MIRATI THERAPEUTICS

Transforming Lives

Developing best-in-class targeted therapies to meaningfully impact the lives of patients with cancer

2021 Annual Report

“2021 was an important year of growth, progress and strong execution for Mirati. I am proud of our accomplishments and the company we are building. We have a broad targeted oncology pipeline along with the financial strength to continue to advance and expand our pipeline and capabilities to position the company for sustained growth. We have an exceptional team who are relentlessly focused on advancing our mission to meaningfully impact the lives of patients with cancer.”

David Meek
Chief Executive Officer,
Mirati Therapeutics, Inc.

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, 2021

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: 1-15803

MIRATI THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**46-2693615**
(State or other jurisdiction of incorporation or organization)	*(IRS Employer Identification No.)*
3545 Cray Court, San Diego, California	**92121**
(Address of principal executive offices)	*(Zip Code)*

(858) 332-3410

(Registrant's Telephone Number, Including Area Code)

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

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

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

None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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 during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

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

The aggregate market value of common stock held by non-affiliates (based on the closing price on the last business day of the registrant's most recently completed second fiscal quarter as reported on The Nasdaq Global Select Market) was $7.4 billion. All executive officers and directors of the registrant and certain shareholders filing a Schedule 13D or Schedule 13G with the Securities and Exchange Commission in respect to registrant's common stock have been deemed, solely for the purpose of the foregoing calculation, to be "affiliates" of the registrant.

As of February 22, 2022, the registrant had 55,488,261 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required to be disclosed in Part III of this report is incorporated by reference from the registrant's definitive Proxy Statement for the 2022 Annual Meeting of Shareholders, which proxy statement will be filed not later than 120 days after the end of the fiscal year covered by this report.

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PART I

Forward-Looking Statements

This Annual Report on Form 10-K (the "Annual Report") and the information incorporated herein by reference includes forward-looking statements regarding our business and the therapeutic and commercial potential of our technologies and products in development. Any statement describing our goals, expectations, financial or other projections, intentions or beliefs, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this Annual Report, including those identified in Item 1A entitled "Risk Factors". Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. As a result, you are cautioned not to rely or place undue reliance on these forward-looking statements. References in this Annual Report to "we", "our", "us", "Mirati" or "the Company" refer to Mirati Therapeutics, Inc. and its subsidiaries.

Summary of Risk Factors

Investing in our securities involves a high degree of risk. Below is a summary of material factors that make an investment in our securities speculative or risky. Importantly, this summary does not address all of the risks that we face. Additional discussion of the risks summarized in this summary of risk factors, as well as other risks that we face, can be found under the heading "Item 1A – Risk Factors" in Part I of this Annual Report.

- *Risks Related to our Business and Industry*
  - *Our research and development programs and product candidates are in development. As a result, we are unable to predict if or when we will successfully develop or commercialize our product candidates.*
  - *All of our product candidates are subject to extensive regulation, which can be costly and time consuming, cause delays or prevent approval of such product candidates for commercialization*
  - *The successful commercialization of our product candidates, if approved, will depend on achieving market acceptance and we may not be able to gain sufficient acceptance to generate significant revenue.*
  - *The COVID-19 pandemic could adversely impact our business including our ongoing and planned clinical trials and preclinical research.*
  - *We rely upon third-party contractors and service providers for the execution of some aspects of our development programs. Failure of these collaborators to provide services of a suitable quality and within acceptable timeframes may cause the delay or failure of our development programs.*
  - *Competition in our targeted market area is intense and this field is characterized by rapid technological change. Therefore, developments by competitors may substantially alter the predicted market or render our product candidates uncompetitive*
  - *Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved product label, or result in significant negative consequences following marketing approval, if any.*
  - *We are subject to competition for our skilled personnel and may experience challenges in identifying and retaining key personnel that could impair our ability to conduct our operations effectively.*

- *Risks Related to our Financial Position and Capital Requirements*
  - *We will require additional financing and may be unable to raise sufficient capital, which could lead us to delay, reduce or abandon development programs or commercialization.*

- *Risks Related to our Intellectual Property*
  - *We may not obtain adequate protection for our product candidates through patents and other intellectual property rights and as such, our competitive advantage in the marketplace may be compromised.*

- *Other factors set forth herein.*

Item 1. Business

BUSINESS

Company Overview

Mirati Therapeutics, Inc. is a clinical-stage oncology company developing novel therapeutics to address the genetic and immunological promoters of cancer.

We have two KRAS inhibitor programs. Adagrasib is an investigational, selective, specific, potent and orally available KRAS G12C inhibitor in clinical development as a monotherapy and in combination with other agents. Adagrasib is the provisionally filed nonproprietary name for MRTX849. MRTX1133 is an investigational, selective, specific and potent KRAS G12D inhibitor in preclinical development.

Sitravatinib is an investigational spectrum-selective kinase inhibitor designed to potently inhibit receptor tyrosine kinases ("RTK"s) and enhance immune responses through the inhibition of immunosuppressive signaling.

MRTX1719 is an internally discovered investigational synthetic lethal PRMT5 inhibitor designed to specifically target the PRMT5/methylthioadensoine (MTA) complex in preclinical development.

The Company also has additional preclinical programs of potentially first-in-class and best-in-class product candidates specifically designed to address mutations and tumors where few treatment options exist. We approach all of our programs with a singular focus: to translate our deep understanding of the molecular drivers of cancer into better therapies and better outcomes for patients.

KRAS Inhibitor Programs

The RAS family of genes is the most commonly mutated oncogene and mutations in this gene family occur in up to approximately 25% of all human cancers. Among the RAS family members, mutations most frequently occur in KRAS (approximately 85% of all RAS family mutations). Tumors characterized by KRAS mutations are commonly associated with poor prognosis and resistance to therapy. Nonclinical studies have demonstrated that cancer cells exhibiting KRAS mutations are highly dependent on KRAS function for cell growth and survival. Our KRAS inhibitor programs are focused on the discovery and development of small molecule compounds that target KRAS G12C and G12D. We are pursuing development of our KRAS G12C and KRAS G12D inhibitor programs in both single agent and rational combination approaches.

Adagrasib, a selective KRAS G12C inhibitor

Adagrasib, our lead KRAS G12C compound, is an investigational, selective, specific, potent and orally available KRAS G12C inhibitor and is in clinical development varying from Phase 1 through Phase 3. Adagrasib is designed to directly inhibit KRAS G12C mutations. KRAS G12C mutations are present in approximately 14% of non-small cell lung cancer ("NSCLC") adenocarcinoma patients, 3-4% of colorectal cancer ("CRC") patients, 2% of pancreatic cancer patients, as well as smaller percentages of several other difficult-to-treat cancers.

We received U.S. Food and Drug Administration ("FDA") authorization of our investigational new drug application ("IND") for adagrasib in November 2018, and in January 2019, we initiated the dose escalation phase of KRYSTAL-1, a Phase 1/2 multiple expansion cohort clinical trial evaluating adagrasib in patients with advanced solid tumors that harbor KRAS G12C mutations both in monotherapy and in combination with other anticancer therapies. Following single agent dose escalation, the KRYSTAL-1 trial was expanded into multiple cohorts in which adagrasib is being evaluated both in monotherapy and in combination with other compounds in patients with NSCLC, CRC and those with other tumors that carry the KRAS G12C mutation.

In December 2021, we completed our New Drug Application ("NDA") submission to the FDA for adagrasib for the treatment of patients with previously treated KRAS G12C-mutated NSCLC who have received prior systemic therapy. In February 2022, the FDA accepted the NDA and assigned a Prescription Drug User Fee Action ("PDUFA") date of December 14, 2022. The NDA is being reviewed by the FDA for Accelerated Approval (Subpart H), which allows for the approval of drugs that treat serious conditions, and that fill an unmet medical need based on a surrogate endpoint. In addition, this application is being reviewed under the FDA Real-Time Oncology Review pilot program, which aims to explore a more efficient review process that ensures safe and effective treatments are made available to patients as early as possible. Adagrasib has also achieved Breakthrough Therapy Designation as a potential treatment for patients with NSCLC who harbor the KRAS G12C mutation following prior systemic therapy. The Company also has an Expanded Access Program for adagrasib for the treatment of eligible patients with KRAS G12C-mutated cancers regardless of tumor type in the United States.

The KRYSTAL-1 trial is evaluating the combination of adagrasib and a PD-1 inhibitor (pembrolizumab) in patients with NSCLC, the combination of adagrasib and a pan-EGFR inhibitor (afatinib) in patients with advanced NSCLC, and the combination of adagrasib and an anti-EGFR antibody (cetuximab) in patients with CRC. In 2020, we initiated KRYSTAL-2, a Phase 1/2 clinical trial evaluating the combination of adagrasib and a SHP-2 inhibitor (TNO-155) in patients with advanced NSCLC and advanced CRC. In 2021, we initiated KRYSTAL-14, a Phase 1/2 clinical trial evaluating the combination of adagrasib and a SOS1 inhibitor (BI 1701963) in patients with advanced NSCLC, and we initiated KRYSTAL-16, a Phase 1/1b clinical trial evaluating the combination of adagrasib and a CDK4/6 inhibitor (palbociclib) in patients with advanced solid tumors with KRAS G12C mutation.

