 31, 2022 and December 31, 2021.

Fair value of financial instruments

The Company determines the fair value of its financial instruments based upon the fair value hierarchy, which prioritizes valuation inputs based on the observable nature of those inputs. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The hierarchy defines three levels of valuation inputs:

Level 1 inputs	Quoted prices in active markets for identical assets or liabilities that the Company can access at the measurement date.
Level 2 inputs	Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.
Level 3 inputs	Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

Items Measured at Fair Value on a Recurring Basis

The following table presents information about the Company's financial instruments that are measured at fair value on a recurring basis (in thousands)

	December 31, 2022			
Description	**Total**	**Level 1**	**Level 2**	**Level 3**
Financial assets				
Cash equivalents	$ 73,613	$ 72,617	$ 996	$ —
Short-term investments	12,961	—	12,961	—
Total financial assets	**$ 86,574**	**$ 72,617**	**$ 13,957**	**$ —**

	December 31, 2021			
Description	**Total**	**Level 1**	**Level 2**	**Level 3**
Financial assets				
Cash equivalents	$ 19,302	$ 19,302	$ —	$ —
Short-term investments	79,004	—	79,004	—
Total financial assets	**$ 98,306**	**$ 19,302**	**$ 79,004**	**$ —**

The investments and cash equivalents have been initially valued at the transaction price and subsequently valued, at the end of each reporting period, utilizing third party pricing services or other market observable data. The pricing services utilize industry standard valuation models, including both income and market-based approaches and observable market inputs to determine value. These observable market inputs include reportable trades, benchmark yields, credit spreads, broker/dealer quotes, bids, offers, current spot rates and other industry and economic events. The Company validates the prices provided by third party pricing services by reviewing their pricing methods and matrices, obtaining market values from other pricing sources, analyzing pricing data in certain instances and confirming that the relevant markets are active. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of December 31, 2022 and 2021.

Fair Value of Financial Instruments

The fair value of the Company's 2018 issued 5.00% Convertible Senior Notes due 2048 (the "2018 Notes") was approximately $0.3 million as of December 31, 2022, which equals the carrying value of the 2018 Notes as of December 31, 2022. The fair value of the 2018 Notes was approximately $0.3 million as of December 31, 2021, which differed from the carrying value of the 2018 Notes of $0.2 million as of December 31, 2021. The fair value of the 2018 Notes is influenced by the Company's stock price, stock price volatility, and current market yields and was determined using Level 3 inputs.

The fair value of the Company's long-term debt is determined using a discounted cash flow analysis with current applicable rates for similar instruments as of the consolidated balance sheet date. The carrying value of the Company's long-term debt as of December 31, 2022, was approximately $24.5 million. The Company estimates that the fair value of its long-term debt was approximately $24.9 million as of December 31, 2022. There was no long-term debt outstanding as of December 31, 2021. The fair value of the Company's long-term debt was determined using Level 3 inputs.

Investments

Investments and cash equivalents consist of investments in a U.S. Government money market funds, overnight repurchase agreements collateralized by government agency securities or U.S. Treasury securities, corporate bonds and commercial paper of publicly traded companies that are classified as available-for-sale pursuant to Accounting Standards Codification (ASC) Topic 320, *Investments—Debt and Equity Securities*. The Company classifies investments available to fund current operations as current assets on its consolidated balance sheets. Debt securities are carried at fair value with unrealized gains and losses included as a component of accumulated other comprehensive income (loss), which is a separate component of stockholders' equity, until such gains and losses are realized. The fair value of these securities is based on quoted prices for identical or similar assets. If a decline in the fair value is considered other-than-temporary, based on available evidence, the unrealized loss is transferred from other comprehensive loss to the consolidated statements of operations and comprehensive loss.

The Company reviews investments for other-than-temporary impairment whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than-temporary, the Company considers the intent to sell, or whether it is more likely than not that the Company will be required to sell, the investment before recovery of the investment's amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company's investment policy, the severity and the duration of the impairment and changes in value subsequent to year end. Realized gains and losses are determined using the specific identification method and are included in interest income in the consolidated statements of operations and comprehensive loss.

There were no realized gains or losses on investments for the years ended December 31, 2022, 2021 or 2020. There were two debt securities and three debt securities in an unrealized loss position as of December 31, 2022 and December 31, 2021, respectively. None of these investments had been in an unrealized loss position for more than 12 months as of December 31, 2022, or December 31, 2021. The fair value of these securities as of December 31, 2022, and December 31, 2021, was $6.0 million and $15.8 million, respectively, and the aggregate unrealized loss was immaterial. The Company considered the decline in the market value for these securities to be primarily attributable to current economic conditions. As it was not more likely than not that the Company would be

required to sell these securities before the recovery of their amortized cost basis, which may be at maturity, the Company did not consider these investments to be other-than-temporarily impaired as of December 31, 2022, and December 31, 2021, respectively.

Cash, cash equivalents, restricted cash and investments consist of the following (in thousands):

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash, cash equivalents & restricted cash:				
Cash and money market accounts	$ 74,794	$ —	$ —	$ 74,794
Corporate bonds, agency bonds and commercial paper (due within 90 days)	995	—	—	995
Total cash, cash equivalents & restricted cash:	$ 75,789	$ —	$ —	$ 75,789
Investments:				
Corporate bonds, agency bonds and commercial paper (due within 1 year)	$ 12,961	$ 2	$ (2)	$ 12,961
Total investments	$ 12,961	$ 2	$ (2)	$ 12,961
Total cash, cash equivalents, restricted cash and investments	**$ 88,750**	**$ 2**	**$ (2)**	**$ 88,750**

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash, cash equivalents & restricted cash:				
Cash and money market accounts	$ 21,493	$ —	$ —	$ 21,493
Total cash, cash equivalents & restricted cash:	$ 21,493	$ —	$ —	$ 21,493
Investments:				
Corporate bonds and commercial paper (due within 1 year)	$ 78,970	$ 48	$ (14)	$ 79,004
Total investments	$ 78,970	$ 48	$ (14)	$ 79,004
Total cash, cash equivalents, restricted cash and investments	**$ 100,463**	**$ 48**	**$ (14)**	**$ 100,497**

Concentrations of credit risk and off-balance sheet risk

Cash and cash equivalents, investments, and trade accounts receivable are financial instruments that potentially subject the Company to concentrations of credit risk. The Company mitigates this risk by maintaining its cash and cash equivalents and investments with high quality, accredited financial institutions. The management of the Company's investments is not discretionary on the part of these financial institutions. As of December 31, 2022, the Company's cash, cash equivalents and investments were deposited at three financial institutions and it has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

As of December 31, 2022, and 2021, there was one customer, Secura, that made up more than 60% of the Company's trade accounts receivable balance. The Company assesses the creditworthiness of all its customers and sets and reassesses customer credit limits to ensure collectability of any trade accounts receivable balances are assured.

For the year ended December 31, 2022 and 2021, one customer, Secura, individually accounted for all of the Company's total revenue. Refer to *Note 13. License, collaboration, and commercial agreements* for a detailed discussion of the Secura APA.

Property and equipment

Property and equipment consist of laboratory equipment, office furniture, computer equipment and leasehold improvements. Expenditures for repairs and maintenance are recorded to expense as incurred, whereas major betterments are capitalized as additions to property and equipment. Depreciation and amortization are calculated using the straight-line method over the following estimated useful lives of the assets:

Laboratory equipment	5 years
Furniture	5 years
Computer equipment	3 years
Leasehold improvements	Lesser of useful life or life of lease

Upon retirement or sale, the cost of the disposed asset and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is recognized.

The Company reviews its long-lived assets for impairment whenever events or changes in business circumstances indicate that the carrying value of assets may not be recoverable. Recoverability is measured by comparison of the asset's book value to future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value, which is measured based on the projected discounted future net cash flows arising from the assets. No impairment losses have been recorded through December 31, 2022.

Research and development costs

The Company expenses research and development costs to operations as incurred. Research and development expenses consist of:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- external research and development expenses incurred under arrangements with third parties, such as clinical research organizations ("CROs"), clinical trial sites, manufacturing organizations and consultants, including the scientific advisory board;
- license fees;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, and laboratory supplies; and

Costs for certain development activities, such as clinical trial expenses, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, and information provided to the Company by its vendor on their actual costs incurred or level of effort expended. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected on the consolidated balance sheets as prepaid expenses and other current assets or accrued expenses.

Stock-based compensation

For service-based equity awards, the Company recognizes stock-based compensation expense for stock options, and restricted stock units ("RSUs") issued to employees, directors, and consultants based on the grant date fair value of the awards on a straight-line basis over the requisite service period, which typically is the vest period. The Company recognized stock-based compensation for shares issued to employees under the Company's employee stock purchase plan ("ESPP") plan.

The Company has granted performance-based RSUs and stock options with terms that allow the recipients to vest in a specific number of shares based upon the achievement of performance-based milestones as specified in the grants. Stock-based compensation expense associated with these performance-based RSUs and stock options is recognized if the performance condition is considered probable of achievement using the Company's best estimates of the time to vesting for the achievement of the performance-based milestones. Awards subject to performance-

based vesting requirements are expensed utilizing an accelerated attribution model if achievement of the performance criteria is determined to be probable.

The grant date fair value of stock options is estimated using the Black-Scholes option pricing model that takes into account the fair value of its common stock, the exercise price, the expected life of the option, the expected volatility of its common stock, expected dividends on its common stock, and the risk-free interest rate over the expected life of the option. The Company applies the simplified method described in the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin ("SAB") Topic 14.D.2 to calculate the expected term as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term for options granted to employees. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its population. The Company has not paid and do not anticipate paying cash dividends on the Company's shares of common stock; therefore, the expected dividend yield is assumed to be zero. The computation of expected volatility is based on the historical volatility of the Company's common stock. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The Company accounts for forfeitures as they occur.

The Company issues shares under the Company's ESPP to employees. Stock-based compensation expense for discounted purchases under the ESPP is measured using the Black-Scholes model to compute the fair value of the lookback provision plus the purchase discount and is recognized as compensation expense over the offering period.

Leases

Leases are accounted for in accordance with ASC Topic 842, Leases ("*ASC 842*"). This standard requires lessees to recognize in the statement of financial position a liability to make lease payments and a right-of-use asset representing its right to use the underlying asset for the lease term for both finance and operating leases.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances within the arrangement. A lease is identified where an arrangement conveys the right to control the use of identified property, plant, and equipment for a period of time in exchange for consideration. Leases which are identified within the scope of ASC 842 and which have a term greater than one year are recognized on the Company's consolidated balance sheets as right-of-use assets, lease liabilities and, if applicable, long-term lease liabilities. The Company has elected not to recognize leases with terms of one year or less on its consolidated balance sheets. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. However, certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rates to calculate the present value of lease payments. Incremental borrowing rates are the rates the Company incurs to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment.

In accordance with ASC 842, components of a lease are split into three categories: lease components (e.g., land, building, etc.), non-lease components (e.g., common area maintenance, maintenance, consumables, etc.), and non-components (e.g., property taxes, insurance, etc.). The fixed and in-substance fixed contract consideration (including any related to non-components) must be allocated based on fair values to the lease components and non-lease components. Although separation of lease and non-lease components is required, certain practical expedients are available. Entities may elect the practical expedient to not separate lease and non-lease components. Rather, they would account for each lease component and the related non-lease component together as a single component. The Company has elected to account for the lease and non-lease components of each of its operating leases as a single lease component and allocate all of the contract consideration to the lease component only. The lease component results in an operating right-of-use asset being recorded on the consolidated balance sheets and amortized on a straight-line basis as lease expense.

Revenue recognition

The Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services in accordance with ASC Topic 606 *Revenue from Contracts with Customers* (ASC 606). To determine revenue recognition for contracts with its customers, the Company performs the following five step assessment: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception and once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract, determines which goods and services are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product revenue, net

Product Revenue, Net – The Company sold COPIKTRA to a limited number of specialty pharmacies and specialty distributors in the United States. These customers subsequently resold COPIKTRA either directly to patients or to community hospitals or oncology clinics with in-office dispensaries who in turn distribute COPIKTRA to patients. In addition to distribution agreements with customers, the Company also entered into arrangements with (1) certain government agencies and various private organizations (Third-Party Payers), which may provide for chargebacks or discounts with respect to the purchase of COPIKTRA, and (2) Medicare and Medicaid, which may provide for certain rebates with respect to the purchase of COPIKTRA.

The Company recognized revenue on sales of COPIKTRA when a customer obtains control of the product, which occurs at a point in time (typically upon delivery). Product revenues are recorded at the wholesale acquisition costs, net of applicable reserves for variable consideration. Components of variable consideration include trade discounts and allowances, Third-Party Payer chargebacks and discounts, government rebates, other incentives, such as voluntary co-pay assistance, product returns, and other allowances that are offered within contracts between the Company and customers, payors, and other indirect customers relating to the Company's sale of COPIKTRA. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable or a current liability. These estimates take into consideration a range of possible outcomes based upon relevant factors such as customer contract terms, information received from third parties regarding the anticipated payor mix for COPIKTRA, known market events and trends, industry data, 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 with respect to sales made.

The amount of variable consideration which is included in the transaction price 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 under contracts will not occur in a future period. The Company's analyses contemplate the application of the constraint in accordance with ASC 606. For the year ended December 31, 2020, the Company determined a material reversal of revenue would not occur in a future period for the estimates detailed below and, therefore, the transaction price was not reduced further. There was not any product revenue, net recorded for the year ended December 31, 2021 and 2022. Actual amounts of consideration ultimately received may differ from the Company's estimates. However, as of December 31, 2022, there are not any reserve balances associated with product revenue, net.

Trade Discounts and Allowances: The Company generally provided customers with invoice discounts on sales of COPIKTRA for prompt payment, which are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company compensated its specialty distributor customers for sales order management, data, and distribution services. The Company has determined such services are not distinct from the Company's sale of COPIKTRA to the specialty distributor customers and, therefore, these payments have also been recorded as a reduction of revenue within the

consolidated statements of operations and comprehensive loss for the year ended December 31, 2020. There were no amounts recorded for the years ended December 31, 2022 and 2021.