In the fourth quarter of 2021, we announced preliminary results from the Phase 1b cohort of the KRYSTAL-1 trial evaluating the combination of adagrasib and a PD-1 inhibitor (pembrolizumab) in eight patients with KRAS G12C-mutated first-line NSCLC. The preliminary results support moving forward with a 400mg twice daily dose ("BID") of adagrasib with full dose pembrolizumab, which will be evaluated in an ongoing Phase 2 clinical trial. The Phase 1b data showed adagrasib 400mg BID plus pembrolizumab had a manageable tolerability profile, with no observed Grade 4 or Grade 5 adverse events. Of the seven patients evaluable for a response as of October 21, 2021, four had a confirmed RECIST-defined partial response and one additional patient, who is still on study, experienced 49% tumor regression in the first scan, which allowed for tumor resection prior to achieving a RECIST-defined confirmed response. The disease control rate ("DCR") was 100%, with all seven patients exhibiting tumor regression ranging from 37% to 92%. With a median follow up of 9.9 months, five of the seven patients remained on treatment, as of the data cutoff date, and had been on treatment for 8 to 11 months.

On September 20, 2021, we announced that we completed an analysis in the intent-to-treat population of the registration enabling cohort of KRYSTAL-1, the Phase 1/2 clinical trial evaluating adagrasib at 600mg BID as a monotherapy treatment for patients in at least 2nd line NSCLC. The analysis showed an objective response rate ("ORR") of 43% and a DCR of 80%, based on central independent review, as of June 15, 2021.

In the third quarter of 2021, we amended KRYSTAL-7, the Phase 2 clinical trial evaluating the combination of adagrasib at 400mg BID and a PD-1 inhibitor (pembrolizumab) in patients with NSCLC stratified by <1% Tumor Proportion Score ("TPS") score and ≥1% TPS score.

In the first quarter of 2021, we initiated two registration-enabling Phase 3 clinical trials. The first clinical trial, KRYSTAL-12, is evaluating adagrasib as a monotherapy randomized against docetaxel in patients with 2nd line NSCLC. The second clinical trial, KRYSTAL-10, is evaluating the combination of adagrasib and an anti-EGFR antibody (cetuximab) randomized against chemotherapy in patients with 2nd line CRC.

On September 19, 2021, at the European Society for Medical Oncology Congress 2021, we presented preliminary results from the cohort of the KRYSTAL-1 Phase 1/2 clinical trial evaluating adagrasib at 600mg BID as both a monotherapy treatment and in combination with cetuximab for patients with heavily pretreated colorectal cancer harboring a KRAS G12C mutation.

- As of May 25, 2021, the adagrasib monotherapy arm (n=46) had a median follow up of 8.9 months. Of the evaluable patients (n=45), preliminary results showed an investigator assessed response rate ("RR") of 22%, including one unconfirmed partial response ("PR"), and a DCR of 87%; the median duration of response ("DOR") was 4.2 months. In all enrolled patients, the median progression free survival ("PFS") was 5.6 months (95% confidence interval ("CI"): 4.1,8.3).

- As of July 9, 2021, the adagrasib plus cetuximab arm (n=32) had a median follow up of 7 months. Of the evaluable patients (n=28), preliminary results showed an investigator assessed RR of 43%, including two unconfirmed PRs and a DCR of 100%. After the data cutoff date, of the two unconfirmed PRs, follow up scans showed one patient had a confirmed PR, and the second patient progressed.

- Adagrasib monotherapy and in combination with cetuximab was well-tolerated in this study, with a manageable safety profile. Grade 3/4 treatment related adverse events ("TRAEs") were observed in 30% of patients treated with adagrasib alone, and in 16% of patients treated with the combination. Treatment related adverse events led to treatment discontinuation in 6% of patients who received combination therapy and in none (0%) of those who received adagrasib monotherapy. No Grade 5 TRAEs were observed in either treatment arm.

On October 9, 2021, at the 33rd EORTC-NCI-AACR Symposium on Molecular Targets and Therapeutics, we presented preliminary results from a cohort of the KRYSTAL-1 clinical trial evaluating adagrasib at 600mg BID as

monotherapy for patients with pancreatic ductal adenocarcinoma harboring a KRAS G12C mutation. arm (n=12). Of the evaluable patients (n=10), preliminary results showed an investigator assessed RR of 50%, including an unconfirmed PR, and a DCR of 100%.

Preliminary efficacy data was assessed as of August 30, 2020 in six patients with advanced solid tumors, other than NSCLC and CRC, treated with adagrasib as a monotherapy at 600mg BID dose from a Phase 1/1b cohort. One patient each with pancreatic, ovarian, endometrial and cholangiocarcinoma tumors were treated and had a confirmed PR to therapy. Two appendiceal cancer patients had stable disease and all six eligible patients remained on treatment.

Adagrasib Development in Collaboration with Zai Lab Ltd. ("Zai")

In May 2021, we entered into a Collaboration and License Agreement with Zai (the "Zai Agreement"). Under the Zai Agreement, we granted Zai the right to research, develop, manufacture and exclusively commercialize adagrasib in all indications in China, Macau, Hong Kong and Taiwan (collectively, the "Zai Licensed Territory"), with Mirati retaining exclusive rights for the development, manufacture and commercialization of adagrasib outside the Zai Territory and certain co-commercialization, manufacture, and development rights in the Zai Licensed Territory.

MRTX1133, a selective KRAS G12D inhibitor

MRTX1133, our lead KRAS G12D compound, has been identified as a clinical development candidate and is an investigational, selective, specific and potent inhibitor of KRAS G12D and is currently in preclinical development. KRAS G12D mutations have been detected in over 25 different types of cancer, including pancreatic, colon, lung and endometrial adenocarcinoma. The prevalence of cancers harboring KRAS G12D mutations exceeds the prevalence of KRAS G12C positive cancers by greater than two-fold and is an area of significant unmet medical need.

On October 25, 2020 we announced initial preclinical in vivo data from MRTX1133. Based on preclinical analyses, MRTX1133 has a projected human half-life of approximately 50 hours and exhibits a low propensity for drug interactions or off-target pharmacology. MRTX1133 demonstrated tumor regression in multiple in vivo tumor models, including pancreatic and colorectal cancers. MRTX1133 has a low predicted target plasma concentration, based on its potency and high unbound fraction, and our goal is to achieve near complete and sustained target inhibition and maximal anti-tumor activity. We have prioritized a long-acting IV injectable drug product strategy, including liposome-based formulations, that are designed to optimize and extend the duration of KRAS G12D target inhibition as we progress towards IND-enabling studies. We are also continuing to evaluate strategies to enhance oral absorption to potentially enable development of a solid oral dose form.

Sitravatinib

Sitravatinib is a spectrum-selective kinase inhibitor in Phase 3 clinical development and is designed to potently inhibit receptor tyrosine kinases ("RTK"s), including TAM family receptors (TYRO3, Axl, Mer), split family receptors (VEGFR2, KIT) and RET. Sitravatinib's potent inhibition of TAM and split family RTKs may overcome resistance to checkpoint inhibitor therapy through targeted reversal of an immunosuppressive tumor microenvironment, enhancing antigen-specific T cell response and expanding dendritic cell-dependent antigen presentation. There are over 100,000 2nd or 3rd line NSCLC patients in the United States and Europe, who have derived prior clinical benefit following treatment with a PD-(L)1 inhibitor, with approximately 70,000 of these patients being of the non-squamous histology.

Sitravatinib in Combination with Nivolumab

As an immuno-oncology agent, sitravatinib is being evaluated in combination with nivolumab (*OPDIVO*®), Bristol-Myers Squibb Company's ("BMS") anti-PD-1 checkpoint inhibitor, in patients with NSCLC who have experienced documented disease progression following treatment with a checkpoint inhibitor. Sitravatinib is also being developed in certain Asian territories in collaboration with BeiGene, Ltd. ("BeiGene") which is evaluating sitravatinib in combination with tislelizumab, BeiGene's anti-PD-1 checkpoint inhibitor, in a number of advanced solid tumors.

We are enrolling an ongoing Phase 3 clinical trial in 2nd line non-squamous NSCLC patients whose tumors have progressed on prior therapy with platinum-chemotherapy in combination with a checkpoint inhibitor or 3rd line non-squamous NSCLC patients who have received chemotherapy followed by a checkpoint inhibitor. The Phase 3 clinical trial is comparing the combination of sitravatinib plus nivolumab randomized to docetaxel. The statistical design of the Phase 3 clinical trial includes an interim analysis of overall survival that we believe, if positive, could support an NDA submission seeking full approval.

In January 2019, we announced a clinical trial collaboration with BMS in connection with the aforementioned Phase 3 clinical trial. Under the terms of the collaboration, we are sponsoring and funding the clinical trial and BMS is providing nivolumab at no cost. We maintain global development and commercial rights to sitravatinib outside of certain Asian territories and Australia and New Zealand, where we have partnered with BeiGene, and we are free to develop the program in combination with other agents.

We also have several Phase 2 clinical trials in which we are evaluating sitravatinib in combination with nivolumab in patients with NSCLC, urothelial carcinoma or other cancers who have experienced documented disease progression following prior treatment with chemotherapy and/or a checkpoint inhibitor. On September 20, 2021, we announced results from a post hoc exploratory analysis of the Phase 2 study, MRTX-500, in patients with nonsquamous NSCLC with prior clinical benefit from checkpoint inhibitor therapy and where anti-PD-(L)1 was the most recent line of therapy (n=68) and a median follow-up of 33.6 months. The median overall survival was 14.9 months (95% CI: 9.3, 21.1), with 56% and 32% of these patients alive at one year and two years, respectively. The ORR was 18%, with 3% of patients achieving a complete response and 15% of patients achieving a PR. The median DOR was 12.8 months.

Sitravatinib Development in Collaboration with BeiGene

In January 2018, we entered into a Collaboration and License Agreement with BeiGene (the "BeiGene Agreement"). Under the BeiGene Agreement, we granted BeiGene an exclusive license to develop, manufacture and commercialize sitravatinib in Asia (excluding Japan and certain other countries), Australia and New Zealand (the "BeiGene Licensed Territory"), and we retained exclusive rights for the development, manufacturing and commercialization of sitravatinib outside the BeiGene Licensed Territory.