Third-Party Payer Chargebacks, Discounts and Fees: The Company executed contracts with Third-Party Payers which allowed for eligible purchases of COPIKTRA at prices lower than the wholesale acquisition cost charged to customers who directly purchase the product from the Company. In some cases, customers charged the Company for the difference between what they paid for COPIKTRA and the ultimate selling price to the Third-Party Payers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable, net. Chargeback amounts are generally determined at the time of resale to the qualified Third-Party Payer by customers, and the Company generally issues credits for such amounts within a few weeks of the customer's notification to the Company of the resale. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at the end of each reporting period that the Company expects will be sold to Third-Party Payers, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit. In addition, the Company compensated certain Third-Party Payers for administrative services, such as account management and data reporting. These administrative service fees have also been recorded as a reduction of product revenue within the consolidated statements of operations and comprehensive loss for the year ended December 31, 2020. There were no amounts recorded for the years ended December 31, 2022 and 2021.

Government Rebates: The Company was subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Other Incentives: Other incentives which the Company offered include voluntary co-pay assistance programs, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive for product that has been recognized as revenue but remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses on the consolidated balance sheets.

Product Returns: Consistent with industry practice, the Company generally offers customers a limited right of return for product that has been purchased from the Company. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. The Company estimates product return liabilities using available industry data and its own sales information, including its visibility into the inventory remaining in the distribution channel.

Subject to certain limitations, the Company's return policy allows for eligible returns of COPIKTRA for credit under the following circumstances:

- Receipt of damaged product;
- Shipment errors that were a result of an error by the Company;
- Expired product that is returned during the period beginning three months prior to the product's expiration and ending six months after the expiration date;
- Product subject to a recall; and
- Product that the Company, at its sole discretion, has specified can be returned for credit.

If taxes should be collected from customers relating to product sales and remitted to governmental authorities, they will be excluded from product revenue. The Company expenses incremental costs of obtaining a contract when incurred if the expected amortization period of the asset that the Company would have recognized is one year or less.

Licenses and sales of intellectual property

Licenses of Intellectual Property - The Company may enter into collaboration and licensing arrangements for research and development, manufacturing, and commercialization activities with collaboration partners for the development and commercialization of its product candidates, which have components within the scope of ASC 606. The arrangements generally contain multiple elements or deliverables, which may include (i) licenses, or options to obtain licenses, to the Company's intellectual property or sale of the Company's license, (ii) research and development activities performed for the collaboration partner, (iii) participation on joint steering committees, and (iv) the manufacturing of commercial, clinical or preclinical material. Payments pursuant to these arrangements typically include non-refundable, upfront payments, milestone payments upon the achievement of significant development events, research and development reimbursements, sales milestones, and royalties on product sales. The amount of variable consideration is constrained until it is probable that the revenue is not at a significant risk of reversal in a future period. The contracts into which the Company enters generally do not include significant financing components.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its collaboration and license agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract within the scope of ASC 606; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above; b) the transaction price under step (iii) above; c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above; and d) the measure of progress in step (v) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties on license arrangements, should be included in the transaction price as described further below.

If a license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a promise or performance obligation is distinct from the other elements, the Company considers factors such as the research, development, manufacturing and commercialization capabilities of the collaboration partner and the availability of its associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from a promise for its intended purpose without the receipt of the remaining elements, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined 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. The Company evaluates the measure as of progress of each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, is subject to estimates by management and may change over the course of the arrangement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Customer Options: If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services such as research and development services or manufacturing services, the goods and services underlying the customer options are not considered to be performance obligations at the inception of the arrangement; rather, such goods and services are contingent on exercise of the option, and the associated option fees are not included in the transaction price. The Company evaluates customer options for material rights or options

to acquire additional goods or services for free or at a discount. If a customer option is determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the estimated probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised.

Milestone Payments: At the inception of each arrangement that includes milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the respective milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

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

For sales of license and intellectual property, that include sale-based royalties, including milestone payments based on a level of sales, the Company evaluates whether the royalties and sales-based milestones are considered probable of being achieved and estimates the amount of royalties to include over the contractual term using the expected value method and estimates the sales-based milestones using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated royalty and milestone value is included in the transaction price. Royalties and sales-based milestones for territories for which there is not regulatory approval are not considered probable until such regulatory approval is achieved. The Company evaluates factors such as whether consideration is outside of the Company's control, timeline for when the uncertainty will be resolved and historical sales of COPIKTRA if applicable. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and amount of royalty revenue to be received and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

Collaborative arrangements

Collaborative Arrangements: Contracts are considered to be collaborative arrangements when they satisfy the following criteria defined in ASC Topic 808, *Collaborative Arrangements* (ASC 808): (i) the parties to the contract must actively participate in the joint operating activity and (ii) the joint operating activity must expose the parties to the possibility of significant risk and rewards, based on whether or not the activity is successful. Payments received from or made to a partner that are the result of a collaborative relationship with a partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction or increase to research and development expense, respectively.

Accounts receivable, net

Accounts receivable, net consists of amounts due from customers, net of applicable revenue reserves. Accounts receivable have standard payments that generally require payment within 30 to 90 days. The Company analyzes accounts that are past due for collectability and provides an allowance for receivables when collection

becomes doubtful. Given the nature and credit profile of the Company's limited number of customers, an allowance for doubtful accounts is not deemed necessary at December 31, 2022.

Income taxes

The Company accounts for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Tax benefits are recognized when it is more likely than not that a tax position will be sustained during an audit. Deferred tax assets are reduced by a valuation allowance if current evidence indicates that it is considered more likely than not that these benefits will not be realized.

The Company recognizes the tax effects of an uncertain tax position only if it is more likely than not that it will be sustained based solely on its technical merits as of the reporting date and only in an amount more likely than not that it will be sustained upon review by the tax authorities. The Company evaluates uncertain tax positions on a quarterly basis and adjust the liability for changes in facts and circumstances, such as new regulations or interpretations by the taxing authorities, new information obtained during a tax examination, significant amendment to an existing tax law, or resolution of an examination. To the extent that the final tax outcome of these matters is different than the amounts recorded, such differences will impact the income tax provision in the period in which such determination is made. The resolution of its uncertain income tax positions is dependent on uncontrollable factors such as law changes, new case law, and the willingness of the income tax authorities to settle, including the timing thereof and other factors. Although the Company does not anticipate significant changes to its uncertain income tax positions in the next twelve months, items outside of its control could cause its uncertain income tax positions to change in the future, which would be recorded in its statements of operations. Interest and/or penalties related to income tax matters are recognized as a component of income tax expense.

Net operating loss ("NOL") and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

The Company experienced a greater than 50% change in ownership as defined under Section 382 and 383 of the Internal Revenue Code as well as similar state provisions during the year ended December 31, 2020. For more details please refer to *Note 11. Income Taxes.*

Net loss per share

Basic net loss per common share is calculated by dividing net loss applicable to common stockholders by the weighted-average number of common shares outstanding during the period. Diluted net loss per common share is calculated by increasing the denominator by the weighted-average number of additional shares that could have been outstanding from securities convertible into common stock, such as stock options, restricted stock units and warrants (using the "treasury stock" method), Notes and Series A Preferred Stock (using the "if-converted" method), unless their effect on net loss per share is antidilutive. The effect of computing diluted net loss per common share was antidilutive for any potentially issuable shares of common stock from the conversion of stock options, restricted stock units and warrants and, as such, have been excluded from the calculation. However, under the "if-converted" method, convertible instruments that are-in-the-money, are assumed to have been converted as of the beginning of the period or when issued, if later. Additionally, the effects of any interest expense and changes in fair value of bifurcated derivatives shall be added back to the numerator of the diluted net loss per share calculation. Refer to *Note 10. Net Loss per share* for further details related to the calculation of net loss per share.

Recently issued accounting standards updates

In June 2016, the FASB issued Accounting Standard Update ("ASU") No. 2016-13, Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"). ASU 2016-13 will replace the incurred loss impairment methodology under current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. In November 2019, the FASB issued ASU 2019-10, Financial Instruments – Credit Losses (Topic 326), Derivatives (Topic 815), and Leases (Topic 842). This ASU delayed the required adoption for SEC filers that are smaller reporting companies as of their determination on November 15, 2019, until annual and interim periods beginning after December 15, 2022, with early adoption permitted. The Company has determined that as of November 15, 2019, it is a smaller reporting company and has not elected to early adopt this standard. The Company is currently evaluating the impact the adoption of the standard will have on its consolidated financial statements and related disclosures.

In August 2020, the FASB issued No. ASU 2020-06, Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815 – 40) ("ASU 2020-06"). ASU 2020-06 simplifies the complexity associated with applying U.S. GAAP for certain financial instruments with characteristics of liabilities and equity. More specifically, the amendments focus on the guidance for convertible instruments and derivative scope exception for contracts in an entity's own equity. The ASU also simplifies the diluted earnings per share ("EPS") calculation in certain areas. For smaller reporting companies, ASU 2020-06 is effective for fiscal years beginning after December 15, 2023, and interim periods within those fiscal years. The Company is currently evaluating the impact ASU 2020-06 will have on its consolidated financial statements and related disclosures.

3. Property and equipment, net

Property and equipment and related accumulated depreciation are as follows (in thousands):

	December 31, 2022	December 31, 2021
Leasehold improvements	$ 146	$ 146
Furniture and fixtures	811	1,074
Computer equipment	665	665
	1,622	1,885
Less: accumulated depreciation	(1,530)	(1,675)
Total property and equipment, net	**$ 92**	**$ 210**

The Company recorded approximately $0.1 million, $0.2 million, and $0.5 million in depreciation expense for the years ended December 31, 2022, 2021, and 2020, respectively.

4. Accrued expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2022	December 31, 2021
Research and development expenses	$ 8,535	$ 9,311
Compensation and related benefits	3,844	3,892
Professional fees	469	785
Consulting fees	902	544
Interest	192	3
Commercialization costs	148	187
Other	893	899
Total accrued expenses	**$ 14,983**	**$ 15,621**

5. Long-term debt

Oxford

On March 25, 2022 (the "Closing Date"), the Company entered into a loan and security agreement (the "Loan Agreement") with Oxford, as collateral agent and a lender, and Oxford Finance Credit Fund III LP, as a lender ("OFCF III" and together with Oxford, the "Lenders"), pursuant to which the Lenders have agreed to lend the Company up to an aggregate principal amount of $150.0 million in a series of term loans (the "Term Loans").

Pursuant to the Loan Agreement, the Company received an initial Term Loan of $25.0 million on the Closing Date and may borrow an additional $125.0 million of Term Loans at its option upon the satisfaction of certain conditions as follows:

i. $15.0 million (the "Term B Loan"), when the Company has either (a) received the Regulatory Milestone Payment (as defined in the Secura APA) from Secura of $35.0 million which is due upon receipt of regulatory approval of COPIKTRA in the United States for the treatment of peripheral T-cell lymphoma ("PTCL") or (b) received at least $50.0 million in unrestricted cash proceeds from the sale or issuance of equity securities after the Closing Date (the "Term B Milestones"). The Company may draw the Term B Loan within 60 days after the occurrence of one of the Term B Milestones, but no later than March 31, 2023.
ii. $25.0 million (the "Term C Loan"), when the Company has received accelerated or full approval from the FDA of avutometinib for the treatment of LGSOC (the "Term C Milestone"). The Company may draw the Term C Loan within 60 days after the occurrence the Term C Milestone, but no later than March 31, 2024.
iii. $35.0 million (the "Term D Loan"), when the Company has achieved at least $50.0 million in gross product revenue calculated on a trailing six-month basis (the "Term D Milestone"). The Company may draw the Term D Loan within 30 days after the occurrence of the Term D Milestone, but no later than March 31, 2025.
iv. $50.0 million (the "Term E Loan"), at the sole discretion of the Lenders.

The Term Loans bear interest at a floating rate equal to (a) the greater of (i) the one-month CME Secured Overnight Financing Rate and (ii) 0.13% plus (b) 7.37%, which is subject to an overall floor and cap. Interest is payable monthly in arrears on the first calendar day of each calendar month. Beginning (i) April 1, 2024, if the Term B Loan is not made, (ii) April 1, 2025, if the Term B Loan is made, or (iii) April 1, 2026, if the Term B Loan is made and either (A) avutometinib has received FDA approval for the treatment of LGSOC or (B) COPIKTRA has received FDA approval for the treatment of PTCL, the Company shall repay the Term Loans in consecutive equal monthly payments of principal, together with applicable interest, in arrears. All unpaid principal and accrued and unpaid interest with respect to each Term Loan is due and payable in full on March 1, 2027.

The Company is required to make a final payment of 5.0% of the original principal amount of the Term Loans that are drawn, payable at maturity or upon any earlier acceleration or prepayment of the Term Loans (the "Final Payment Fee"). The Company may prepay all, but not less than all, of the Term Loans, subject to a prepayment fee equal to (i) 3.0% of the principal amount of the applicable Term Loan if prepaid on or before the first anniversary date of the funding date of such Term Loan, (ii) 2.0% of the principal amount of the applicable Term Loan if prepaid after the first anniversary and on or before the second anniversary of the funding date of such Term Loan, and (iii) 1.0% of the principal amount of the applicable Term Loan if prepaid after the second anniversary of the applicable funding date of such Term Loan. All Term Loans are subject to a facility fee of 0.5% of the principal amount.

The Loan Agreement contains no financial covenants. The Loan Agreement includes customary events of default, including, among others, payment defaults, breach of representations and warrants, covenant defaults, judgment defaults, insolvency and bankruptcy defaults, and a material adverse change. The occurrence of an event of default could result in the acceleration of the obligations under the Loan Agreement, termination of the Term Loan commitments and the right to foreclose on the collateral securing the obligations. During the existence of an event of default, the Term Loans will accrue interest at a rate per annum equal to 5.0% above the otherwise applicable interest rate.

In connection with the Loan Agreement, the Company granted Oxford a security interest in all of the Company's personal property now owned or hereafter acquired, excluding intellectual property (but including the right to payments and proceeds of intellectual property), and a negative pledge on intellectual property.

The Company assessed all terms and features of the Loan Agreement in order to identify any potential embedded features that would require bifurcation. As part of this analysis, the Company assessed the economic characteristics and risks of the Loan Agreement, including put and call features. The Company determined that all features of the Loan Agreement were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's financial statements. The Company reassesses the features on a quarterly basis to determine if they require separate accounting. There have been no changes to the Company's assessment through December 31, 2022.

The debt issuance costs and the Final Payment Fee have been recorded as a debt discount which are being accreted to interest expense through the maturity date of the Term Loan using the effective interest method. The components of the carrying value of the debt as of December 31, 2022 (in thousands):

	December 31, 2022
Principal loan balance	$ 25,000
Final Payment Fee	225
Debt issuance costs, net of accretion	(699)
Long-term debt, net of discount	**$ 24,526**

As of December 31, 2022, future principal payments due are as follows (in thousands):

2023	—
2024	6,250
2025	8,333
2026	8,333
2027	2,084
Total principal payments	**$ 25,000**

Hercules

On March 21, 2017, the Company entered into a term loan facility of up to $25.0 million with Hercules Capital, Inc. ("Hercules"). The term loan facility was governed by a loan and security agreement, dated March 21, 2017 (the "Original Loan Agreement"). The Original Loan Agreement was amended on January 4, 2018, March 6, 2018, October 11, 2018, April 23, 2019, and November 14, 2019 (the "Amended Loan Agreement") to increase the total borrowing limit under the Original Loan Agreement from $25.0 million to up to $75.0 million, pursuant to certain conditions of funding. The Amended Term Loan was scheduled to mature on December 1, 2022.

On November 9, 2020, the Company repaid in full all principal, accrued and unpaid interest, fees, and expenses under the Amended Loan Agreement with Hercules in an aggregate amount of $37.4 million (the "Payoff Amount"). The Payoff Amount included the principal balance of $35.0 million, final payment fee of $1.8 million, prepayment penalty fee of $0.5 million, and accrued and unpaid interest of $0.1 million. On November 9, 2020 the Amended Loan Agreement was terminated along with Hercules' commitment to provide funding under any future term loans. All liens on substantially all of the Company's assets to secure the loans under the Amended Loan Agreement have been terminated and released. The Payoff Amount, excluding accrued interest, exceeded the carrying amount of the Hercules debt on November 9, 2020 by $1.6 million. As a result, the Company recorded a loss on debt extinguishment of $1.6 million included in the statements of operations and comprehensive loss for the year ended December 31, 2020.

6. Leases

On April 15, 2014, the Company entered into a lease agreement for approximately 15,197 square feet of office and laboratory space in Needham, Massachusetts. The lease term commenced on April 15, 2014 and it was scheduled to expire on September 30, 2019. Effective February 15, 2018, the Company amended its lease agreement to relocate within the facility to another location consisting of 27,810 square feet of office space (the Amended Lease Agreement). The Amended Lease Agreement extends the expiration date of the lease from September 2019 through June 2025. Pursuant to the Amended Lease Agreement, the initial annual base rent amount is approximately $0.7 million, which increases during the lease term to $1.1 million for the last twelve-month period.

The Company has accounted for its Needham, Massachusetts office space as an operating lease. The Company's lease contains an option to renew and extend the lease terms and an option to terminate the lease prior to the expiration date. The Company has not included the lease extension or the termination options within the right-of-use asset and lease liability on the consolidated balance sheets as neither option is reasonably certain to be exercised. The Company's lease includes variable non-lease components (e.g., common area maintenance, maintenance, consumables, etc.) that are not included in the right-of-use asset and lease liability and are reflected as an expense in the period incurred. The Company does not have any other operating or finance leases.

In calculating the present value of future lease payments, the Company has elected to utilize its incremental borrowing rate based on the remaining lease term at the date of adoption of ASC 842. The Company has elected to account for lease components and associated non-lease components as a single lease component and has allocated all of the contract consideration to the lease components only. This will potentially result in the initial and subsequent measurement of the balances of the right-of-use asset and lease liability for leases being greater than if the policy election was not applied.

As of December 31, 2022, a right-of-use asset of $1.8 million and lease liability of $2.3 million are reflected on the consolidated balance sheets. The elements of lease expense were as follows (dollar amounts in thousands):

	Year ended December 31,	
	2022	2021
Lease Expense		
Operating lease expense	$ 885	$ 885
Total Lease Expense	**$ 885**	**$ 885**
Other Information - Operating Leases		
Operating cash flows paid for amounts included in measurement of lease liabilities	$ 1,039	$ 1,019

	December 31, 2022
Other Balance Sheet Information - Operating Leases	
Weighted average remaining lease term (in years)	2.5
Weighted average discount rate	14.6%
Maturity Analysis	
2023	1,060
2024	1,081
2025	546
Total	**$ 2,687**
Less: Present value discount	(423)
Lease Liability	**$ 2,264**

7. Common stock

As of December 31, 2022 and 2021, the Company had reserved the following shares of common stock for the issuance of common stock for vested restricted stock units, the exercise of stock options, employee stock purchase plan, 2018 Notes and Series A Preferred Stock conversions to shares of common stock (in thousands):

	December 31,	
	2022	2021
Shares reserved under equity compensation plans	34,739	36,234
Shares reserved for inducement grants	3,928	3,991
Shares reserved for 2018 Notes	42	42
Shares reserved for ESPP	1,068	1,190
Shares reserved for Series A Preferred Stock	10,000	—
Total shares reserved	**49,777**	**41,457**

Each share of common stock is entitled to one vote. The holders of the common stock are also entitled to receive dividends whenever funds are legally available and when declared by the board of directors.

Series A Preferred Stock

Under the amended and restated certificate of incorporation, the Company's board of directors has the authority, without further action by the stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

On November 4, 2022, the Company entered into an exchange agreement (the "Exchange Agreement") with Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS

LP and MSI BVF SPV, LLC (collectively referred to as "BVF"), pursuant to which BVF exchanged 10,000,000 shares of the Company's common stock for 1,000,000 shares of newly designated Series A convertible preferred stock, par value $0.0001 per share (the "Series A Preferred Stock") (the "Exchange").

Each share of the Series A Preferred Stock is convertible into 10 shares of common stock at the option of the holder at any time, subject to certain limitations, including that the holder will be prohibited from converting Preferred Stock into common stock if, as a result of such conversion, the holder, together with its affiliates, would beneficially own a number of shares of common stock above a conversion blocker, which is initially set at 9.99% (the "Conversion Blocker") of the total common stock then issued and outstanding immediately following the conversion of such shares of Preferred Stock. Holders of the Series A Preferred Stock are permitted to increase the Conversion Blocker to an amount not to exceed 19.99% upon 60 days' notice.

Shares of Series A Preferred Stock will generally have no voting rights, except as required by law and except that the consent of a majority of the holders of the outstanding Series A Preferred Stock will be required to amend the terms of the Series A Preferred Stock. In the event of the Company's liquidation, dissolution or winding up, holders of Series A Preferred Stock will participate pari passu with any distribution of proceeds to holders of common stock. Holders of Series A Preferred Stock are entitled to receive when, as and if dividends are declared and paid on the common stock, an equivalent dividend, calculated on an as-converted basis. Shares of Series A Preferred Stock are otherwise not entitled to dividends.

The Series A Preferred Stock ranks (i) senior to any class or series of capital stock of the Company hereafter created specifically ranking by its terms junior to the Series A Preferred Stock; (ii) on parity with the common stock and any class or series of capital stock of the Company created specifically ranking by its terms on parity with the Series A Preferred Stock; and (iii) junior to any class or series of capital stock of the Company created specifically ranking by its terms senior to any Series A Preferred Stock, in each case, as to distributions of assets upon liquidation, dissolution or winding up of the Company, whether voluntarily or involuntarily.

The Company evaluated the Series A Preferred Stock for liability or equity classification under ASC 480, *Distinguishing Liabilities from Equity*, and determined that equity treatment was appropriate because the Series A Preferred Stock did not meet the definition of the liability under ASC 480. Additionally, the Series A Preferred Stock is not redeemable for cash or other assets (i) on a fixed or determinable date, (ii) at the option of the holder, or (iii) upon the occurrence of an event that is not solely within control of the Company. As such, the Company recorded the Series A Preferred Stock as permanent equity.

At-the-market equity offering programs

On March 30, 2017, the Company established an at-the-market equity offering program pursuant to which it was able to offer and sell up to $35.0 million of its common stock at then-current market prices from time to time through Cantor Fitzgerald & Co. ("Cantor"), as sales agent. On August 28, 2017, the Company amended its sales agreement with Cantor to increase the maximum aggregate offering price of shares of common stock that can be sold under the at-the-market equity offering program to $75.0 million. The Company did not make any sales under this program during the year ended December 31, 2021. During the year ended December 31, 2020, the Company sold 6,769,559 shares under this program for net proceeds of approximately $12.2 million (after deducting commissions and other offering expenses).

In August 2021, the Company entered into a sales agreement with Cantor pursuant to which the Company can offer and sell up to $100.0 million of its common stock at the current market prices from time to time through Cantor as sales agent (the "August 2021 ATM"). During the year-ended December 31, 2022 and 2021, the Company sold 23,573,403 shares and 2,930,585 shares, respectively, under the August 2021 ATM for net proceeds of approximately $27.4 million and $6.8 million, respectively, (after deducting commissions and other offering expenses).

Private Investment in Public Equity (PIPE)

On February 27, 2020, the Company entered into a Securities Purchase Agreement (the "Purchase Agreement") with certain institutional investors in which the Company agreed to sell 46,511,628 shares of common stock at a purchase price of $2.15 per share, which represents 12.6% premium to the last reported sale price of the Company's common stock of $1.91 per share on February 27, 2020. On March 3, 2020, the closing occurred. The aggregate proceeds net of underwriting discounts and offering costs, were approximately $93.8 million.

8. Stock-based compensation

Stock-based compensation expense as reflected in the Company's consolidated statements of operations and comprehensive loss was as follows (in thousands):

	Year ended December 31,		
	2022	2021	2020
Research and development	$ 1,766	$ 2,099	$ 1,935
Selling, general and administrative	4,281	5,612	6,183
Total stock-based compensation expense	**$ 6,047**	**$ 7,711**	**$ 8,118**

All of the $6.0 million, $7.7 million, and $8.1 million of stock-based compensation expense recorded during the years ended December 31, 2022, 2021, and 2020, respectively, was recorded to additional paid-in capital.

The Company has awards outstanding under two equity compensation plans, the 2021 Equity Incentive Plan (the "2021 Plan"), and the Amended and Restated 2012 Incentive Plan (the "2012 Plan"), as well as the inducement award program. As of December 31, 2022 and 2021, there were no awards outstanding under the 2010 Equity Incentive Plan (the "2010 Plan"). Terms of stock award agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the individual plans.

2021 Plan

During 2021, the Company's stockholders approved the 2021 Plan. Upon effectiveness of the 2021 Plan, the Company ceased making awards under the 2012 Plan. The 2021 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, RSUs and other stock-based awards. The number of shares of common stock initially reserved for issuance under the 2021 Plan is (i) 23,900,000 which is the sum of 13,250,124 shares plus the number of shares available for issuance under the 2012 Plan as of the date the Company's Board of Directors approved the 2021 Plan (10,649,876 shares) plus (ii) the number of shares of the Company's common stock underlying awards under the 2012 Plan and the 2010 Plan that expire, terminate or are surrendered without delivery of shares, are forfeited to or repurchased by the Company, or otherwise become available again for grant under the terms of the 2012 Plan or the 2010 Plan, as applicable.

As of December 31, 2022, under the 2021 Plan, the Company has granted stock options for 4,685,445 shares of common stock, of which 404,850 have been forfeited and 0 have been exercised, and granted RSUs for 2,032,397 shares of common stock, of which 213,400 have been forfeited and 541,012 have vested. As of December 31, 2022, 20,996,662 shares remain available for future issuance. The exercise price of each option has been equal to the closing price of a share of the Company's common stock on the grant date.

2012 Plan

The 2012 Plan became effective immediately upon the closing of the Company's IPO in February 2012. Upon effectiveness of the 2012 Plan, the Company ceased making awards under the 2010 Plan. The 2012 Plan initially allowed the Company to grant awards for up to 3,428,571 shares of common stock, plus the number of shares of common stock available for grant under the 2010 Plan as of the effectiveness of the 2012 Plan (which was an additional 30,101 shares), plus that number of shares of common stock related to awards outstanding under the 2010 Plan which terminate by expiration, forfeiture, cancellation or otherwise. The 2012 Plan included an "evergreen provision" that allowed for an annual increase in the number of shares of common stock available for

issuance under the 2012 Plan. The annual increase was added on the first day of each year from 2013 through 2018 and was equal to the lesser of 1,285,714 shares of common stock and 4.0% of the number of shares of common stock outstanding, or a lesser amount as determined by the board of directors. On each of January 1, 2018, January 1, 2017 and January 1, 2016, the number of shares available for issuance under the 2012 Plan increased by 1,285,714 under this provision. On December 18, 2018, the shareholders of the Company approved the Amended and Restated 2012 Incentive Plan which increased the maximum number of shares available for issuance under the 2012 Plan to 16,628,425 and eliminated the evergreen provision. On May 19, 2020, the shareholders of the Company approved the Amended and Restated 2012 Incentive Plan which increased the maximum number of shares available for issuance by 13,000,000 shares.

Awards under the 2012 Plan may include the following award types: incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock awards, RSUs, other stock-based or cash-based awards and any combination of the foregoing. As of December 31, 2022, under the 2012 Plan, the Company has granted stock options for 22,098,207 shares of common stock, of which 11,915,465 have been forfeited and 2,296,645 have been exercised, and granted RSUs for 6,678,621 shares of common stock, of which 1,049,068 have been forfeited and 5,302,060 have vested. The exercise price of each option has been equal to the closing price of a share of the Company's common stock on the grant date. Upon adoption of the 2021 Plan, the Company ceased issuing awards from the 2012 Plan.

Inducement Award Program

In December 2014, the Company established an inducement award program (in accordance with Nasdaq Listing Rule 5635(c)(4)) under which it may grant non-statutory stock options to purchase, and RSUs in respect of up to an aggregate of 750,000 shares of common stock to new or prospective employees as inducement to enter into employment with the Company. In December 2016, the Board of Directors authorized and reserved 580,000 additional shares of common stock under this program. In December 2017, the Board of Directors authorized and reserved 2,500,000 additional shares of common stock under this program. In June and December 2018, the Board of Directors authorized and reserved 1,700,000 and 1,250,000 additional shares of common stock under this program, respectively. In February 2020, the Board of Directors authorized the reduction of 2,033,367 shares available for issuance under this program. The program is governed by the terms of the 2021 Plan, but shares issued pursuant to the program are not issued under the 2021 Plan. As of December 31, 2022, the Company had granted options for 7,875,009 shares of common stock under the program, of which 5,439,075 have been forfeited and 584,016 have been exercised, and granted RSUs for 873,063 shares, of which 243,294 have been forfeited and 160,280 have vested. As of December 31, 2022, 1,605,930 shares remain available for future issuance.