In November 2018, we dosed the first patient under the BeiGene Agreement to assess the safety and tolerability, pharmacokinetics and preliminary anti-tumor activity of sitravatinib in combination with BeiGene's investigational anti-PD-1 antibody, tislelizumab, in patients with advanced solid tumors. BeiGene's clinical trials will evaluate the combination of sitravatinib and tislelizumab in patients with solid tumors including NSCLC, renal cell carcinoma, hepatocellular cancer, gastric cancer and ovarian cancer.

MRTX1719, a synthetic lethal MTA cooperative PRMT5 inhibitor

MRTX1719, our lead synthetic MTA cooperative lethal PRMT5 inhibitor is an investigational, selective, potent and orally available inhibitor targeting the PRMT5/MTA complex in methylthioadenosine phosphorylase (MTAP)-deleted cancers and is in Phase 1/2 clinical development. The MTAP deletion is present in approximately 10 percent of all cancers and is the most frequently observed gene deletion event (MTAP/CDKN2A) across several cancer types. Cancers with an MTAP deletion, such as pancreatic, lung, and bladder cancers, are associated with a poor prognosis, representing a significant unmet medical need.

In preclinical studies, MRTX1719 has demonstrated a greater than 70-fold selectivity for MTAP-deleted cells relative to normal cells and demonstrated near complete and sustained inhibition of PRMT5 in tumor xenografts resulting in significant tumor growth inhibition or tumor regression in MTAP-deleted tumor models. The ability to target the PRMT5/MTA complex provides an opportunity to selectively target tumor cells harboring the MTAP gene deletion which exhibit an abnormally high level of MTA (methylthioadenosine) compared with normal cells. This is anticipated to provide an increased therapeutic index relative to first generation PRMT5 inhibitors that do not specifically target the PRMT5/MTA complex. In the first quarter of 2022, we initiated a Phase 1/2 multiple expansion cohort trial to evaluate MRTX1719 in patients with advanced, unresectable or metastatic solid tumor malignancy with homozygous deletion of the MTAP gene.

Market and Competition

NSCLC Market

The National Cancer Institute estimates that in 2021, approximately 236,000 patients in the United States ("U.S.") were diagnosed with lung cancer and 132,000 died due to the disease. Lung cancer represents almost 12% of all new cancer cases in the U.S., and 22% of all cancer deaths. According to the American Cancer Society, approximately 84% of lung cancers are NSCLC. The five-year survival rate for lung cancer patients is 25%, indicating a significant need for novel therapies to extend overall survival in this patient population.

The prognosis for advanced NSCLC is poor, and the primary objective of treating late-stage disease is to prolong overall survival, delay disease progression and control symptoms. The treatment algorithm for advanced NSCLC has changed

significantly following recent approvals and label expansions of immuno-oncology agents, specifically immune checkpoint inhibitors. In 2015, the FDA approved *OPDIVO*®, an anti-PD-1 monoclonal antibody, and the first immuno-oncology agent approved for the treatment of squamous NSCLC. The approval of *OPDIVO*® in NSCLC was subsequently followed by FDA approval of three additional immuno-oncology agents in NSCLC, *KEYTRUDA*®, *TECENTRIQ*®, and *IMFINZI*®. These four agents, approved for multiple indications including NSCLC, accounted for over $27 billion in global sales in 2020.

Despite the advances in patient outcomes demonstrated by approved immuno-oncology therapies in NSCLC, a significant patient need remains. The percentage of patients who respond to approved immuno-oncology treatments is quite low, and of the patients that respond, the majority will still experience disease progression.

NSCLC represents a heterogeneous patient population with diverse tumor histology and underlying genomic aberrations. The clinical and commercial success of leading targeted agents across multiple indications, including NSCLC, demonstrates the potential of new targeted treatments for cancer.

Competition

KRAS G12C

We are aware of at least six companies who currently have competing commercial or clinical-stage direct KRAS G12C inhibitor programs: Amgen, Inc., F. Hoffman-LaRoche Ltd., Eli Lilly and Company, Merck & Co., Inc., Novartis AG and Boehringer Ingelheim International GmbH.

Sitravatinib in Combination with Immune Checkpoint Inhibitors

There are several immune checkpoint inhibitors currently approved for use as single agents to treat multiple tumor types, including NSCLC. To augment the efficacy of these agents, combination studies are being conducted with a variety of potentially synergistic mechanisms, including inhibitors of CTLA-4, LAG3, TIM-3, TIGIT and CSF-1R, among others. Most of these combination studies are being conducted in patients who are naïve to immune checkpoint inhibitor therapy. Direct mechanistic competitors to sitravatinib in combination with checkpoint inhibitors in NSCLC patients who had previously failed checkpoint inhibitor therapy include *CABOMETYX*® (Exelixis, Inc.) and *LENVIMA*® (Eisai Co., Ltd.), both anti-VEGF agents that also inhibit other receptor tyrosine kinases. Additionally, there are numerous other potential competitors with kinase inhibitors that are being evaluated in combination with checkpoint inhibitors in NSCLC patients who had previously failed checkpoint inhibitor therapy in earlier lines of treatment.

Oncology

In addition to companies that have kinase 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. Other important competitors, in addition to those mentioned above, are small and large biotechnology companies, specialty and regional pharmaceutical companies and multinational pharmaceutical companies, including but not limited to AbbVie Inc., AstraZeneca plc, Bristol-Myers Squibb Company, Gilead Sciences, Inc., GlaxoSmithKline plc, Johnson & Johnson, Pfizer Inc., Sanofi S.A., and Takeda Pharmaceutical Co.

Intellectual Property

Our goal is to obtain, maintain and enforce patent protection wherever appropriate for our product candidates, formulations, processes, methods and any other proprietary technologies both in the United States and in other countries. We typically file for patents in the United States with counterparts in certain countries in Europe and certain key market countries in the rest of the world, thereby covering the major pharmaceutical markets. As of December 31, 2021, we own or co-own U.S. patents and patent applications and their foreign counterparts, including 34 issued U.S. patents, including one for KRAS inhibitors and 15 for sitravatinib and other kinase inhibitors. Mirati's patents and patent applications have expiration dates ranging from 2023-2041. In some instances, patent terms can be increased or decreased, depending on the laws and regulations of the country or jurisdiction that issued the patent.

Manufacturing

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we plan to develop our own manufacturing operations in the foreseeable future. We currently depend on third-party contract manufacturers for all of our required raw materials and finished products for our preclinical and clinical trials.

Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's Current Good Manufacturing Practices ("cGMP") regulations. cGMP regulations require, among other things, quality control and quality assurance, as well as corresponding maintenance of records and documentation. Pharmaceutical product manufacturers and other entities involved in the manufacture and distribution of approved pharmaceutical products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an NDA, including withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented.

Government Regulation

The Regulatory Process for Drug Development

Our business activities, including the manufacturing of our product candidates and our ongoing research and development activities are subject to extensive regulation by numerous governmental authorities in the United States and other countries. Regulation by these government authorities is a significant component in the development, manufacture and commercialization of pharmaceutical products and services. Before marketing in the United States, any new drug developed must undergo rigorous preclinical testing, clinical trials and an extensive regulatory clearance process implemented by the FDA under the Federal Food, Drug, and Cosmetic Act, as amended (the "FDCA"). The FDCA and other various federal, state and foreign statutes govern or influence the research, testing, manufacture, safety, labeling, storage, recordkeeping, approval, promotion, marketing, distribution, post-approval monitoring and reporting, sampling, quality, and import and export of our medicines. State, local, and other authorities also regulate pharmaceutical manufacturing.

Applicable legislation requires licensing of manufacturing and contract research facilities, carefully controlled research and testing of products, and governmental review and/or approval of results prior to marketing therapeutic products. Additionally, adherence to good laboratory practices ("GLP") and good clinical practices ("GCP") during nonclinical and clinical testing and cGMP during production is required. Our manufacturing CMOs are subject to periodic inspection by the FDA and other foreign equivalents to ensure that they are operating in compliance with cGMP requirements. In addition, marketing authorization for each new medicine may require a rigorous manufacturing pre-approval inspection by regulatory authorities. Post approval, there are strict regulations regarding changes to the manufacturing process, and, depending on the significance of the change, changes may require prior FDA approval. 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.

In addition, we are subject to other state and federal laws, including, among others, anti-kickback laws, fraud and abuse, false claims laws, Sunshine Act, patient protection and affordable care, data privacy and security laws and regulations, and transparency laws that restrict certain business practices in the pharmaceutical industry. Violations of these healthcare laws can result in significant penalties, including civil, criminal and administrative penalties. Moreover, government coverage and reimbursement policies will both directly and indirectly impact our ability to successfully commercialize any future approved products, and such coverage and reimbursement policies will be impacted by enacted and any applicable future healthcare reform and drug pricing measures.