Stock Options

Most options granted by the Company vest twenty-five percent (25%) one year from vesting start date and six and a quarter percent (6.25%) for each successive three-month period, thereafter (subject to acceleration of vesting in the event of certain change of control transactions) subject to the employee's continued employment with, or service to, the Company on such vesting date and are exercisable for a period of ten years from the date of grant.

A summary of the Company's stock option activity and related information for the year ended December 31, 2022, is as follows:

	Shares	Weighted-average exercise price per share	Weighted-average remaining contractual term (years)	Aggregate intrinsic value (in thousands)
Outstanding at December 31, 2021	16,264,098	$ 3.56	6.7	$ 2,601
Granted	1,547,998	0.95		
Exercised	(98,176)	1.20		
Forfeited/cancelled	(3,695,310)	5.41		
Outstanding at December 31, 2022	14,018,610	$ 2.80	7.1	$ 18
Vested at December 31, 2022	8,686,694	$ 3.28	6.1	$ 2

The fair value of each stock option was estimated using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year ended December 31,		
	2022	2021	2020
Risk-free interest rate	3.13 %	1.15 %	0.60 %
Volatility	88 %	89 %	96 %
Dividend yield	—	—	—
Expected term (years)	5.8	6.0	6.0

The Company recorded stock-based compensation expense associated with employee and non-employee stock options of $4.2 million, $4.1 million, and $4.3 million, for the years ended December 31, 2022, 2021, and 2020, respectively. The weighted-average grant date fair value of options granted in the years ended December 31, 2022, 2021, and 2020 was $0.69, $1.82, and $1.62 per share, respectively. The fair value of options that vested during the years ended December 31, 2022, 2021, and 2020 was $4.4 million, $3.8 million, and $7.4 million, respectively. The aggregate intrinsic value of options exercised (i.e., the difference between the market price at exercise and the price paid by employees to exercise the option) during the years ended December 31, 2022 and 2021 was less than $0.1 million and $0.8 million, respectively.

At December 31, 2022 there was $6.6 million of total unrecognized compensation cost related to unvested stock options and the Company expects to recognize this cost over a remaining weighted-average period of 2.6 years.

Restricted Stock Units ("RSUs")

Each RSU entitles the holder to receive one share of the Company's common stock when the RSU vests. The RSUs generally vest (i) twenty-five percent (25%) one year from vesting start date and six and a quarter percent (6.25%) for each successive three-month period, thereafter, (ii) two tranches for 50% of the award with the second and final vesting date on the one year anniversary of the vesting commencement date and (iii) 100 percent within two years of the vesting commencement date. The RSUs are subject to acceleration of vesting in the event of certain change of control transactions and subject to the employee's continued employment with, or service to, the Company on such vesting date. Compensation expense is recognized on a straight-line basis.

A summary of RSU activity during the year ended December 31, 2022, is as follows:

	Shares	Weighted-average grant date fair value per share
Outstanding at December 31, 2021	2,805,004	$ 2.44
Granted	398,413	$ 0.92
Vested	(876,829)	$ 2.63
Forfeited/cancelled	(251,621)	$ 2.29
Outstanding at December 31, 2022	2,074,967	$ 2.09

The Company recorded stock-based compensation expense associated with employee and non-employee RSUs of $1.8 million, $3.5 million, and $3.7 million, for the years ended December 31, 2022, 2021, and 2020, respectively. The total fair value of restricted stock units vested during the years ended December 31, 2022, 2021, and 2020 was approximately $2.3 million, $3.7 million, and $3.8 million, respectively.

At December 31, 2022, there was $4.3 million of total unrecognized compensation cost related to unvested RSUs and the Company expects to recognize this cost over a remaining weighted-average period of 2.8 years.

On March 27, 2020, the Company amended all outstanding stock options and RSUs awards held by employees (including executive officers), other than certain performance-based awards, to provide that, in the event of a change of control, such equity awards currently held by employees that are outstanding and unvested immediately prior to a change of control of the Company will become fully vested and, if applicable, exercisable immediately prior to, and subject to the consummation of, such change of control. The amendment was implemented to provide assurance to the Company's existing employees and not in response to any change of control offer for the Company. The modification affected 93 employees and resulted in incremental stock compensation expense of $0.2 million that was recognized over the remaining requisite service period for each award. The modification resulted in incremental stock compensation expense of $0.0 million, $0.1 million, and $0.1 million recognized in the years ended December 31, 2022, 2021 and 2020, respectively.

The Company modified all unvested equity awards held by 41 employees included in the August 2020 Restructuring discussed in *Note 14. Restructurings*. On September 30, 2020, the Company accelerated all unvested awards held by employees included in the August 2020 Restructuring to be fully vested on September 30, 2020. As a result of the modification, the Company recognized incremental stock compensation cost of approximately $0.5 million during year ended December 31, 2020 within selling, general and administrative expense in the consolidated statements of operations and comprehensive loss.

Employee stock purchase plan

At the Special Meeting of Stockholders, held on December 18, 2018, the stockholders approved the 2018 Employee Stock Purchase Plan ("2018 ESPP"). On June 21, 2019, the board of directors of the Company amended and restated the 2018 ESPP, to account for certain non-material changes to the plan's administration (the "Amended and Restated 2018 ESPP"). The Amended and Restated 2018 ESPP provides eligible employees with the opportunity, through regular payroll deductions, to purchase shares of the Company's common stock at 85% of the lesser of the fair market value of the common stock (a) on the date the option is granted, which is the first day of the purchase period, and (b) on the exercise date, which is the last business day of the purchase period. The Amended and Restated 2018 ESPP generally allows for two six-month purchase periods per year beginning in January and July, or such other periods as determined by the compensation committee of the Company's board of directors. The Company has reserved 2,000,000 shares of common stock for the administration of the Amended and Restated 2018 ESPP. The fair value of shares expected to be purchased under the Amended and Restated 2018 ESPP was calculated using the Black-Scholes model with the following weighted-average assumptions:

	Year ended December 31,		
	2022	2021	2020
Risk-free interest rate	1.56 %	0.07 %	1.04 %
Volatility	77 %	68 %	109 %
Dividend yield	—	—	—
Expected term (years)	0.5	0.5	0.5

The Company has recognized $0.1 million of stock-based compensation expense under the Amended and Restated 2018 ESPP, for each of the years ended December 31, 2022, 2021, and 2020. During the year ended December 31, 2022, 2021, and 2020, the Company issued 122,332 shares, 110,060 shares and 358,193 shares, respectively, of common stock for proceeds of $0.2 million, $0.2 million and $0.4 million, respectively under the Amended and Restated 2018 ESPP.

9. Convertible Senior Notes

2018 Notes

On October 17, 2018, the Company closed a registered direct public offering of $150.0 million aggregate principal amount of the Company's 2018 Notes for net proceeds of approximately $145.3 million. The 2018 Notes are governed by the terms of a base indenture for senior debt securities (the "2018 Base Indenture"), as supplemented by the first supplemental indenture thereto (the "Supplemental Indenture" and together with the "2018 Base Indenture", the "2018 Indenture"), each dated October 17, 2018, by and between the Company and Wilmington Trust, National Association, ("Wilmington") as trustee. The 2018 Notes are senior unsecured obligations of the Company and bear interest at a rate of 5.00% per annum, payable semi-annually in arrears on May 1 and November 1 of each year, beginning on May 1, 2019. The 2018 Notes will mature on November 1, 2048, unless earlier repurchased, redeemed or converted in accordance with their terms.

The 2018 Notes are convertible into shares of the Company's common stock, par value $0.0001 per share, together, if applicable, with cash in lieu of any fractional share, at an initial conversion rate of 139.5771 shares of common stock per $1,000 principal amount of the 2018 Notes, which corresponds to an initial conversion price of approximately $7.16 per share of common stock and represents a conversion premium of approximately 15.0% above the last reported sale price of the common stock of $6.23 per share on October 11, 2018. Upon conversion, converting noteholders will be entitled to receive accrued interest on their converted 2018 Notes. To the extent the Company has insufficient authorized but unissued shares to settle conversions in shares of common stock, the Company would be required to settle the deficiency in cash.

The Company will have the right, exercisable at its option, to cause all Notes then outstanding to be converted automatically if the "Daily VWAP" (as defined in the 2018 Indenture) per share of the Company's common stock equals or exceeds 130% of the conversion price on each of at least 20 VWAP Trading Days (as defined in the 2018 Indenture), whether or not consecutive, during any 30 consecutive VWAP Trading Day period commencing on or after the date the Company first issued the 2018 Notes.

The conversion rate is subject to adjustment from time to time upon the occurrence of certain events, including, but not limited to, the issuance of stock dividends and payment of cash dividends, but will not be adjusted for any accrued and unpaid interest.

Prior to November 1, 2022, the Company will not have the right to redeem the 2018 Notes. On or after November 1, 2022, the Company may elect to redeem the 2018 Notes, in whole or in part, at a cash redemption price equal to the principal amount of the 2018 Notes to be redeemed, plus accrued and unpaid interest, if any.

Unless the Company has previously called all outstanding 2018 Notes for redemption, the 2018 Notes will be subject to repurchase by the Company at the holders' option on each of November 1, 2023, November 1, 2028, November 1, 2033, November 1, 2038 and November 1, 2043 (or, if any such date is not a business day, on the next business day) at a cash repurchase price equal to the principal amount of the 2018 Notes to be repurchased, plus accrued and unpaid interest, if any.

If a "Fundamental Change" (as defined in the 2018 Indenture) occurs at any time, subject to certain conditions, holders may require the Company to purchase all or any portion of their 2018 Notes at a purchase price equal to 100% of the principal amount of the 2018 Notes to be purchased, plus accrued and unpaid interest. If a "Fundamental Change" occurs on or before November 1, 2022 and a holder elects to convert its Notes in connection with such change, such holder may be entitled to an increase in the conversion rate in certain circumstances as set forth in the Indenture.

The 2018 Indenture includes customary covenants and set forth certain events of default after which the 2018 Notes may be declared immediately due and payable and set forth certain types of bankruptcy or insolvency events of default involving the Company or certain of its subsidiaries after which the 2018 Notes become automatically due and payable.

The Company assessed all terms and features of the 2018 Notes in order to identify any potential embedded features that would require bifurcation. As part of this analysis, the Company assessed the economic characteristics and risks of the 2018 Notes, including the conversion, put and call features. The conversion feature was initially bifurcated as an embedded derivative but subsequently qualified for a scope exception to derivative accounting upon the Company's stockholders approving an increase in the number of authorized shares of Common Stock in December 2018. The Company determined that all other features of the 2018 Notes were clearly and closely associated with the debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's consolidated financial statements. The Company reassesses the features on a quarterly basis to determine if they require separate accounting. There have been no changes to the Company's original assessment through December 31, 2022.

2019 Notes

On November 14, 2019 and December 23, 2019, the Company entered into privately negotiated agreements to exchange approximately $114.3 million and $7.4 million, respectively, aggregate principal amount of the 2018 Notes for (i) approximately $62.9 million and $4.0 million, respectively, aggregate principal amount of newly issued 5.00% Convertible Senior Second Lien Notes due 2048 (the "2019 Notes"), (ii) an aggregate of $11.4 million and $0.7 million, respectively, in 2018 Notes principal repayment and (iii) accrued interest on the 2018 Notes through November 14, 2019 and December 23, 2019, respectively. The 2019 Notes are governed by the terms of an indenture (the "2019 Indenture"). The 2019 Notes are senior secured obligations of the Company and bear interest at 5.00% per annum, payable semi-annually in arrears on May 1 and November 1 of each year. The 2019 Notes will mature on November 1, 2048, unless earlier repurchased, redeemed or converted in accordance with the terms.

The Company determined 2019 Notes exchange met the definition of a troubled debt restructuring under ASC 470-60, *Troubled Debt Restructurings by Debtors*, as the Company was experiencing financial difficulties and the lenders granted a concession. The future undiscounted cash flows of the 2019 Notes after the exchange exceeded the carrying value of the converted 2018 Notes prior to the exchange. As such no gain was recognized as a result of the exchange. The Company reduced the carrying value of the 2019 Notes by the cash given and the change in fair value of the conversion option driven by the reduction in conversion price. The change in fair value of the conversion option was determined to be $13.6 million.

The 2019 Notes were convertible into shares of the Company's common stock, par value $0.0001 per share, together, if applicable, with cash in lieu of any fractional share, at an initial conversion rate of 606.0606 shares of common stock per $1,000 principal amount of the 2019 Notes, which corresponds to an initial conversion price of approximately $1.65 per share of common stock. In addition, if the holders converted the 2019 Notes with a conversion date that is on or prior to November 1, 2020, then the consideration due upon any such conversion will also include a cash interest make-whole payment for all future scheduled interest payments on the converted 2019 Notes through November 1, 2020 ("2019 Notes Interest Make-Whole Provision").

The Company assessed all terms and features of the 2019 Notes in order to identify any potential embedded features that would require bifurcation. As part of this analysis, the Company assessed the economic characteristics and risks of the 2019 Notes, including the conversion, put and call features. In consideration of the 2019 Notes Interest Make-Whole Provision, the Company concluded the provision required bifurcation as a derivative. The fair

value of the 2019 Interest Make-Whole Provision was determined using a Monte Carlo model. It was determined that the fair value of the derivative upon the November 14, 2019 and December 23, 2019 issuance of the 2019 Notes was $0.2 million in aggregate; and recorded this amount as a derivative liability and the offsetting amount as a debt discount as a reduction to the carrying value of the 2019 Notes on the closing dates. During the period November 14, 2019 to December 31, 2019, 2019 Note holders converted $9.5 million aggregate principal of 2019 Notes in exchange for 5,767,872 shares of common stock, $0.4 million of cash for 2019 Interest Make-Whole Provision payments, and accrued interest.

During the first quarter of 2020, 2019 Note holders converted $57.4 million aggregate principal of 2019 Notes in exchange for 34,796,350 shares of common stock, $1.8 million of cash for the 2019 Note Interest Make-Whole Provision, and accrued interest. The Company recorded $1.3 million for the year ended December 31, 2020, as other expense for the change in fair value of the 2019 Notes Interest Make-Whole Provision in the consolidated statements of operations and comprehensive loss. The Company determined that all other features of the 2019 Notes were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's consolidated financial statements. As of March 31, 2020, all 2019 Notes have converted into shares of common stock.