U.S. Pharmaceutical Product Development Process

To establish a new product candidate's safety and efficacy, the FDA requires companies seeking approval to market a pharmaceutical drug product to submit extensive preclinical and clinical data, along with other information, for each indication for which the product will be labeled. The data and information are submitted to the FDA in the form of a New Drug Application (NDA), which must be accompanied by payment of a significant user fee unless a waiver or exemption applies. Generating the required data and information for an NDA takes many years and requires the expenditure of substantial resources. Information generated in this process is susceptible to varying interpretations that could delay, limit or prevent regulatory approval at any stage of the process. The failure to demonstrate adequately the quality, safety and efficacy of a

product candidate under development would delay or prevent regulatory approval of the product candidate. Under applicable laws and FDA regulations, each NDA submitted for FDA approval is given an internal administrative review within 60 days following submission of the NDA. If deemed sufficiently complete to permit a substantive review, the FDA will "file" the NDA. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established internal goals of eight months from submission for priority review of NDAs that cover new product candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists, and 12 months from submission for the standard review of NDAs. However, the FDA is not legally required to complete its review within these periods, these performance goals may change over time and the review is often extended by FDA requests for additional information or clarification. Moreover, the outcome of the review, even if generally favorable, may not be an actual approval but a "complete response letter" that describes additional work that must be done before the NDA can be approved. Before approving an NDA, the FDA can choose to inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with GMPs. The FDA may also audit sites at which clinical trials have been conducted to determine compliance with GCPs and data integrity. The FDA's review of an NDA may also involve review and recommendations by an independent FDA advisory committee, particularly for novel indications. The FDA is not bound by the recommendation of an advisory committee. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling.

FDA Regulation of Companion Diagnostics

As part of our clinical development plans, we are exploring the use of companion diagnostics to identify patients most likely to respond to our product candidates. Companion diagnostics are classified as medical devices under the FDCA in the United States and similarly in other foreign regulations. In the United States, the FDA regulates the medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, reporting, recordkeeping, advertising and promotion, export and import, sales and distribution, and post-market surveillance of medical devices. Unless an exemption applies, companion diagnostics require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval ("PMA").

The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to the cancer treatment to obtain a 510(k) clearance or PMA simultaneously with approval of the drug. Based on the draft guidance, and the FDA's past treatment of companion diagnostics, we believe that the FDA will require a PMA for one or more companion diagnostics to identify patient populations suitable for our product candidates. The review of these companion diagnostics in conjunction with the review of our product candidates involves coordination of review by the FDA's Center for Drug Evaluation and Research and by the FDA's Center for Devices and Radiological Health.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and adequate reimbursement from third-party payors, including government authorities, managed care providers, private health insurers and other organizations. In the United States, private health insurers and other third-party payors often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such products and services. There is no uniform coverage and reimbursement policy among third-party payors in the United States; however, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Third-party payors are increasingly examining the medical necessity and cost-effectiveness of medical products and services in addition to their safety and efficacy and, accordingly, significant uncertainty exists as to the coverage and reimbursement status of newly approved therapeutics. In particular, in the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which often has resulted in average selling prices that are lower than they would otherwise be. The increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and utilization, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. As a result, coverage and adequate third-party reimbursement may not be available for our product candidates to enable us to realize an appropriate return on our investment in research and product development.

The market for our product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or may otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. In addition, because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming and costly process. We would be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any of our product candidates for which we may receive approval and could have a negative effect on our future revenue and operating results. We cannot be certain that our product candidates will be considered cost-effective. If we are unable to obtain coverage and adequate payment levels for our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition, and future success.

Human Capital Resources

Successful execution of our strategy is dependent on attracting, developing, and retaining key employees and members of our executive leadership team. The skills, experience and industry knowledge of our employees significantly benefit our operations and performance. We continuously evaluate, modify, and enhance our internal processes and technologies to increase employee engagement, productivity, and efficiency. The Company works diligently to attract the best talent from a diverse range of sources in order to meet the current and future demands of our business. We offer a strong employee value proposition and our compensation programs are designed to align the compensation of our employees with the Company's performance and to provide the proper incentives to attract, retain and motivate employees. The structure of our compensation programs incentivizes both short-term and long-term performance and we believe in a total rewards experience, specifically:

- We provide employee wages that are competitive and consistent with employee positions, skill levels, experience, and knowledge. Our competitive benefits packages include equity grants such as stock options and restricted stock units; performance-based bonuses; recognition awards; an employee stock purchase plan; retirement savings plan with company matching contributions; medical, dental and life insurance; an employee assistance program; work/life balance arrangements, including core hours and flexible work arrangements; paid time off and holidays; and volunteer hours.

- We engage nationally recognized independent compensation and benefits consulting firms to evaluate the effectiveness of our executive compensation and benefit programs and to provide benchmarking against our peers within the industry.

- Annual increases and incentive compensation, which are communicated to employees at the time of hiring and documented through our talent management process as part of our review procedures.

We also make significant investments in training, development and engagement, using development programs such as our Leadership Model Sessions program, comprised of interactive workshops to gain insight into leading at the Company, and our Mirati Mentor Program, in which employees self-nominate as mentors or mentees and facilitates meaningful relationships supporting new employees' career and development goals.

As of December 31, 2021, we had 418 employees of which 413 were full-time, exempt employees, one was a part-time, exempt employee, and the remaining were full-time, non-exempt employees. None of our employees are represented by a collective bargaining agreement

Culture

Fostering and maintaining a strong, healthy culture is fundamental to the success of our business. Our core values reflect who we are and the way our employees interact with one another, our partners, and stakeholders. Urgency, open-mindedness, accountability, and collaboration ground our work and behavior. These shared values are central to who we are, what we do, and how we do it. No matter the role, we are unified by our passion for helping patients, and we are inspired by a single vision – to unlock the science behind the promise of a life beyond cancer. We believe our culture creates strong engagement, which is measured through an annual employee-wide, anonymous survey to assess our performance on metrics including mission and vision, development and empowerment, our ability to adapt and overall employee satisfaction.

Diversity, Equity and Inclusion

We believe diverse professional experiences and an inclusive culture can drive better outcomes for patients. Our culture is one where we challenge norms, have high risk tolerance and celebrate an entrepreneurial and courageous attitude full of grit and determination to make a difference. In 2021, we initiated a Diversity, Equity and Inclusion ("DE&I") program, for which we took the following initials steps: established a DE&I Committee, comprised of cross-functional representatives including from medical affairs, supply chain, financial planning, business development, commercial and human resources, and surveyed all employees to inform the Company's DE&I objectives and future employee training. Based on data as of November 1, 2021, 46% of our Company's employees identify as women, including 43% of our executive leadership team; and 40% of our Company's employees identify as being a racial or ethnic minority, including 14% of our executive leadership team. As of December 31, 2021, 30% of the Company's board of directors, identify as women and 30% identify as being a racial or ethnic minority. We are committed to diversifying the representation of our organization.

COVID-19 Health and Safety

We are committed to providing a healthy and safe work environment for our employees, partners and consultants. In early 2020 as the pandemic began, we assembled a cross-functional COVID-19 response team that included members of our executive leadership. At the start of the pandemic, we quickly moved to a work-from-home mandate and adopted a flexible work schedule. We are continuing to allow for flexible work schedules, including remote and hybrid options. To allow employees to work from home seamlessly, we provide the necessary technology and collaboration tools and developed an internal task force to identify support opportunities for employees working from home and homeschooling children.

In response to employee feedback and as part of our commitment to supporting our employees and families in meaningful ways throughout the pandemic, we put in place the following programs: a work-from-home stipend for all employees whose jobs are not regularly remote; caregiver resources, including a tax-free subsidy to help with unplanned dependent care costs; an Employee Assistance Program that includes free resources and confidential counseling for employees and their household members; and fully-covered COVID-19 testing for employees.

As we move towards having more of our workforce onsite, we implemented the following protocols based on recent COVID-19 science and local/federal government advice: requiring the COVID-19 vaccination as a condition to be at our corporate headquarters, with certain exceptions; Company personnel who are onsite are highly recommended to wear face masks when unable to physically distance, regardless of vaccination status; providing disposable masks; face masks and a negative COVID-19 test result are required for those who are unvaccinated for each week they are approved to come on-site; and all personnel complete a touch-free temperature check and "check" to the site via a third-party app to help keep track of employees coming to the site for potential contact tracing needs. We continually evaluate our approach in line with our principles to meet our company goals, while maintaining the well-being and productivity of our teams.

Corporate Information

We were originally incorporated in Canada as MethylGene, Inc. ("MethylGene") and reincorporated in Delaware on April 29, 2013 as Mirati Therapeutics, Inc. with headquarters in San Diego, California. We have two wholly-owned subsidiaries: Methylgene, Inc, in Canada, and Mirati Therapeutics B.V., in the Netherlands. We maintain a website at www.mirati.com, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the Securities and Exchange Commission ("SEC"), are available free of charge through our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Interested persons can subscribe to our website for email alerts that are sent automatically when we issue press releases, file our reports with the SEC or post certain other information to our website. Information contained in our website does not constitute a part of this report or our other filings with the SEC. Our common stock is listed under the ticker symbol "MRTX" on the Nasdaq Global Select Market since June 5, 2018, and was previously listed on the Nasdaq Capital Market since July 15, 2013.

Item 1A. Risk Factors

RISK FACTORS

Risks Related to Our Business and Industry

Our research and development programs and product candidates are in development. As a result, we are unable to predict if or when we will successfully develop or commercialize our product candidates.

Our clinical-stage product candidates as well as our other pipeline assets will require significant further investment and regulatory approvals prior to commercialization. Adagrasib is in Phase 3 and Phase 1/2 clinical trials, sitravatinib is in a Phase 3 clinical trial, and Phase 1/2 clinical trials, MRTX1719 is in a Phase 1 clinical trial, and MRTX1133 is in preclinical development. We recently submitted an NDA to the FDA to adagrasib. Each of our product candidates will require the selection of suitable patients for our clinical trials and additional clinical development, management of clinical, preclinical and manufacturing activities, obtaining regulatory approval, obtaining manufacturing supply, continued build out of a commercial organization, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. The treatment of cancer is a rapidly evolving field and will continue to evolve. By such time, if ever, as we may receive necessary regulatory approvals for our product candidates, the standard of care for the treatment of cancers may have evolved such that it would be necessary to modify our plans for full approval and commercial acceptance of our products may be limited by a change in the standard of care. In addition, some of our product development programs contemplate the development of companion diagnostics. Companion diagnostics are subject to regulation as medical devices and we or our collaborators may be required to obtain marketing approval for accompanying companion diagnostics before we may commercialize our product candidates.

Even if we obtain the required financing or establish a collaboration to enable us to conduct late-stage clinical development of our product candidates and pipeline assets, we cannot be certain that such clinical development would be successful, or that we will obtain regulatory approval or be able to successfully commercialize any of our product candidates and generate revenue. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the clinical trial process may fail to demonstrate that our product candidates are safe and effective for their proposed uses. Any such failure could cause us to abandon further development of any one or more of our product candidates and may delay development of other product candidates. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Any delay in, or termination of, our clinical trials will delay and possibly preclude the submission of any new drug applications ("NDA") with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenue.

We recently submitted an NDA to the FDA. We, however, have not previously submitted an NDA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to market one or more of our product candidates, our revenues will be dependent, in part, upon our current collaborators' and future collaborators' ability to obtain regulatory approval for the companion diagnostics to be used with our product candidates, if required, and upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

Further, even if any product candidate we develop was to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to bear the risks that the FDA or similar foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies.

All of our product candidates are subject to extensive regulation, which can be costly and time consuming, cause delays or prevent approval of such product candidates for commercialization.

The clinical development of product candidates is subject to extensive regulation by the FDA in the United States and by comparable regulatory authorities in foreign markets. Product development is a very lengthy and expensive process, and its outcome is inherently uncertain. The product development timeline can vary significantly based upon the product candidate's novelty and complexity and the applicable regulatory authority. For example, we are pursuing an expansion strategy to bring

our leading product candidate to countries within the European Economic Area ("EEA") and the United Kingdom ("UK"). The regulatory approval in other countries may include all the risks associated with FDA approval as well as additional, presently unanticipated, risks. Regulations are subject to change and regulatory agencies have significant discretion in the approval process.

Numerous statutes and regulations govern human testing and the manufacture and sale of human therapeutic products in the United States, Europe and other countries and regions where we intend to market our products. Such legislation and regulation bears upon, among other things, the approval of trial protocols and human testing, the approval of manufacturing facilities, safety of the product candidates, testing procedures and controlled research, review and approval of manufacturing, preclinical and clinical data prior to marketing approval including adherence to good manufacturing practices ("GMP") during production and storage as well as regulation of marketing activities including advertising and labeling.

In order to obtain regulatory approval, including an NDA or marketing authorization application, for the commercial sale of any of our product candidates in the United States, EEA and other foreign market, we must demonstrate through preclinical studies and clinical trials, as well as extensive information regarding chemistry, manufacturing and controls ("CMC"), that the potential product is safe and effective for use in humans for each target indication. The failure to adequately demonstrate the safety and efficacy of a product under development could delay or prevent regulatory approval of our product candidates. 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.

No assurance can be given that current regulations relating to regulatory approval will not change or become more stringent in the United States or foreign markets. Regulatory agencies may also require that additional trials be run in order to provide additional information regarding the safety or efficacy of any drug candidates for which we seek regulatory approval or require additional administrative review periods, including obtaining reimbursement and pricing approval in select markets. Moreover, any regulatory approval of a drug which is eventually obtained may entail limitations on the indicated uses for which that drug may be marketed. Furthermore, product approvals may be withdrawn or limited in some way if problems occur following initial marketing or if compliance with regulatory standards is not maintained. Regulatory agencies could become more risk averse to any side effects or set higher standards of safety and efficacy prior to reviewing or approving a product. This could result in a product not being approved. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

The successful commercialization of our product candidates, if approved, will depend on achieving market acceptance and we may not be able to gain sufficient acceptance to generate significant revenue.

Even if our product candidates are successfully developed and receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors such as private insurers or governments and other funding parties and the medical community. The degree of market acceptance for any of our products will depend on a number of factors, including:

- demonstration of the clinical efficacy and safety of our products;
- the prevalence and severity of any adverse side effects;
- limitations or warnings contained in the product's approved labeling;
- cost-effectiveness and availability of acceptable pricing;
- competitive product profile versus alternative treatment methods and the superiority of alternative treatment or therapeutics;
- the effectiveness of marketing and distribution methods and support for the products; and
- the availability of coverage and adequate reimbursement from third-party payors to the extent that our products receive regulatory approval.

Disease indications may be small subsets of a disease that could be parsed into smaller and smaller indications as different subsets of diseases are defined. This increasingly fine characterization of diseases could have negative consequences; including creating an approved indication that is so small as not to have a viable market for us. If future technology allows characterization of a disease in a way that is different from the characterization used for large pivotal studies, it may make those

studies invalid or reduce their usefulness, and may require repeating all or a portion of the studies. Future technology may supply better prognostic ability which could reduce the portion of patients projected to need a new therapy. Even after being cleared by regulatory authorities, a product may later be shown to be unsafe or not to have its purported effect, thereby preventing its widespread use or requiring withdrawal from the market.

We may not be successful in establishing development and commercialization collaborations which could adversely affect, and potentially prohibit, our ability to develop our product candidates.

Developing pharmaceutical products, conducting clinical trials, obtaining regulatory approval, establishing manufacturing capabilities and marketing approved products is expensive, and therefore we may seek to enter into additional collaborations with companies that have more resources and experience in order to continue to develop and commercialize our product candidates. We also may be required due to financial or scientific constraints to enter into additional collaboration agreements to research and/or to develop and commercialize our product candidates. The establishment and realization of such collaborations may not be possible or may be problematic. There can be no assurance that we will be able to establish such additional collaborations on favorable terms, if at all, or that our current or future collaborative arrangements will be successful or maintained for any specific product candidate or indication. If we are unable to reach successful agreements with suitable collaboration partners for the ongoing development and commercialization of our product candidates, we may face increased costs, we may be forced to limit the scope and number of our product candidates we can commercially develop or the territories in which we commercialize such product candidates, and we may be unable to commercialize products or programs for which a suitable collaboration partner cannot be found. If we fail to achieve successful collaborations, our operating results and financial condition will be materially and adversely affected.

In addition, the terms of any collaboration agreements may place restrictions on our activities with respect to other products, including by limiting our ability to grant licenses or develop products with other third parties, or in different indications, diseases or geographical locations, or may place additional obligations on us with respect to development or commercialization of our product candidates. If we fail to comply with or breach any provision of a collaboration agreement, a collaborator may have the right to terminate, in whole or in part, such agreement or to seek damages.

Some of our collaboration agreements, including the BeiGene Agreement and Zai Agreement, are complex and involve sharing or division of ownership of certain data, know-how and intellectual property rights among the various parties. Accordingly, our collaborators could interpret certain provisions differently than we or our other collaborators which could lead to unexpected or inadvertent disputes with collaborators. In addition, these agreements might make additional collaborations, partnering or mergers and acquisitions difficult.

There is no assurance that a collaborator who is acquired by a third party would not attempt to change certain contract provisions that could negatively affect our collaboration. The acquiring company may also not accept the terms or assignment of our contracts and may seek to terminate the agreements. Any one of our collaborators could breach covenants, restrictions and/or sub-license agreement provisions leading us into disputes and potential breaches of our agreements with other partners.

We have no experience in clinical or commercial manufacturing and depend on others for the production of our product candidates at suitable levels of quality and quantity. Any problems or delays in the manufacture of our products would have a negative impact on our ability to successfully execute our development and commercialization strategies.

We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our clinical drug supplies for use in the conduct of our clinical trials, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. We rely on collaborators and/or third parties for development, scale-up, formulation, optimization, management of clinical trial and commercial scale manufacturing and commercialization. There are no assurances we can scale-up, formulate or manufacture any product candidate in sufficient quantities with acceptable specifications for the conduct of our clinical trials or for the regulatory agencies to grant approval of such product candidate. We have not yet commercialized any products and have no commercial manufacturing experience. To be successful, our products must be properly formulated, scalable, stable and safely manufactured in clinical trial and commercial quantities in compliance with GMP and other regulatory requirements and at acceptable costs. Should any of our suppliers or our collaborators be unable to supply or be delayed in supplying us with sufficient supplies, no assurance can be given that we will be able to find alternative means of supply in a short period of time. Should such parties' operations suffer a material adverse effect, the manufacturing of our products would also be adversely affected. Furthermore, key raw materials could become scarce or unavailable. There may be a limited number of third parties who can manufacture our products. We may not be able to meet specifications previously established for product candidates during scale-up and manufacturing.

Our reliance on third parties to manufacture our product candidates will expose us and our partners to risks including the following, any of which could delay or prevent the commercialization of our products, result in higher costs, or deprive us of potential product revenue:

- Contract manufacturers can encounter difficulties in achieving the scale-up, optimization, formulation, or volume production of a compound as well as maintaining quality control with appropriate quality assurance. They may also experience shortages of qualified personnel. Contract manufacturers are required to undergo a satisfactory GMP inspection prior to regulatory approval and are obliged to operate in accordance with FDA, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("ICH"), European and other nationally mandated GMP regulations and/or guidelines governing manufacturing processes, stability testing, record keeping and quality standards. A failure of these contract manufacturers to follow GMP and to document their adherence to such practices or failure of an inspection by a regulatory agency may lead to significant delays in the availability of our product candidate materials for clinical study, leading to delays in our trials.