2020 Notes

On November 6, 2020, the Company entered into a privately negotiated agreement with an investor who was a holder of the Company's 2018 Notes to exchange approximately $28.0 million aggregate principal amount of 2018 Notes for approximately $28.0 million aggregate principal amount of newly issued 5.00% Convertible Senior Notes due 2048 (the "2020 Notes" and together with the 2018 Notes and 2019 Notes referred to as the "Notes"). The issuance of the 2020 Notes closed on November 13, 2020. The 2020 Notes were governed pursuant to the Base Indenture between the Company and Wilmington, as trustee and collateral agent, dated as of October 17, 2018 as supplemented by the second supplemental indenture thereto dated as of November 13, 2020 (the "2020 Notes Supplemental Indenture" and together with the Base Indenture, the "2020 Indenture").

The Company had the right, exercisable at its option, to cause all 2020 Notes then outstanding to be converted automatically if the "Daily VWAP" (as defined in the 2020 Indenture) per share of the Company's common stock equaled or exceeded 123.08% of the conversion price on each of at least 20 "VWAP Trading Days" (as defined in the 2020 Indenture), whether or not consecutive, during any 30 consecutive VWAP Trading Day period commencing on or after the date the Company first issued the 2020 Notes (the "2020 Notes Mandatory Conversion Option").

The initial conversion rate for the 2020 Notes was 307.6923 shares of the Company's common stock per $1,000 principal amount of the 2020 Notes, which is equivalent to an initial conversion price of approximately $3.25 per share. The conversion rate was subject to adjustment from time to time upon the occurrence of certain events, including, but not limited to, the issuance of stock dividends and payment of cash dividends, but was not subject to adjustment for any accrued and unpaid interest.

Prior to November 1, 2023, the Company did not have the right to redeem the 2020 Notes. On or after November 1, 2023, the Company had the option to redeem the 2020 Notes, in whole or in part, at a cash redemption price equal to the principal amount of the 2020 Notes to be redeemed, plus accrued and unpaid interest, if any.

Unless the Company had previously called all outstanding 2020 Notes for redemption, the 2020 Notes were subject to repurchase by the Company at the holders' option on each of November 1, 2023, November 1, 2028, November 1, 2033, November 1, 2038 and November 1, 2043 (or, if any such date is not a business day, on the next business day) at a cash repurchase price equal to the principal amount of the 2020 Notes to be repurchased, plus accrued and unpaid interest, if any.

The Company determined the 2020 Notes exchange met the definition of a debt modification under ASC 470-50, *Modifications and Extinguishments*. The Company reduced the carrying value of the 2020 Notes by the change in fair value of the conversion option driven by the reduction in conversion price. The change in fair value of the conversion option was determined to be $2.3 million.

The Company determined that all features of the 2020 Notes were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's consolidated financial statements.

On July 1, 2021, the Company exercised the Company's 2020 Notes Mandatory Conversion Option for the aggregate principal amount of $28.0 million of the Company's 2020 Notes. On July 16, 2021, the aggregate principal of $28.0 million of 2020 Notes was converted into 8,615,384 shares of common stock. As a result, as of September 30, 2021, all 2020 Notes have converted into shares of common stock. Upon conversion of the 2020 Notes, holders received a cash payment equal to the accrued and unpaid interest on the converted 2020 Notes. Pursuant to ASC 815-15-40-1, upon conversion, the Company recorded the remaining discount on the 2020 Notes of $7.8 million as interest expense in the statements of operations and comprehensive loss during the year ended December 31, 2021.

All Notes

The Company determined that the expected life of the 2018 Notes, 2019 Notes, and 2020 Notes was equal to the period through November 1, 2023, as this represents the point at which the 2018 Notes, 2019 Notes, and 2020 Notes were initially subject to repurchase by the Company at the option of the holders. Accordingly, for the 2018 Notes, the total debt discount, inclusive of the fair value of the embedded conversion feature derivative at issuance is being amortized using the effective interest method through November 1, 2023. For the 2019 Notes and 2020 Notes, the total debt discount, inclusive of the fair value of the embedded conversion feature derivative at issuance and change in fair value of conversion option upon exchange, was being amortized using the effective interest method through November 1, 2023. Pursuant to ASC 815-15-40-1, upon conversion of the 2019 Notes and 2020 Notes into common stock, the remaining debt discount on the conversion date was recorded to interest expense in the statements of operations and comprehensive loss. For the year ended December 31, 2022, the Company recognized less than $0.1 million of interest expense related to the 2018 Notes.

10. Net Loss per Share

ASC Topic 260, *Earnings Per Share,* requires the Company to calculate its net loss per share based on basic and diluted net loss per share, as defined. Basic EPS excludes dilution and is computed by dividing net loss by the weighted average number of shares outstanding for the period. For the years ended December 31, 2022, 2021, and 2020 net loss, basic and diluted EPS are the same as the assumed exercise of stock options, restricted stock units, and the Notes are anti-dilutive.

The following potentially dilutive securities were excluded from the calculation of diluted net loss per share due to their anti-dilutive effect:

	Year Ended December 31,		
	2022	2021	2020
Outstanding stock options	14,018,610	16,264,098	12,690,745
Outstanding restricted stock units	2,074,967	2,805,004	2,649,317
2018 Notes	41,873	41,873	41,873
2020 Notes	—	—	8,615,384
Employee stock purchase plan	82,496	57,636	53,372
Series A Preferred Stock	10,000,000	—	—
Total potentially dilutive securities	**26,217,946**	**19,168,611**	**24,050,691**

11. Income Taxes

As of December 31, 2022, the Company had federal and state NOL carryforwards of approximately $436.6 million and $203.3 million, respectively, which are available to reduce future taxable income. The Company also had federal and state tax credits of $5.6 million and $1.9 million, respectively, which may be used to offset future tax liabilities. The NOL and tax credit carryforwards will expire at various dates through 2042, except for $240.9 million of federal NOL carryforwards which may be carried forward indefinitely.

During the year ended December 31, 2020, the Company recorded income tax expense of $0.2 million, which primarily related to state income tax as a result of the sale of COPIKTRA license and related assets to Secura. Refer to *Note 13. License, collaboration and commercial agreements* for further discussion of the sale to Secura.

For the years ended December 31, 2022, 2021, and 2020 income tax expense consisted of the following (in thousands):

	Year ended December 31,		
	2022	2021	2020
Current tax expense:			
Federal	$ —	$ —	$ —
State	—	—	194
Current income tax expense	—	—	194
Deferred			
Federal	—	—	—
State	—	—	—
Deferred income tax expense	—	—	—
Total income tax expense	**$ —**	**$ —**	**$ 194**

A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations follows:

	December 31,	
	2022	2021
Income tax benefit using U.S. federal statutory rate	21.00 %	21.00 %
State tax benefit, net of federal benefit	2.15 %	3.01 %
Research and development tax credits	2.81 %	2.71 %
Stock-based compensation	(2.17)%	— %
Permanent items	(0.08)%	(0.44)%
Change in the valuation allowance	(21.41)%	(21.23)%
NOL and tax credit expiration under Section 382	(2.26)%	(4.34)%
Other	(0.04)%	(0.71)%
	— %	— %

The principal components of the Company's deferred tax assets and liabilities are as follows (in thousands):

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 103,243	$ 98,777
Capitalized research and development	11,621	1,276
Research and development credits	7,107	4,516
Stock-based compensation	3,450	4,200
Installment sale	7,768	8,819
Lease liability	538	730
Other deferred tax assets	587	411
Total deferred tax assets	134,314	118,729
Deferred tax liabilities:		
Right-of-use asset	(425)	(574)
Debt discount	(4)	(11)
Other deferred tax liability	(29)	(91)
Total deferred tax liabilities	(458)	(676)
Net deferred tax asset prior to valuation allowance	133,856	118,053
Valuation allowance	(133,856)	(118,053)
Net deferred tax asset	**$ —**	**$ —**

The Tax Cuts and Jobs Act ("TCJA") requires taxpayers to capitalize and amortize research and development ("R&D") expenditures under section 174 for tax years beginning after December 31, 2021. This rule became effective for the Company during 2022 and resulted in capitalized R&D costs of $44.5 million as of December 31, 2022. The Company will amortize these costs for tax purposes over 5 years for R&D performed in the U.S. and over 15 years for R&D performed outside the U.S.

The Company has recorded a valuation allowance against its deferred tax assets at December 31, 2022 and 2021 because the Company's management believes that it is more likely than not that these assets will not be fully realized. The increase in the valuation allowance of approximately $15.8 million in the year ended December 31, 2022, primarily relates to the capitalization of research and development expenses, the generation of NOLs and R&D credits.

Section 382 of the Internal Revenue Code and similar provisions under state law limit the utilization of U.S. NOL carryforwards, state NOL carryforwards, R&D credits, and Orphan Drug ("OD") credits following certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%. Based on the Company's analysis under Section 382, the Company believes that its federal NOL carryforwards, its state NOL carryforwards, R&D credits, and OD credits are limited by Section 382 and similar provisions under state law as of December 31, 2022. The portion of federal NOL carryforwards, state NOL carryforwards, R&D credits, and OD credits that were determined to be limited have been written off as of December 31, 2022. The remaining unused carryforwards and credits remain available for future periods. Due the Company's full valuation allowance the write off of NOL carryforwards and R&D and OD credits did not have any impact to the statements of operation and comprehensive loss.

The Company's reserves related to taxes are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. From inception and through December 31, 2022, the Company had no unrecognized tax benefits or related interest and penalties accrued. The Company has not conducted a study of R&D credit carryforwards. This study may result in an adjustment to the Company's R&D credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's R&D credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated balance sheet or statement of operations if an adjustment were required. The Company would recognize both accrued interest and penalties related to unrecognized benefits in income tax expense. The Company's uncertain tax positions are related to years that remain

subject to examination by relevant tax authorities. Since the Company is in a loss carryforward position, the Company is generally subject to examination by the U.S. federal, state and local income tax authorities for all tax years in which a loss carryforward is available.

12. Commitments and contingencies

The Company has entered into a lease agreement for approximately 27,810 square feet of office space in Needham, Massachusetts. Please refer to *Note 6. Leases* for further details regarding the minimum aggregate future lease commitments as of December 31, 2022. In conjunction with the execution of the Amended Lease Agreement, the Company has provided a security deposit in the form of a letter of credit in the amount of $0.2 million as of December 31, 2022, and 2021. The amount is included in non-current restricted cash on the consolidated balance sheets as of December 31, 2022, and 2021.

Pursuant to the terms of various agreements, the Company may be required to pay various development, regulatory and commercial milestones. In addition, if any products related to these agreements are approved for sale, the Company may be required to pay significant royalties on future sales. The payment of these amounts, however, is contingent upon the occurrence of various future events, which have a high degree of uncertainty of occurring.

13. License, collaboration and commercial agreements

Secura Bio, Inc. ("Secura")

On August 10, 2020, the Company and Secura signed the Secura APA and on September 30, 2020, the transaction closed.

Pursuant to the Secura APA, the Company sold to Secura its exclusive worldwide license, including related assets, for the research, development, commercialization, and manufacture in oncology indications of products containing duvelisib. The sale included certain intellectual property related to duvelisib in oncology indications, certain existing duvelisib inventory, claims and rights under certain contracts pertaining to duvelisib. Pursuant to the Secura APA, Secura assumed all operational and financial responsibility for activities that were part of the Company's duvelisib oncology program, including all commercialization efforts related to duvelisib in the United States and Europe, as well as the Company's ongoing duvelisib clinical trials. Further, Secura assumed all obligations with existing collaboration partners developing and commercializing duvelisib, which include Yakult Honsha Co., Ltd. ("Yakult"), CSPC Pharmaceutical Group Limited ("CSPC"), and Sanofi. Additionally, Secura assumed all royalty payment obligations due under the amended and restated license agreement with Infinity Pharmaceuticals, Inc. ("Infinity") ("Infinity License Agreement").

Pursuant to the terms of the Secura APA, Secura has paid the Company an up-front payment of $70.0 million in September 2020 and has agreed to pay the Company (i) regulatory milestone payments up to $45.0 million, consisting of a payment of $35.0 million upon receipt of regulatory approval of COPIKTRA in the United States for the treatment of peripheral T-cell lymphoma and a payment of $10.0 million upon receipt of the first regulatory approval for the commercial sale of COPIKTRA in the European Union for the treatment of peripheral T-cell lymphoma, (ii) sales milestone payments of up to $50.0 million, consisting of $10.0 million when total worldwide net sales of COPIKTRA exceed $100.0 million, $15.0 million when total worldwide net sales of COPIKTRA exceed $200.0 million and $25.0 million when total worldwide net sales of COPIKTRA exceed $300.0 million, (iii) low double-digit royalties on the annual aggregate net sales above $100.0 million in the United States, European Union, and the United Kingdom of Great Britain and Northern Ireland and (iv) 50% of all royalty, milestone and sublicense revenue payments payable to Secura under the Company's existing license agreements with Sanofi, Yakult, and CSPC, and 50% of all royalty and milestone payments payable to Secura under any license or sublicense agreement entered into by Secura in certain jurisdictions.

In connection with the Secura APA, the Company and Secura entered into a transition services agreement ("Secura TSA"). Under the terms of the Secura TSA, the Company provided certain support functions at Secura's direction for a term of less than one year from the date of execution ("Secura TSA Services"). Services performed were paid at a mutually agreed upon rate.

The Company evaluated the Secura APA and Secura TSA in accordance with ASC 606 as the Company concluded that the counterparty, Secura, is a customer. The Company identified the following performance obligations under the Secura APA and Secura TSA:

- a bundled performance obligation consisting of delivery of the duvelisib global license and intellectual property, certain existing duvelisib inventory, certain duvelisib contracts and clinical trials, certain regulatory approvals, and certain regulatory documentation and books and records (the "Bundled Secura Performance Obligation"); and

- Secura TSA Services.

The Company concluded that the duvelisib global license and intellectual property were not distinct within the context of the contract (i.e. separately identifiable) because the other assets including certain existing duvelisib inventory, certain duvelisib contracts and clinical trials, certain regulatory approval, and certain regulatory documentation and books and records do not have stand-alone value from other duvelisib global license and intellectual property and Secura could not benefit from them without the duvelisib global license and intellectual property. Consistent with the guidance under ASC 606-10-25-16A, the Company disregarded immaterial promised goods and services when determining performance obligations.