- For each of our current product candidates we will initially rely on a limited number of contract manufacturers. Changing these or identifying future manufacturers may be difficult. Changing manufacturers requires re-validation of the manufacturing processes and procedures in accordance with FDA, ICH, European and other mandated GMP regulations and/or guidelines. Such re-validation may be costly and time-consuming. It may be difficult or impossible for us to quickly find replacement manufacturers on acceptable terms.

- Our contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to produce, store and distribute our products successfully.

A variety of risks associated with operating our business internationally could adversely affect our business.

In addition to our operations in the United States, we have operations in the Netherlands, and are pursuing further European expansion to support the planned commercialization of our product candidates in the EEA and UK. We face risks associated with our international operations, including possible unfavorable political, tax and labor conditions, which could harm our business. We are subject to numerous risks associated with international business activities, including:

- difficulties in staffing and managing foreign operations;

- foreign government taxes, regulations and permit requirements;

- United States and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;

- anti-corruption laws, including the Foreign Corrupt Practices Act ("FCPA");

- economic weakness, including inflation, natural disasters, war, events of terrorism or political instability in particular foreign countries;

- fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenues, and other obligations related to doing business in another country;

- compliance with tax, employment, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;

- workforce uncertainty in countries where labor unrest is more common than in the United States;

- production shortages resulting from any events affecting raw material supply or manufacturing capabilities aboard; and

- changes in diplomatic and trade relationships.

Our business activities outside of the United States are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA and similar anti-corruption laws generally prohibit offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to non-U.S. government officials in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions

of the company and to devise and maintain an adequate system of internal accounting controls. As described above, our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers may be subject to regulation under the FCPA. Recently the Securities and Exchange Commission ("SEC") and the U.S. Department of Justice ("DOJ") have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd–Frank Wall Street Reform and Consumer Protection Act, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. We are engaged in ongoing efforts that are designed to ensure our compliance with these laws, including due diligence, training, policies, procedures and internal controls. However, there is no certainty that all employees and third-party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of manufacturers and other third-party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

We are or may become subject to tax audits in the Netherlands or other countries into which we expand our operations, and such jurisdictions may assess additional income tax against us. The final determination of tax audits could be materially different from our recorded income tax provisions and accruals. The ultimate results of an audit could have a material adverse effect on our operating results or cash flows in the period or periods for which that determination is made and could result in increases to our overall tax expense in subsequent periods.

These and other risks associated with our international operations may materially adversely affect our business, financial condition and results of operations.

The COVID-19 pandemic could adversely impact our business including our ongoing and planned clinical trials and preclinical research.

Our business could be materially adversely affected by the effects of health epidemics. For example, since December 2019, a novel strain of coronavirus, SARS-CoV-2, causing a disease referred to as COVID-19, has spread worldwide. In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic and the U.S. government-imposed travel restrictions on travel between the U.S., Europe and certain other countries. In addition, the Governor of the State of California issued a number of stay-at-home orders and health directives. As a result of such orders, we implemented work-from-home policies for most of our employees and generally suspended business-related travel. Although many of these orders and directives have since been lifted, in response to the spread of various variants of COVID-19 and to protect the health and welfare of our employees, we continue to maintain flexible work-from-home policies for most of our employees. The effects of these work-from-home and travel policies have thus far had a limited impact on our business.

Our business could be materially adversely affected by health epidemics in regions where we or our partners have concentrations of clinical trial sites or other business operations and could cause significant disruption in the operations of third-party manufacturers and contract research organizations upon whom we rely.

Quarantines, shelter-in-place, executive and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, could impact personnel at third-party manufacturing facilities in the U.S. and other countries, or the availability or cost of materials, which would disrupt our supply chain. We have experienced impacts to our clinical trial operations due to the COVID-19 pandemic. Some examples of these impacts include:

- we have experienced impact on clinical site initiation and patient enrollment due to restrictions imposed as a result of the COVID-19 pandemic;
- some patients have not been able to comply with clinical trial protocols as quarantines have impeded patient movement and interrupted healthcare services;
- we have experienced some impact on our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19; and
- we have experienced some delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel.

The global COVID-19 pandemic continues to rapidly evolve. While we have not yet experienced material adverse effects to our business as a result of the COVID-19 pandemic the ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and could have negative impact our business, financial condition and operating results.

We rely upon third-party contractors and service providers for the execution of some aspects of our development programs. Failure of these collaborators to provide services of a suitable quality and within acceptable timeframes may cause the delay or failure of our development programs.

We outsource certain functions, tests and services to CROs, medical institutions and collaborators and outsource manufacturing to collaborators and/or contract manufacturers, and we rely on third parties for quality assurance, clinical monitoring, clinical data management and regulatory expertise. In particular, we rely on CROs to run our clinical trials on our behalf and contract manufacturers to manufacture our product candidates. There is no assurance that such individuals or organizations will be able to provide the functions, tests, drug supply or services as agreed upon or to acceptable quality standards, and we could suffer significant delays in the development of our products or processes. In particular, certain third party service providers may be unable to comply with their contractual obligations to us due to disruptions caused by the COVID-19 pandemic, including reduced operations or headcount reductions, or otherwise, and in certain cases we may have limited recourse if the non-compliance is due to factors outside of the service provider's control.

In some cases, there may be only one or few providers of such services, including manufacturing services. In addition, the cost of such services could increase significantly over time. We rely on third parties as mentioned above to enroll qualified patients and conduct, supervise and monitor our clinical trials. Our reliance on these third parties and collaborators for clinical development activities reduces our control over these activities, but does not relieve us of our regulatory responsibilities, including ensuring that our clinical trials are conducted in accordance with good clinical practices ("GCP") regulations and the investigational plan and protocols contained in the regulatory agency applications. In addition, these third parties may not complete activities on schedule or may not manufacture compounds under GMP conditions. Preclinical studies may not be performed or completed in accordance with good laboratory practices, regulatory requirements or our trial design. If we or our CROs fail to comply with GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the European Medicines Agency ("EMA") or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving any marketing applications. If these third parties or collaborators do not successfully carry out their contractual duties or meet expected deadlines, obtaining regulatory approval for manufacturing and commercialization of our product candidates may be delayed or prevented. We rely substantially on third-party data managers for our clinical trial data. There is no assurance that these third parties will not make errors in the design, management or retention of our data or data systems. There is no assurance that these third parties will pass FDA or regulatory audits, which could delay or prohibit regulatory approval.

Our CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could harm our competitive position. If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Further, switching or adding additional CROs involves additional cost and requires management time and attention. In addition, there is a natural transition period when a new CRO commences work. As a result, delays may occur, which could materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Competition in our targeted market area is intense and this field is characterized by rapid technological change. Therefore, developments by competitors may substantially alter the predicted market or render our product candidates uncompetitive.

We are aware of at least six companies who currently have competing commercial or clinical-stage direct KRAS G12C inhibitor programs: Amgen, Inc., F. Hoffman-LaRoche Ltd., Eli Lilly and Company, Merck & Co., Inc, Novartis AG and Boehringer Ingelheim International GmbH.

There are several immune checkpoint inhibitors currently approved for use as single agents to treat multiple tumor types, including NSCLC. To augment the efficacy of these agents, combination studies are being conducted with a variety of potentially synergistic mechanisms, including inhibitors of CTLA-4, LAG3, TIM-3, TIGIT and CSF-1R, among others. Most of these combination studies are being conducted in patients who are naïve to immune checkpoint inhibitor therapy. Direct mechanistic competitors to sitravatinib in combination with checkpoint inhibitors in NSCLC patients who had previously failed checkpoint inhibitor therapy include *CABOMETYX*® (Exelixis, Inc.) and *LENVIMA*® (Eisai Co., Ltd.), both anti-VEGF agents

that also inhibit other receptor tyrosine kinases. Additionally, there are numerous other potential competitors with kinase inhibitors that are being evaluated in combination with checkpoint inhibitors in NSCLC patients who had previously failed checkpoint inhibitor therapy in earlier lines of treatment.

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. Other important competitors, in addition to those mentioned above, are small and large biotechnology companies, specialty and regional pharmaceutical companies and multinational pharmaceutical companies, including but not limited to AbbVie Inc., AstraZeneca plc, Bristol-Myers Squibb Company, Gilead Sciences, Inc., GlaxoSmithKline plc, Johnson & Johnson, Pfizer Inc., Sanofi S.A., and Takeda Pharmaceutical Co.

Developments by others may render our products or technologies non-competitive or we may not be able to keep pace with technological developments. Our competitors may have developed or may be developing technologies which may be the basis for competitive products. Some of these products may prove to be more effective and less costly than the products developed or being developed by us. Our competitors may obtain regulatory approval for their products more rapidly than we do which may change the standard of care in the indications we are targeting, rendering our technology or products non-competitive. For example, with the recent approval of immunotherapy agents for the treatment of NSCLC and other cancers, the standard of care for the treatment of cancer is evolving and will continue to evolve which could require us to change the design and timelines for our registration trials and may limit the commercial acceptance of our products in the future. Others may develop treatments or cures superior to any therapy we are developing or will develop. Moreover, alternate, less toxic forms of medical treatment may be developed which may be competitive with our products.

Many of the organizations which could be considered to be our competitors have substantially more financial and technical resources, more extensive discovery research, preclinical research and development capabilities and greater manufacturing, marketing, distribution, production and human resources than we do. Many of our current or potential competitors have more experience than we do in research, preclinical testing and clinical trials, drug commercialization, manufacturing and marketing, and in obtaining domestic and foreign regulatory approvals. In addition, failure, unacceptable toxicity, lack of sales or disappointing sales or other issues regarding competitors' products or processes could have a material adverse effect on our product candidates, including our clinical candidates or our lead compounds. Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and brand recognition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA, EMA or other regulatory approval or discovering, developing and commercializing medicines before we do, which would have a material adverse impact on our business.

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

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our trials could reveal a high and unacceptable 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 product candidates for any or all targeted indications. Treatment-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial, or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the product label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;

- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of any product candidate, if approved, and could significantly harm our business, results of operations and prospects.

We are subject to competition for our skilled personnel and may experience challenges in identifying and retaining key personnel that could impair our ability to conduct our operations effectively.

Our future success depends on our ability to retain our executive officers and to attract, retain and motivate qualified personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. Although we have not experienced problems attracting and retaining highly qualified personnel in the recent past, our industry has experienced a high rate of turnover of management personnel in recent years. Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, whose services are critical to the successful implementation of our product candidates, development and regulatory strategies, as well as the management of our financial operations. We are not aware of any present intention of any of these personnel to leave our Company. In order to induce valuable employees to continue their employment with us, we have provided equity awards that vest over time. The value to employees of equity awards that vest over time is significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could harm our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel.

We will continue to experience growth in the number of our employees and the scope of our operations. This growth will place a significant strain on our management, operations and financial resources and we may have difficulty managing this future potential growth. No assurance can be provided that we will be able to attract new employees to assist in our growth. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. We also may employ consultants or part-time and contract employees. There can be no assurance that these individuals are retainable. While we have been able to attract and retain skilled and experienced personnel and consultants in the past, no assurance can be given that we will be able to do so in the future.

We have attempted to obtain FDA approval of adagrasib, sitravatinib or other product candidates through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to await the completion of planned or ongoing clinical trials or conduct additional clinical trials, which could increase the expense of obtaining, and delay the receipt of, necessary approval. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We may in the future seek an accelerated approval for our one or more of our product candidates. Under the accelerated approval program, the FDA may grant accelerated approval to a product candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the

drug's clinical benefit. If such post-approval studies fail to confirm the drug's clinical benefit, the FDA may withdraw its approval of the drug.

Prior to seeking accelerated approval for any of our product candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA for accelerated approval. If we decide to submit an application for accelerated approval for our product candidates, there can be no assurance that such submission or application will be accepted or that review or approval will be granted on a timely basis, or at all. A failure to obtain accelerated approval would result in a longer time period to commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

If we or third parties are unable to successfully develop companion diagnostics for our product candidates, or experience significant delays in doing so, we may not achieve marketing approval or realize the full commercial potential of such product candidates.

A key part of our development strategy for our product candidates is to identify subsets of patients with specific types of tumors that express specific genetic markers. Identification of these patients will require the use and development of companion diagnostics. The FDA generally will either require approval or clearance of the diagnostic at the same time the FDA approves the therapeutic product, or as a post-marketing commitment at the time of the therapeutic product's approval. We do not have experience or capabilities in developing or commercializing diagnostics and plan to rely in large part on third parties to perform these functions.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and will likely require separate regulatory approval prior to commercialization. If we or third parties are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so:

- the development of these product candidates may be delayed because it may be difficult to identify patients for enrollment in our clinical trials in a timely manner;
- these product candidates may not receive marketing approval if their safe and effective use depends on a companion diagnostic; and
- we may not realize the full commercial potential of these product candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients or types of tumors with the specific genetic alterations targeted by these product candidates.

Even if our product candidates and any associated companion diagnostics are approved for marketing, the need for companion diagnostics may slow or limit adoption of our product candidates. Although we believe genetic testing is becoming more prevalent in the diagnosis and treatment of cancer, our product candidates may be perceived negatively compared to alternative treatments that do not require the use of companion diagnostics, either due to the additional cost of the companion diagnostic or the need to complete additional procedures to identify genetic markers prior to administering our product candidates.

If any of these events were to occur, our business and growth prospects would be harmed, possibly materially.

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

From time to time, we may publicly disclose preliminary, interim or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change as patient enrollment and treatment continues and more patient data become available. Adverse differences between previous preliminary or interim data and future interim or final data could significantly harm our business prospects. We may also announce topline data following the completion of a preclinical study or clinical trial, which may be subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim, topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary, interim, or topline data also remain subject to audit and

verification procedures that may result in the final data being materially different from the data we previously published. As a result, preliminary, interim, and topline data should be viewed with caution until the final data are available.

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

The timelines of our clinical trials may be impacted by numerous factors and any delays may adversely affect our ability to execute our current business strategy.

Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. We may experience delays in clinical trials at any stage of development and testing of our product candidates. Our planned clinical trials may not begin on time, have an effective design, enroll a sufficient number of subjects, or be completed on schedule, if at all.

Events which may result in a delay or unsuccessful completion of clinical trials include:

- inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA or other regulatory authorities on final trial design;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in obtaining required institutional review board approval at each site;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- delays caused by subjects dropping out of a trial due to side effects or otherwise;
- delays caused by or relating to the COVID-19 pandemic;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites; and
- delays by our contract manufacturers to produce and deliver a sufficient supply of clinical trial materials.

Furthermore, enrollment may depend on the availability of suitable companion diagnostics to identify genetic markers we are targeting and the capability and willingness of clinical sites to conduct genetic screening of potential patients.

If initiation or completion of any of our clinical trials for our product candidates are delayed for any of the above reasons or for other reasons, our development costs may increase, our approval process could be delayed, any periods after commercial launch and before expiration of patent protection may be reduced and our competitors may have more time to bring products to market before we do. Any of these events could impair the commercial potential of our product candidates and could have a material adverse effect on our business.

If we experience delays or difficulties in the enrollment of patients in clinical trials, those clinical trials could take longer than expected to complete and our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or complete 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. In particular, because we are focused on patients with

specific genetic alterations in some of our trials, our pool of suitable patients may be smaller and more selective and our ability to enroll a sufficient number of suitable patients may be limited or take longer than anticipated. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications, including NSCLC, where we are studying adagrasib in monotherapy and in combination with other anticancer therapies, and sitravatinib in combination with checkpoint inhibitors, or target the same genetic alterations as our product candidates. Therefore, patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment for any of our clinical trials may also be affected by other factors, including without limitation:

- the severity of the disease under investigation
- the frequency of the genetic alteration we are seeking to target in the applicable trial, and the ability to effectively identify such alteration;
- the willingness of clinical sites and principal investigators to subject candidate patients to genetic screening;
- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the availability, effectiveness and safety of other treatment options;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of a sufficient number of clinical trial sites that are willing to comply with the requirements of our clinical protocols.

For example, due to the targeted indications and patient populations we intend to focus on for development of our product candidates, the number of study sites and patient populations available to us may be limited, and therefore enrollment of suitable patients to participate in clinical trials for these product candidates may take longer than would be the case if we were pursuing broader indications or patient populations.

We are and continue to be subject to stringent government regulations concerning the clinical testing of our products. We will also continue to be subject to government regulation of any product that receives regulatory approval.

Numerous statutes and regulations govern human testing and the manufacture and sale of human therapeutic products in the United States, EEA, UK and other countries where we intend to market our products. Such legislation and regulation bears upon, among other things, the approval of trial protocols and human testing, the approval of manufacturing facilities, testing procedures, CMC and controlled research, the review and approval of manufacturing, preclinical and clinical data prior to marketing approval, including adherence to GMP during production and storage, and marketing activities including advertising and labeling.

Clinical trials may be delayed or suspended at any time by us or by the FDA or other similar regulatory authorities if it is determined at any time that patients may be or are being exposed to unacceptable health risks, including the risk of death, or if compounds are not manufactured under acceptable GMP conditions or with acceptable quality. Current regulations relating to regulatory approval may change or become more stringent. The agencies may also require additional trials be run in order to provide additional information regarding the safety, efficacy or equivalency of any product candidate for which we seek regulatory approval.

Moreover, any regulatory approval of a drug which is eventually obtained may entail limitations on the indicated uses for which that drug may be marketed or on the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with GMPs and GCPs for any clinical trials that we conduct post-approval. In addition, if the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. For example, prescription drugs may be promoted only for the

approved indications in accordance with 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. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments, but the FDA does restrict manufacturer's communications on the subject of off-label use of their products. Furthermore, product approvals may be withdrawn or limited in some way if problems occur following initial marketing or if compliance with regulatory standards is not maintained. Similar restrictions are imposed in foreign markets. Regulatory agencies could become more risk averse to any side effects or set higher standards of safety and efficacy prior to reviewing or approving a product. This could result in a product not being approved.

If we, or any future marketing collaborators or contract manufacturers, fail to comply with applicable regulatory requirements, we may be subject to sanctions including fines, product recalls or seizures and related publicity requirements, injunctions, total or partial suspension of production, civil penalties, suspension or withdrawals of previously granted regulatory approvals, warning or untitled letters, refusal to approve pending applications for marketing approval of new products or of supplements to approved applications, import or export bans or restrictions, and criminal prosecution and penalties. Any of these penalties could delay or prevent the promotion, marketing or sale of our products and product candidates.

The FDA's policies, and policies of comparable foreign regulatory authorities, 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 to adopt new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

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

We received breakthrough therapy designation for adagrasib for the treatment of patients with NSCLC with the KRAS G12C mutation following prior systemic therapy, and we may seek breakthrough therapy designation for future product candidates. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug, or biologic, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, sponsors may obtain more frequent interaction with and communication with the FDA to help to identify the most efficient path for clinical development.

The receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval and does not change the approval standards or assure ultimate approval by the FDA. In addition, the FDA may later decide that the product no longer meets the conditions for qualification. As such, there can be no assurance that even if we do receive breakthrough therapy designation, that such designation will have a material impact on our development program.