The Company has determined that the upfront payment of $70.0 million, future potential milestone payments and royalties including from Secura's sublicensees should be allocated to the delivery of the Bundled Secura Performance Obligation. The Company has the right to consideration for TSA services in an amount that corresponds directly with the value to Secura of the Company's performance to date. Consideration allocated to the Secura TSA Services will be recognized as such services are provided over the performance period using an output method based on the amount to which the Company has a right to invoice.

The Company determined $0.1 million of future potential royalties the Company expects to receive pursuant to the Secura APA were not constrained as of December 31, 2022. When estimating the amount of royalties to be received that were not constrained, the Company used the expected value method as there are a range of possible outcomes. When estimating royalties expected to be received, the Company used a combination of internal projections and forecasts and data from external sources. The Company determined that all other future potential royalties were constrained under the guidance as of December 31, 2022. As part of the Company's evaluation of the constraint on future royalties, the Company considered a number of factors in determining whether there is significant uncertainty associated with the future events that would result in royalty payments. Those factors include: the likelihood and magnitude of revenue reversals related to future royalties, the amount of variable consideration is highly susceptible to factors outside of the Company's influence, the amount of time to resolve the uncertainty, and lack of significant history of selling COPIKTRA outside of the United States.

As the consideration for future royalties is conditional, the Company recorded a corresponding contract asset for the expected future royalties. Portions of the contract asset are reclassified to accounts receivable when the right to consideration becomes unconditional. As of December 31, 2022, the $0.1 million contract asset has been recorded within prepaid and other current assets on the consolidated balance sheet.

The following table presents changes in the Company's contract asset for the year ended December 31, 2022 (in thousands):

Contract Asset:	December 31, 2021	Additions	Reclassification to receivable	December 31, 2022
Contract asset - Secura	$ 170	$ 96	$ (170)	$ 96
Total	$ 170	$ 96	$ (170)	$ 96

During the year ended December 31, 2022, one regulatory milestone was achieved by Secura's sublicensee, CSPC, of which 50% of the milestone or $2.5 million was paid to the Company pursuant to the Secura APA. The Company determined all other future potential milestones were excluded from the transaction price, as all other milestone amounts were fully constrained under the guidance as of December 31, 2022. As part of the Company's

evaluation of the constraint, the Company considered a number of factors in determining whether there is significant uncertainty associated with the future events that would result in the milestone payments. Those factors included: the likelihood and magnitude of revenue reversals related to future milestones, the amount of variable consideration that is highly susceptible to factors outside of the Company's influence and the uncertainty about the consideration is not expected to be resolved for a long period of time. All other future potential milestone payments were fully constrained as the risk of significant revenue reversal related to these amounts has not yet been resolved.

During the year ended December 31, 2022, the Company recognized $2.6 million of sale of COPIKTRA license and related assets revenue within the statements of operations and comprehensive loss. The sale of COPIKTRA license and related assets revenue for the year ended December 31, 2022 related to one regulatory milestone for $2.5 million achieved by Secura's sublicensee, CSPC, and $0.1 million related to royalties on COPIKTRA sales in the year ended December 31, 2022, and future royalties expected to be received pursuant to the Secura APA that were not constrained.

During the year ended December 31, 2021, the Company recognized $1.4 million of sale of COPIKTRA license and related assets revenue within the statements of operations and comprehensive loss. The sale of COPIKTRA license and related assets revenue for the year ended December 31, 2021 primarily related to two regulatory milestone for $1.3 million achieved by Secura's sublicensee and $0.2 million related to royalties received and expected to be received pursuant to the Secura APA. During the year ended December 31, 2021, the Company also recognized $0.6 million in transition services revenue within the statements of operations and comprehensive loss.

During the year ended December 31, 2020, the Company recognized $70.0 million as sale of COPIKTRA license and related assets revenue related to delivery of the Bundled Secura Performance Obligation and $0.4 million in transition services revenue within the statements of operations and comprehensive loss. The Company recognized approximately $31.2 million of cost of sales – sale of COPIKTRA license and related assets within the statements of operations and comprehensive loss which consisted of $19.2 million, $6.0 million, $5.8 million and $0.2 million for the intangible asset, certain duvelisib inventory, net duvelisib contract prepaid balances and manufacturing equipment, respectively, which were delivered to Secura as part of the sale.

Chugai Pharmaceutical Co., Ltd (Chugai)

On January 7, 2020, the Company entered into a license agreement with Chugai (the "Chugai Agreement") whereby Chugai granted the Company an exclusive worldwide license for the development, commercialization and manufacture of products containing avutometinib, a dual RAF/MEK inhibitor.

Under the terms of the Chugai Agreement, the Company received an exclusive right to develop and commercialize products containing avutometinib at the Company's own cost and expense. The Company is required to pay Chugai a non-refundable payment of $3.0 million which was paid in February 2020. The Company is further obligated to pay Chugai double-digit royalties on net sales of products containing avutometinib, subject to reduction in certain circumstances. Chugai also obtained opt back rights to develop and commercialize avutometinib (a) in the European Union, which option may be exercised through the date the Company submits a NDA to the FDA for a product which contains avutometinib as the sole active pharmaceutical ingredient and (b) in Japan and Taiwan, which option may be exercised through the date the Company receives marketing authorization from the FDA for a product which contains avutometinib as the sole active pharmaceutical ingredient. As consideration for executing either option, Chugai would have to make a payment to the Company calculated on the Company's development costs to date. Chugai has communicated their intention not to exercise their opt back rights for Japan, Taiwan, or the European Union. Chugai and the Company have made customary representations and warranties and have agreed to certain customary covenants, including confidentiality and indemnification.

Unless earlier terminated, the Chugai Agreement will expire upon the fulfillment of the Company's royalty obligations to Chugai for the sale of any products containing avutometinib, which royalty obligations expire on a product-by-product and country-by-country basis, upon the last to occur, in each specific country, of (a) expiration of valid patent claims covering such product or (b) 12 years from the first commercial sale of such product in such country.

The Company may terminate the Chugai Agreement upon 180 days' written notice. Subject to certain limitations, Chugai may terminate the Chugai Agreement upon written notice if the Company challenges any patent licensed by Chugai to the Company under the Chugai Agreement. Either party may terminate the license agreement in its entirety with 120 days' written notice for the other party's material breach if such party fails to cure the breach. Either party may also terminate the Chugai Agreement in its entirety upon certain insolvency events involving the other party.

The Company evaluated the license agreement with Chugai under ASC Topic 805, *Business Combinations* ("ASC 805") and concluded that as the fair value of the gross assets acquired is concentrated in a single identifiable asset or group of similar assets, the transaction did not meet the requirements to be accounted for as a business combination and therefore was accounted for as an asset acquisition. The Company recorded the up-front payment of $3.0 million as research and development expense within the consolidated statement of operations and comprehensive loss for the year ended December 31, 2020.

Infinity Pharmaceuticals, Inc. ("Infinity")

In November 2016, the Company entered into the Infinity License Agreement with Infinity under which the Company acquired an exclusive worldwide license for the research, development, commercialization, and manufacture of products in oncology indications containing duvelisib.

Pursuant to the terms of the Infinity License Agreement, the Company was obligated to pay Infinity royalties on worldwide net sales of any products in an oncology indication containing duvelisib ranging from the mid-single digits to the high single-digits. In addition to the foregoing, the Company was obligated to pay Infinity an additional royalty of 4% on worldwide net sales of any products in an oncology indication containing duvelisib to cover the reimbursement of research and development costs owed by Infinity to Mundipharma International Corporation Limited and Purdue Pharmaceutical Products L.P.

During the year ended December 31, 2022, 2021, and 2020, the Company recorded royalty expense of $0.0 million, $0.0 million, and $1.3 million, respectively related to the Infinity License Agreement, which are included in costs of sales - product within the consolidated statements of operation and comprehensive loss.

As discussed above under heading *Secura Bio, Inc. ("Secura")* as of September 30, 2020, Secura has assumed from the Company all responsibilities and obligations under the Infinity License Agreement. All royalties due pursuant to the Infinity License Agreement are the sole responsibility of Secura.

Sanofi

On July 25, 2019, the Company entered into a license and collaboration agreement with Sanofi (the "Sanofi Agreement"), under which the Company granted exclusive rights to Sanofi to develop and commercialize products containing duvelisib in Russia, the Commonwealth of Independent States ("CIS"), Turkey, the Middle East and Africa (collectively the "Sanofi Territory") for the treatment, prevention, palliation or diagnosis of any oncology indication in humans or animals.

Sanofi paid the Company an upfront, non-refundable payment of $5.0 million in August 2019. The Company is also entitled to receive aggregate payments of up to $42.0 million if certain regulatory and commercial milestones are successfully achieved. Sanofi is obligated to pay the Company double-digit royalties on net sales of products containing duvelisib in the Sanofi Territory, subject to reduction in certain circumstances.

The Company satisfied the performance obligation upon delivery of the license and initial technology transfer and recognized the upfront payment of $5.0 million as license and collaboration revenue during the year ended December 31, 2019. For the year ended December 31, 2020, the Company recognized $2.5 million of license revenue upon achievement of two development milestones which were paid in the year ended December 31, 2020.

As discussed above under heading *Secura Bio, Inc. ("Secura")* as of September 30, 2020, Secura has assumed from the Company all responsibilities and obligations under the Sanofi Agreement. After September 30, 2020, the Company is entitled to 50% of future milestone payments and royalties pursuant to the Secura APA

discussed under heading *Secura Bio, Inc. ("Secura")* above. Future milestone and royalty payments pursuant to the Sanofi Agreement will be paid by Sanofi to Secura. The Company's portion of such milestone and royalty payments will be subsequently remitted to the Company by Secura.

Yakult Honsha Co., Ltd. (Yakult)

On June 5, 2018, the Company entered into a license and collaboration agreement (the Yakult Agreement) with Yakult, under which the Company granted exclusive rights to Yakult to develop and commercialize products containing duvelisib in Japan for the treatment, prevention, palliation or diagnosis of all oncology indications in humans or animals.

Yakult paid the Company an upfront, non-refundable payment of $10.0 million in June 2018. The Company is also entitled to receive aggregate payments of up to $90.0 million if certain development, regulatory and commercial milestones are successfully achieved. Yakult is obligated to pay the Company a double-digit royalty on net sales of products containing duvelisib in Japan, subject to reduction in certain circumstances, and to fund certain global development costs related to worldwide clinical trials conducted by the Company in which Yakult has opted to participate (Global Clinical Trials) on a pro-rata basis.

As discussed above under heading *Secura Bio, Inc. ("Secura")* as of September 30, 2020, Secura has assumed from the Company all responsibilities and obligations under the Yakult Agreement. After September 30, 2020, the Company is entitled to 50% of future milestone payments and royalties pursuant to the Secura APA discussed under heading *Secura Bio, Inc. ("Secura")* above. Payments pursuant to the Yakult Agreement will be paid by Yakult to Secura. The Company's portion of such milestone and royalty payments will be subsequently remitted to the Company by Secura.

CSPC Pharmaceutical Group Limited (CSPC)

On September 25, 2018, the Company entered into a license and collaboration agreement with CSPC (the CSPC Agreement), under which the Company granted exclusive rights to CSPC to develop and commercialize products containing duvelisib in the People's Republic of China (China), Hong Kong, Macau and Taiwan (collectively, the "CSPC Territory") for the treatment, prevention, palliation or diagnosis of all oncology indications in humans.

CSPC paid the Company an aggregate upfront, non-refundable payment of $15.0 million, less the previously paid $5.0 million Exclusivity Fee. The Company is also entitled to receive aggregate payments of up to $160.0 million if certain development, regulatory and commercial milestones are successfully achieved. CSPC is obligated to pay the Company a double-digit royalty on net sales of products containing duvelisib in the CSPC Territory, subject to reduction in certain circumstances, and to fund certain global development costs related to worldwide clinical trials conducted by the Company in which CSPC has opted to participate ("Global Clinical Trials") on a pro-rata basis.

As discussed above under heading *Secura Bio, Inc. ("Secura")* as of September 30, 2020 Secura has assumed from the Company all responsibilities and obligations under the CSPC Agreement. After September 30, 2020, the Company is entitled to 50% of future milestone payments and royalties pursuant to the Secura APA discussed under heading *Secura Bio, Inc. ("Secura")* above. Payments pursuant to the CSPC Agreement will be paid by CSPC to Secura. The Company's portion of such milestone and royalty payments will be subsequently remitted to the Company by Secura.

14. Restructurings

On February 27, 2020, following further analysis of the Company's strategy, the Company committed to an operational plan to reduce overall operating expenses, including the elimination of approximately 31 positions across the Company and other cost-saving measures (the "February 2020 Restructuring"). The February 2020 Restructuring is designed to streamline operations, speed execution of the Company's clinical development of avutometinib and defactinib, and reflect a focused, account-based approach in the field.

In August 2020, in connection with the duvelisib sale to Secura pursuant to the Secura APA, the Company committed to a strategic restructuring (the "August 2020 Restructuring"). The restructuring included a workforce reduction of approximately 41 positions primarily in the Company's commercial operations department.

During the year-ended December 31, 2020, the Company recorded an aggregate expense of $4.6 million for the February 2020 Restructuring and August 2020 Restructuring for one-time termination benefits for employee severance, benefits, and related costs. This expense is reflected in the consolidated statements of operation and comprehensive loss as selling general, and administrative expense for $4.1 million, and research and development expense for $0.5 million. There were no restructuring expenses for the years ended December 31, 2022 and 2021.

15. Employee benefit plan

In June 2011, the Company adopted a 401(k) retirement and savings plan (the 401(k) Plan) covering all employees. The 401(k) Plan allows employees to make pre-tax or post-tax contributions up to the maximum allowable amount set by the Internal Revenue Service. Under the 401(k) Plan, the Company may make discretionary contributions as approved by the board of directors. The Company made contributions to the 401(k) Plan of approximately $0.8 million, $0.8 million, and $0.9 million for the years ended December 31, 2022, 2021, and 2020, respectively.

16. Subsequent events

The Company reviews all activity subsequent to year end but prior to the issuance of the consolidated financial statements for events that could require disclosure or that could impact the carrying value of assets or liabilities as of the consolidated balance sheet date. The Company is not aware of any material subsequent events other than the following:

Securities Purchase Agreement

On January 24, 2023, the Company entered into a Securities Purchase Agreement (the "Purchase Agreement") with BVF, pursuant to which the Company agreed to sell and issue to BVF in a private placement (the "Private Placement") up to 2,144,160 shares of its Series B convertible preferred stock, par value $0.0001 per share (the "Series B Preferred Stock"), in two tranches. The Series B Preferred Shares will be convertible into the Company's common stock at the option of the holders at any time, subject to certain limitations, at a conversion rate equal to $0.5901 per share.

The Company agreed to sell and issue in the first tranche of the Private Placement 1,200,000 shares of Preferred Stock at a purchase price of $25.00 per share of Preferred Stock (equivalent to $0.5901 per share of common stock). The first tranche of the Private Placement closed on January 27, 2023 and the Company received gross proceeds from the first tranche of the Private Placement of approximately $30.0 million, before deducting fees to the placement agent and other offering expenses.

In addition, the Company agreed to sell and issue in the second tranche of the Private Placement 944,160 shares of Series B Preferred Stock at a purchase price of $31.77 per share of Preferred Stock (equivalent to $0.75 per share of common stock) if at any time within 18 months following the closing of the first tranche the 10-day volume weighted average price of the Company's Common Stock (as quoted on Nasdaq and as calculated by Bloomberg) should reach at least $1.125 per share (adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction as needed) with aggregate trading volume during the same 10-

day period of at least $25 million within 18 months from the closing date of the initial tranche. The second tranche of the Private Placement is expected to close within seven trading days of meeting the second tranche conditions and will be subject to additional, customary closing conditions. If the second tranche conditions are satisfied, the Company anticipates receiving gross proceeds from the second tranche of the Private Placement of approximately $30.0 million, before deducting fees to the placement agent and other offering expenses payable by the Company.

Silicon Valley Bank

On March 10, 2023, Silicon Valley Bank ("SVB"), based in Santa Clara, California, was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. On March 12, 2023, the Department of the Treasury, the Federal Reserve, and the FDIC announced that all depositors of SVB will be fully protected and have access to all their money starting March 13, 2023. As of March 13, 2023, the Company's deposit balance at SVB was approximately $2 million. The Company is continually monitoring developments related to the recovery of its uninsured funds at SVB.

DESCRIPTION OF THE REGISTRANT'S SECURITIES

DESCRIPTION OF CAPITAL STOCK

General

The following is a summary of information concerning the capital stock of Verastem, Inc. ("Verastem" or "the Company"). The summaries and descriptions below do not purport to be complete and are subject to and qualified in their entirety by reference to the Delaware General Corporation Law, the Company's Restated Certificate of Incorporation, as amended (the "Certificate of Incorporation"), and Amended and Restated Bylaws (the "Bylaws") each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this exhibit is a part.

Common Stock

Under the Certificate of Incorporation, Verastem has authority to issue up to 300,000,000 shares of common stock, par value $0.0001 per share. As of February 28, 2023, 200,673,570 shares of common stock were issued and outstanding.

Holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by the Company's stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by the Company's board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of the Company's liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that the Company may designate and issue in the future.

Preferred Stock

Under the Certificate of Incorporation, Verastem has authority to issue up to 5,000,000 shares of preferred stock, $0.0001 par value per share and the Company's board of directors is authorized to establish, from the authorized shares of preferred stock, one or more classes or series of shares, to designate each such class and series, and fix the rights and preferences of each such class of preferred stock, which shall have voting powers, preferences, participating, optional or other special rights, qualifications and limitations or restrictions as adopted by the board of directors prior to the issuance of any such preferred shares. The Company's board of directors has designated 1,000,000 shares of Series A convertible preferred stock, par value $0.0001 per share (the "Series A Preferred Stock") and 2,144,160 shares of Series B convertible preferred stock, par value $0.0001 per share (the "Series B Preferred Stock"). As of February 28, 2023, there were 1,000,000 and 1,200,000 shares issued and outstanding of the Series A Preferred Stock and Series B Preferred Stock, respectively.

Series A Preferred Stock

The Series A Preferred Stock have the following rights and preferences:

- Each share of Series A Preferred Stock is convertible into 10 shares of common stock.
- The Series A Preferred Stock generally has no voting rights, except as required by law and except that the consent of a majority of the holders of the outstanding Series A Preferred Stock will be required to amend the terms of the Series A Preferred Stock.

- In the event of the Company's liquidation, dissolution or winding up, holders of Series A Preferred Stock will participate pari passu with any distribution of proceeds to holders of common stock.
- Holders of Series A Preferred Stock are entitled to receive when, as and if dividends are declared and paid on the common stock, an equivalent dividend, calculated on an as-converted basis. Shares of Series A Preferred Stock are otherwise not entitled to dividends.
- The Series A Preferred Stock ranks:
    a. senior to any class or series of capital stock of the Company hereafter created specifically ranking by its terms junior to the Series A Preferred Stock;
    b. on parity with the common stock and any class or series of capital stock of the Company created specifically ranking by its terms on parity with the Series A Preferred Stock; and
    c. junior to any class or series of capital stock of the Company created specifically ranking by its terms senior to any Series A Preferred Stock, in each case, as to distributions of assets upon liquidation, dissolution or winding up of the Company, whether voluntarily or involuntarily.

Series B Preferred Stock

The Series B Preferred Stock have the following rights and preferences:

- Each share of Series B Preferred Stock is convertible into 42.3657 shares of common stock.
- The Series B Preferred Stock generally has no voting rights. The Company shall not, without the affirmative vote or consent of the holders of majority of the shares of the Series B Preferred Stock then-outstanding, given in person or by proxy, either in writing or at a meeting, in which the holders of the Series B Preferred Stock vote separately as a class:
    a. amend, alter, modify or repeal (whether by merger, consolidation or otherwise) the certificate of designation of the preference rights, and limitations of Series B Preferred Stock, the Certificate of Incorporation, or the Bylaws in any manner that adversely affects the rights, preferences, privileges or the restrictions provided for the benefit of, the Series B Preferred Stock;
    b. issue further shares of Series B Preferred Stock or increase or decrease (other than by conversion) the number of authorized shares of Preferred Stock;
    c. authorize or issue any class or series of capital stock hereafter creating specifically ranking by its terms senior to the Series B Preferred Stock ("Senior Stock") or;
    d. enter into any agreement to do any of the foregoing that is not expressly made conditional on obtaining the affirmative vote or written consent of the majority of then-outstanding Series B Preferred Stock.
- In the event of the Company's liquidation, dissolution or winding up, holders of Series B Preferred Stock will be entitled to an amount equal to $1.00 per share of Series B Preferred Stock, plus an additional amount equal to any dividends declared but unpaid on such shares, before any distributions or payments are made to holders of common stock or other classes ranking junior to the Series B Preferred Stock.
- Holders of Series B Preferred Stock are entitled to receive when, as and if dividends are declared and paid on the common stock, an equivalent dividend, calculated on an as-converted basis. Shares of Series B Preferred Stock are otherwise not entitled to dividends.
- The Series B Preferred Stock rank:
    a. senior to common stock;
    b. senior to all other classes and series of equity securities of the Company that by their terms do not rank senior to the Series B Preferred Stock;
    c. senior to all shares of the Series A Preferred Stock;

d. on parity with any class or series of capital stock of the Company hereafter created specifically ranking by its terms on parity with the Series B Preferred Stock;

e. junior to any class or series of capital stock of the Company hereafter created specifically ranking by its terms senior to the Series B Preferred Stock; and

f. junior to all of the Company's existing and future debt obligations, including convertible or exchangeable debt securities, in each case, as to distributions of assets upon liquidation, dissolution or winding up of the Corporation, whether voluntarily or involuntarily and as to the right to receive dividends.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware law

Verastem is subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly-traded Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of a corporation's board of directors, the business combination is approved by a corporation's board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of the outstanding voting stock of the corporation in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving the Company and an "interested stockholder" and the sale of more than 10% of the Company's assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of the Company's outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Staggered board

Verastem's Certificate of Incorporation and Bylaws divide its board of directors into three classes with staggered three-year terms. In addition, the Certificate of Incorporation and Bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of the shares of capital stock present in person or by proxy and entitled to vote. Under the Certificate of Incorporation and Bylaws, any vacancy on the Company's board of directors, including a vacancy resulting from an enlargement of the board of directors, may be filled only by vote of a majority of the directors then in office. Furthermore, the Certificate of Incorporation provides that the authorized number of directors may be changed only by the resolution of the board of directors. The classification of the board of directors and the limitations on the ability of the Company's stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of the Company.

Stockholder action; special meeting of stockholders; advance notice requirements for stockholder proposals and director nominations

Verastem's Certificate of Incorporation and Bylaws provide that any action required or permitted to be taken by its stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. The Certificate of Incorporation and Bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by the Company's chairman of the board, president or chief executive officer or the board of directors. In addition, the Company's Bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to the board of directors. Stockholders at an annual meeting may consider only proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to the Company's secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of the Company's outstanding voting securities. These provisions also could discourage a third party from making a tender offer for the Company's common stock, because even if it acquired a

majority of the outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-majority voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Verastem's bylaws may be amended or repealed by a majority vote of the Company's board of directors or the affirmative vote of the holders of at least 75% of the votes that the Company's stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that the Company's stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of Verastem's Certificate of Incorporation described above.

Transfer Agent and Registrar

The transfer agent and registrar for the common stock is Computershare Trust Company, N.A.

Listing

The Company's common stock is listed on The Nasdaq Global Market under the symbol "VSTM."

Exhibit 21.1

List of Registrant's Subsidiaries

Verastem Securities Company, incorporated in Massachusetts, a wholly owned subsidiary.

Verastem Europe GmbH, incorporated in Germany, a wholly owned subsidiary.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-180475) pertaining to the 2010 Equity Incentive Plan and the 2012 Incentive Plan of Verastem, Inc.,
(2) Registration Statement (Form S-8 No. 333-190578) pertaining to the 2012 Incentive Plan of Verastem, Inc.,
(3) Registration Statement (Form S-8 No. 333-201075) pertaining to the 2014 Inducement Award Program of Verastem, Inc.,
(4) Registration Statement (Form S-8 No. 333-201076) pertaining to the 2012 Incentive Plan of Verastem, Inc.,
(5) Registration Statement (Form S-8 No. 333-211235) pertaining to the 2012 Incentive Plan of Verastem, Inc.,
(6) Registration Statement (Form S-8 No. 333-218768) pertaining to the 2014 Inducement Award Program of Verastem, Inc.,
(7) Registration Statement (Form S-8 No. 333-218769) pertaining to the 2012 Incentive Plan of Verastem, Inc.,
(8) Registration Statement (Form S-8 No.333-223616) pertaining to the 2014 Inducement Award Program of Verastem, Inc.,
(9) Registration Statement (Form S-8 No.333-228309) pertaining to the 2014 Inducement Award Program of Verastem, Inc.,
(10) Registration Statement (Form S-8 No.333-229430) pertaining to the 2018 Employee Stock Purchase Plan, 2012 Amended and Restated Incentive Plan, and 2014 Inducement Award Program of Verastem, Inc.,
(11) Registration Statement (Form S-8 No. 333-238877) pertaining to the 2012 Amended and Restated 2012 Incentive Plan of Verastem, Inc.,
(12) Registration Statement (Form S-3 No. 333-237332) of Verastem, Inc.,
(13) Registration Statement (Form S-8 No. 333-257111) pertaining to the 2021 Equity Incentive Plan of Verastem, Inc. and,
(14) Registration Statement (Form S-3 No. 333-258372) of Verastem, Inc.

of our report dated March 14, 2023 with respect to the consolidated financial statements of Verastem, Inc. included in this Annual Report (Form 10-K) of Verastem, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 14, 2023

Exhibit 31.1

CERTIFICATIONS

I, Brian M. Stuglik certify that:

1. I have reviewed this Annual Report on Form 10-K of Verastem, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ BRIAN M. STUGLIK
Brian M. Stuglik
Chief Executive Officer

Date: March 14, 2023

Exhibit 31.2

CERTIFICATIONS

I, Daniel Calkins, certify that:

1. I have reviewed this Annual Report on Form 10-K of Verastem, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ DANIEL CALKINS
Daniel Calkins
Vice President, Finance

Date: March 14, 2023

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Verastem, Inc. (the "Company") for the period ended December 31, 2022 as filed with the Securities and Exchange Commission (the "SEC") on the date hereof (the "Report"), the undersigned, Brian M. Stuglik, Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ BRIAN M. STUGLIK
Brian M. Stuglik
Chief Executive Officer

Date: March 14, 2023

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the SEC or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Verastem, Inc. (the "Company") for the period ended December 31, 2022 as filed with the Securities and Exchange Commission (the "SEC") on the date hereof (the "Report"), the undersigned, Daniel Calkins, Vice President, Finance of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ DANIEL CALKINS
Daniel Calkins
Vice President, Finance

Date: March 14, 2023

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the SEC or its staff upon request.

Exhibit 99.1

Verastem Oncology Reports Fourth Quarter and Full Year 2022 Financial Results and Highlights Recent Company Progress

Positive Interim Data Read-Out of RAMP 201 and Productive FDA Meeting Support Avutometinib + Defactinib Combination in Recurrent Low-Grade Serous Ovarian Cancer (LGSOC)

Studies of Avutometinib Combinations in Other RAS Pathway-Driven Cancers Advancing

Company Cash, Cash Equivalents, and Investments of $87.9 Million as of December 31, 2022; Pro-Forma $117.9 Million Including the Sale of Series B Convertible Preferred Stock

BOSTON, MA – March 14, 2023 – Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients with cancer, today reported financial results for the three months and full year ended December 31, 2022, and highlighted recent progress.

"Building on our breakthrough therapy designation, we have made significant progress advancing our LGSOC program, including selecting the combination of avutometinib and defactinib as the go-forward treatment regimen in recurrent disease regardless of KRAS mutation with the goal of filing for accelerated approval upon data maturity in the RAMP 201 trial and initiation of a confirmatory study," said Brian Stuglik, Chief Executive Officer of Verastem Oncology. "We believe we are well-positioned to bring this potential new combination therapy to patients who have been waiting for the first U.S. Food and Drug Administration (FDA) approved medicine for this disease. Our debt facility and recent private placement offering add flexibility to our financial strength and are expected to support the continued development of avutometinib in combinations across RAS pathway-driven cancers of high unmet need."

Fourth Quarter 2022 and Recent Highlights

Low Grade Serous Ovarian Cancer (LGSOC)

- The Company held a productive meeting with the FDA to discuss the encouraging results to date of the ongoing RAMP 201 LGSOC trial evaluating avutometinib ± defactinib among patients with recurrent LGSOC, confirmed the go forward treatment regimen selection of avutometinib and defactinib based on a planned interim analysis with prespecified criteria and discussed the regulatory path forward.

- Of the 29 patients evaluable for response by blinded independent central review (BICR) in the combination arm, the initial results showed a confirmed objective response rate (ORR) of 28% in all patients and 27% vs 29% in KRAS mutant (n=15) and KRAS wild-type (n=14) LGSOC, respectively. Three additional patients with KRAS mutant LGSOC showed an unconfirmed partial response. The overall disease control rate (stable disease plus partial response) was 93%. Most evaluable patients (62%) were still on study treatment on the combination arm at the time of the data cut with a

minimum follow-up of five months. No new safety signals were reported with a continued favorable safety and tolerability profile.

- Completed enrollment in primary cohort of 72 patients in the combination arm of RAMP 201. Continued enrollment in the combination arm of RAMP 201 is ongoing to expand the clinical experience in anticipation of initiation of a confirmatory study.

- The Company intends to include mature data from RAMP 201, the Verastem sponsored clinical trial, and the FRAME study, led by The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust, to potentially support filing for accelerated approval.

Other Programs

- In the Company's RAMP 203 and RAMP 204 clinical trials, evaluating the combination of avutometinib with Amgen's LUMAKRAS® (sotorasib) (RAMP 203) and with Mirati's KRAZATI® (adagrasib) (RAMP 204) in KRAS G12C mutant NSCLC, RAMP 203 progressed to the final dose escalation cohort and enrollment was initiated and dose escalation is ongoing in RAMP 204.

- Initiated RAMP 205, a Phase 1b/2 clinical trial of avutometinib and defactinib to evaluate a more complete blockade of KRAS signaling with standard of care chemotherapy ((GEMZAR® (gemcitabine) and ABRAXANE®)). The trial is supported by the Company's receipt of the first "Therapeutic Accelerator Award" from the Pancreatic Cancer Network (PanCAN).

Corporate Updates

- The Company entered into a definitive agreement to sell up to approximately 2.1 million shares of its Series B convertible preferred stock to affiliates of BVF Partners L.P. in a private placement to raise aggregate gross proceeds of up to approximately $60 million in two tranches. On January 27, 2023, Verastem Oncology closed on the initial tranche of 1.2 million shares of its Series B convertible preferred stock with gross proceeds of $30 million.

- The Company has achieved the Term B Milestone pursuant to its credit facility with Oxford and plans to draw down an additional $15 million in March 2023. Under the credit facility, Verastem has the ability to access up to an additional $110 million in a series of tranches, $60 million of which are based on certain pre-determined milestones and $50 million of which are at the lender's discretion.

- Intermittent dosing intellectual property for both avutometinib alone and in combination with defactinib was recently allowed, extending patent coverage up to 2038 and 2040, respectively.

- Appointed Anil Kapur, Executive Vice President, Corporate Strategy and Chief Commercial Officer at Geron Corporation and Robert Gagnon, the Chief Financial Officer and Operating Partner at Gurnet Point Capital to its Board of Directors.

Fourth Quarter 2022 Financial Results

Verastem Oncology ended the fourth quarter of 2022 with cash, cash equivalents and investments of $87.9 million. On a pro forma basis, inclusive of the $30 million gross proceeds raised through issuance of Series B convertible preferred stock, cash, cash equivalents and investments were $117.9 million as of December 31,

2022. Additionally, the Company plans to draw down $15 million on the Oxford Loan and Security Agreement in March 2023.

Total operating expenses for the three months ended December 31, 2022 (the "2022 Quarter") were $16.8 million, compared to $17.1 million for the three months ended December 31, 2021 (the "2021 Quarter").

Research & development expenses for the 2022 Quarter were $10.7 million, compared to $11.4 million for the 2021 Quarter. The decrease of $0.7 million, or 6.1%, primarily resulted from a decrease in investigator fees and drug product and drug substance costs.

Selling, general & administrative expenses for the 2022 Quarter were $6.1 million, compared to $5.7 million for the 2021 Quarter. The increase of $0.4 million, or 7.0%, was primarily related to additional costs in anticipation of potential commercialization of avutometinib and defactinib in LGSOC.

Net loss for the 2022 Quarter was $16.8 million, or $0.08 per share (basic and diluted), compared to net loss of $16.5 million, or $0.09 per share (basic and diluted) for the 2021 Quarter.

For the 2022 Quarter, non-GAAP adjusted net loss was $15.4 million, or $0.08 per share (diluted), compared to non-GAAP adjusted net loss of $14.9 million, or $0.08 per share (diluted) for the 2021 Quarter. Please refer to the GAAP to Non-GAAP Reconciliation attached to this press release.

Full-Year 2022 Financial Results

Total revenue for the year ended December 31, 2022 ("2022 Period") was $2.6 million, compared to $2.1 million for the year ended December 31, 2021 ("2021 Period"). Revenue for the 2022 Period was primarily comprised of one regulatory milestone achieved by Secura Bio, Inc.'s ("Secura") sublicensee, CSPC Pharmaceutical Group Limited. Revenue for the 2021 Period was primarily comprised of two regulatory milestones achieved by Secura's sublicensee, Sanofi, and transition services revenue for certain support functions provided to Secura pursuant to the Secura transition services agreement, which was entered into in connection with the sale of COPIKTRA to Secura.

Total operating expenses for the 2022 Period were $75.5 million, compared to $63.5 million for the 2021 Period.

Research & development expenses for the 2022 Period were $50.6 million, compared to $39.3 million for the 2021 Period. The increase of $11.3 million, or 28.8%, was primarily related to an increase in drug substance and drug product costs and contract research organization costs.

Selling, general & administrative expenses for the 2022 Period were $25.0 million, compared to $24.1 million for the 2021 Period. The increase of $0.9 million, or 3.7%, was primarily related to additional costs in anticipation of potential commercialization of avutometinib and defactinib in LGSOC.

Net loss for the 2022 Period was $73.8 million, or $0.38 per share (basic and diluted), compared to $71.2 million, or $0.41 per share (basic and diluted) for the 2021 Period.

For the 2022 Period, non-GAAP adjusted net loss was $67.4 million, or $0.35 per share (diluted), compared to non-GAAP adjusted net loss of $54.1 million, or $0.31 per share (diluted), for the 2021 Period. Please refer to the GAAP to Non-GAAP Reconciliation attached to this press release.

Use of Non-GAAP Financial Measures

To supplement Verastem Oncology's condensed consolidated financial statements, which are prepared and presented in accordance with generally accepted accounting principles in the United States (GAAP), the Company uses the following non-GAAP financial measures in this press release: [pro-forma cash], non- GAAP adjusted net loss and non-GAAP net loss per share. These non-GAAP financial measures exclude certain amounts or expenses from the corresponding financial measures determined in accordance with GAAP. Management believes this non-GAAP information is useful for investors, taken in conjunction with the Company's GAAP financial statements, because it provides greater transparency and period-over- period comparability with respect to the Company's operating performance and can enhance investors' ability to identify operating trends in the Company's business. Management uses these measures, among other factors, to assess and analyze operational results and trends and to make financial and operational decisions. Non-GAAP information is not prepared under a comprehensive set of accounting rules and should only be used to supplement an understanding of the Company's operating results as reported under GAAP, not in isolation or as a substitute for, or superior to, financial information prepared and presented in accordance with GAAP. In addition, these non-GAAP financial measures are unlikely to be comparable with non-GAAP information provided by other companies. The determination of the amounts that are excluded from non-GAAP financial measures is a matter of management judgment and depends upon, among other factors, the nature of the underlying expense or income amounts. Reconciliations between these non-GAAP financial measures and the most comparable GAAP financial measures for the three months and year ended December 31, 2022 and 2021 are included in the tables accompanying this press release after the unaudited condensed consolidated financial statements.

About Avutometinib (VS-6766)

Avutometinib is a RAF/MEK clamp that induces inactive complexes of MEK with ARAF, BRAF and CRAF potentially creating a more complete and durable anti-tumor response through maximal RAS pathway inhibition. Avutometinib is currently in late-stage development.

In contrast to other MEK inhibitors, avutometinib blocks both MEK kinase activity and the ability of RAF to phosphorylate MEK. This unique mechanism allows avutometinib to block MEK signaling without the compensatory activation of MEK that appears to limit the efficacy of other inhibitors. The U.S. Food and Drug Administration granted Breakthrough Therapy designation for the combination of Verastem Oncology's investigational RAF/MEK clamp avutometinib, with defactinib, its FAK inhibitor, for the

treatment of all patients with recurrent low-grade serous ovarian cancer (LGSOC) regardless of KRAS status after one or more prior lines of therapy, including platinum-based chemotherapy.

Verastem Oncology is currently conducting clinical trials with its RAF/MEK clamp avutometinib in RAS- driven tumors as part of its (**R**af **A**nd **M**ek **P**rogram). RAMP 201 is a registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC. Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS® (sotorasib) and KRAZATI® (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 and RAMP 204 trials, respectively. As part of the "Therapeutic Accelerator Award" Verastem Oncology received from PanCAN, Verastem Oncology is conducting RAMP 205, a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/nab-paclitaxel in patients with front-line metastatic pancreatic cancer.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a development-stage biopharmaceutical company committed to the development and commercialization of new medicines to improve the lives of patients diagnosed with cancer. Our pipeline is focused on novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and focal adhesion kinase (FAK) inhibition. For more information, please visit www.verastem.com.

Forward-Looking Statements Notice

This press release includes forward-looking statements about Verastem Oncology's strategy, future plans and prospects, including statements related to its financial condition, its potential borrowings, the potential clinical value of various of its clinical trials, the timing of commencing and completing trials, including topline data reports, interactions with regulators and potential for additional development programs involving Verastem Oncology's lead compound. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward- looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement.

Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including avutometinib in combination with other compounds, including defactinib, LUMAKRAS® and others; the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis or result in unmanageable safety profiles as compared to their levels of efficacy; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the scope, timing, and outcome of any legal proceedings; decisions by regulatory authorities regarding trial design, labeling and other matters that could affect the timing, availability or commercial potential of our product candidates; whether preclinical testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that third- party payors (including government agencies) may not reimburse; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that our product candidates will experience

manufacturing or supply interruptions or failures; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned, including as a result of conducting additional studies; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that we or our other collaboration partners may fail to perform under our collaboration agreements; that we may not have sufficient cash to fund our contemplated operations; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that Secura will achieve the milestones that result in payments to us under our asset purchase agreement with Secura; that we will be unable to execute on our partnering strategies for avutometinib in combination with other compounds; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

Other risks and uncertainties include those identified under the heading "Risk Factors" in Verastem Oncology's Annual Report on Form 10-K for the year ended December 31, 2022 as filed with the Securities and Exchange Commission (SEC) on March 14, 2023 and in any subsequent filings with the SEC. The forward-looking statements contained in this press release reflect Verastem Oncology's views as of the date hereof, and Verastem Oncology does not assume and specifically disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

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Verastem Oncology
Condensed Consolidated Balance Sheets
(in thousands)
(unaudited)

	December 31, 2022	December 31, 2021
Cash, cash equivalents, & investments	$ 87,894	$ 100,256
Accounts receivable, net	31	516
Prepaid expenses and other current assets	4,945	4,968
Property and equipment, net	92	210
Right-of-use asset, net	1,789	2,302
Restricted cash and other assets	299	410
Total assets	**$ 95,050**	**$ 108,662**
Current Liabilities	$ 21,663	$ 18,590
Long term convertible senior notes	—	249
Long term debt	24,526	—
Lease Liability, long-term	1,470	2,264
Stockholders' equity	47,391	87,559
Total liabilities and stockholders' equity	**$ 95,050**	**$ 108,662**

Verastem Oncology
Condensed Consolidated Statements of Operations
(in thousands, except per share amounts)
(unaudited)

	Three months ended December 31,		Year ended December 31,	
	2022	**2021**	**2022**	**2021**
Revenue:				
Sale of COPIKTRA license and related assets revenue	$ —	$ 545	$ 2,596	$ 1,447
Transition services revenue	—	—	—	606
Total revenue	—	545	2,596	2,053
Operating expenses:				
Research and development	10,740	11,396	50,558	39,347
Selling, general and administrative	6,106	5,660	24,975	24,115
Total operating expenses	16,846	17,056	75,533	63,462
Loss from operations	(16,846)	(16,511)	(72,937)	(61,409)
Other income (expense)	(7)	—	47	—
Interest income	769	40	1,215	181
Interest expense	(724)	(10)	(2,137)	(9,972)
Net loss	$ (16,808)	$ (16,481)	$ (73,812)	$ (71,200)
Net loss per share—basic and diluted	$ (0.08)	$ (0.09)	$ (0.38)	$ (0.41)
Weighted average common shares outstanding used in computing:				
Net loss per share – basic and diluted	204,501	182,672	193,654	174,406

Verastem Oncology
Reconciliation of GAAP to Non-GAAP Financial Information
(in thousands, except per share amounts)
(unaudited)

	Three months ended December 31,		Year ended December 31,	
	2022	2021	2022	2021
Net loss reconciliation				
Net loss (GAAP basis)	$ (16,808)	$ (16,481)	$ (73,812)	$ (71,200)
Adjust:				
Stock-based compensation expense	1,287	1,574	6,047	7,711
Non-cash interest, net	(3)	44	228	9,331
Severance and other	109	—	109	40
Adjusted net loss (non-GAAP basis)	$ (15,415)	$ (14,863)	$ (67,428)	$ (54,118)
Reconciliation of net loss per share				
Net loss per share – diluted (GAAP basis)	$ (0.08)	$ (0.09)	$ (0.38)	$ (0.41)
Adjust per diluted share				
Stock-based compensation expense	—	0.01	0.03	0.04
Non-cash interest, net	—	—	—	0.06
Severance and other	—	—	—	—
Adjusted net loss per share – diluted (non-GAAP basis)	$ (0.08)	$ (0.08)	$ (0.35)	$ (0.31)
Weighted average common shares outstanding used in computing net loss per share—diluted	204,501	182,672	193,654	174,406