The failure to (i) maintain the BeiGene Agreement or the failure of BeiGene to perform its obligations under the BeiGene Agreement and/or (ii) maintain the Zai Agreement or the failure of Zai to perform its obligations under the Zai Agreement, could, in each case, negatively impact our business.

Pursuant to the terms of the BeiGene Agreement, we granted to BeiGene an exclusive license to develop, manufacture and commercialize sitravatinib in the BeiGene Licensed Territory. Consequently, our ability to generate any revenues from sitravatinib in the BeiGene Licensed Territory depends on our ability to maintain our collaboration with BeiGene. We have limited control over the amount and timing of resources that BeiGene will dedicate to these efforts.

Pursuant to the terms of the Zai Agreement, we granted Zai the right to research, develop, manufacture and exclusively commercialize adagrasib in the Zai Licensed Territory. Consequently, our ability to generate any revenues from adagrasib in the Zai Licensed Territory depends on our ability to maintain our collaboration with Zai. We have limited control over the amount and timing of resources that Zai will dedicate to these efforts.

We are subject to a number of other risks associated with our dependence on the BeiGene Agreement with respect to sitravatinib in the BeiGene Licensed Territory and the Zai Agreement with respect to adagrasib in the Zai Licensed Territory, including:

- BeiGene or Zai may not comply with applicable regulatory guidelines with respect to developing, manufacturing or commercializing sitravatinib or adagrasib, respectively, which could adversely impact sales or future development of sitravatinib in or outside of the BeiGene Licensed Territory or adagrasib in or outside of the Zai Licensed Territory, respectively;

- There may be disputes between us and BeiGene or Zai, including disagreements regarding the BeiGene Agreement or the Zai Agreement, respectively; and

- BeiGene or Zai may not properly 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 intellectual property rights or expose us to potential litigation.

Each of the BeiGene Agreement and Zai Agreement are also subject to early termination, including through BeiGene's and Zai's (as applicable) right to terminate without cause upon advance notice to us. If the agreement is terminated early, we may not be able to find another collaborator for the further development and commercialization of (i) with respect to BeiGene, sitravatinib in the BeiGene Licensed Territory and/or (ii) with respect to Zai, adagrasib in the Zai Licensed Territory, in each case on acceptable terms, or at all, and we may be unable to pursue continued development and commercialization of sitravatinib in the BeiGene Licensed Territory and/or adagrasib in the Zai Licensed Territory on our own.

If we fail to obtain coverage and adequate reimbursement for our products, our revenue-generating ability will be diminished and there is no assurance that the anticipated market for our products will be sustained.

We believe that there will be many different applications for products successfully derived from our technologies and that the anticipated market for products under development will continue to expand. However, due to competition from existing or new products and the yet-to-be established commercial viability of our products, no assurance can be given that these beliefs will prove to be correct. Physicians, patients, formularies, payors or the medical community in general may not accept or utilize any products that we or our collaborative partners may develop. Other drugs may be approved during our clinical testing which could change the accepted treatments for the disease targeted and make our product candidates obsolete.

Our and our collaborators' ability to commercialize our products successfully will depend, in part, on the extent to which coverage and adequate reimbursement for such products and related treatments will be available from governmental health payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers, managed care plans and other organizations. No assurance can be given that third-party payor coverage and adequate reimbursement will be available that will allow us to maintain price levels sufficient for the realization of an appropriate return on our investment in product development.

Coverage and adequate reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and private health insurers, managed care plans and other organizations is critical to new product acceptance. There is no uniform coverage and reimbursement policy among third-party payors in the United States; however, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Additionally, coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Even if we obtain coverage for our product candidates, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates.

Additionally, we or our collaborators may develop companion diagnostic tests for use with our product candidates. We or our collaborators will be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our product candidates, once approved. While we have not yet developed any companion diagnostic test for use with our product candidates, if we do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our product candidates.

In the United States and in many other countries, pricing and/or profitability of some or all prescription pharmaceuticals and biopharmaceuticals are subject to varying degrees of government control. In the United States, there has recently been increased government enforcement and government and payor scrutiny relating to drug pricing and price increases. For example, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal

level, the Trump administration used several means to propose implementing drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, President Trump signed several executive orders aimed at lowering drug prices. As a result, the FDA released a final rule and guidance in September 2020 providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the U.S. Department of Health and Human Services ("HHS") finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, Centers for Medicare & Medicaid Services ("CMS") issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinded the Most Favored Nation model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of other reform initiatives. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. These changes may adversely impact the prices we or our future collaborators may charge for our products candidates, if commercialized.

Outside of the United States, the successful commercialization of our products will depend largely on obtaining and maintaining government coverage, because in many countries, patients are unlikely to use prescription drugs that are not covered by their government healthcare programs. Negotiating coverage and reimbursement with governmental authorities can delay commercialization by 12 months or more. Coverage and reimbursement policies may adversely affect our ability to sell our products on a profitable basis. In many international markets, governments control the prices of prescription pharmaceuticals, including through the implementation of reference pricing, price cuts, rebates, revenue-related taxes and profit control, and we expect prices of prescription pharmaceuticals to decline over the life of the product or as volumes increase.

Healthcare reform and controls on healthcare spending may limit the price we charge for any products and the amounts thereof that we can sell. In particular, in the United States, the federal government and private insurers have changed, and have considered ways to change, the manner in which healthcare services are provided. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, "ACA") became law in the United States. With respect to pharmaceutical products, the ACA, among other things, expanded and increased industry rebates for drugs covered by Medicaid and made changes to the coverage requirements under Medicare Part D, Medicare's prescription drug benefits program. Some of the provisions of the ACA have yet to be fully implemented, and there have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, on June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the health reform measures of the Biden administration will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013 and, as amended by subsequent legislation including the Bipartisan Budget Act of 2018, will stay in effect through 2030, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. Under current legislation, the actual reduction in

Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which 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. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

We anticipate that the ACA, as well as alternative or replacement healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the reimbursement we may receive for any approved product. It is possible that additional governmental action will be taken in response to the COVID-19 pandemic. Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives.

In addition, levels of reimbursement may be impacted by other current and future legislation, regulation or reimbursement policies of third-party payors in a manner that may harm the demand and reimbursement available for our products, including for companion diagnostics for our products, which in turn, could harm our future product pricing and sales. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Our potential future relationships with customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

As a clinical-stage company that could potentially become a commercial pharmaceutical company, even though we will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights will be applicable to our business. Our potential future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, which may constrain the business or financial arrangements and relationships through which we may sell, market and distribute any drugs for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which 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, or in return for, either the referral of an individual for, or the purchase, order, lease, furnishing, prescribing or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs, such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The ACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate, in order to commit a violation;

- federal civil and criminal false claims laws, including the federal False Claims Act which can be enforced by private individuals on behalf of the government through civil whistleblower or qui tam actions, and civil monetary penalty laws prohibit individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, 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. Entities can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers, promoting a product off-label, or for providing medically unnecessary services or items. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying,

concealing or covering up a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of or payment for healthcare benefits, items or services;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, which impose obligations on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as individuals and entities that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, known as business associates, as well as their covered subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in U.S. federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal Open Payments program, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to "payments or other transfers of value" made to physicians, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, other health care professionals (such as physician assistances and nurse practitioners), and teaching hospitals and ownership and investment interests held by such healthcare professionals and their immediate family members; and

- analogous state and foreign 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; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. To the extent that any of our product candidates is ultimately sold in countries other than the United States, we may be subject to similar laws and regulations in those countries. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, 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, exclusion from participation in government healthcare programs, and the curtailment or restructuring of our operations, any of which could have a material adverse effect on our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including any of our collaborators, is found not to be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusion from participation in government healthcare programs, which could also materially affect our business.

We are subject to stringent and changing obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations, reputational harm, and other adverse business impacts.

In the ordinary course of business, we process personal data and other sensitive data, including proprietary and confidential business data, trade secrets, intellectual property, data we collect about trial participants in connection with clinical trials, and sensitive third-party data. Our data processing activities also subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts, and other obligations that govern the processing of personal data by us and on our behalf.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, and consumer protection laws. The California Consumer Privacy Act of 2018 ("CCPA") imposes obligations on businesses to which it applies. These obligations include, without limitation, providing specific disclosures in privacy notices, affording California residents certain rights related to their personal data, and requiring businesses subject to the CCPA to implement certain measures to effectuate California residents' personal

data rights. The CCPA allows for statutory fines for noncompliance (up to $7,500 per violation). In addition, it is anticipated that the California Privacy Rights Act of 2020 ("CPRA"), effective January 1, 2023, will expand the CCPA. For example, the CPRA establishes a new California Privacy Protection Agency to implement and enforce the CCPA (as amended), which could increase the risk of an enforcement action. Other states have enacted data privacy laws. For example, Virginia passed its Consumer Data Protection Act, and Colorado passed the Colorado Privacy Act, both of which differ from the CPRA and become effective in 2023.

Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, the European Union's General Data Protection Regulation ("EU GDPR") and the UK's GDPR ("UK GDPR") impose strict requirements for processing the personal data of individuals located, respectively, within the EEA and the UK. For example, under the EU GDPR, government regulators may impose temporary or definitive bans on data processing, as well as fines up to 20 million euros or 4% of the annual global revenue, whichever is greater. Further, individuals may initiate litigation related to our processing of their personal data.

Certain jurisdictions have enacted data localization laws and cross-border personal data transfers laws. For example, absent appropriate safeguards or other circumstances, the EU GDPR generally restricts the transfer of personal data to countries outside of the EEA, such as the United States, which the European Commission does not consider to provide an adequate level of personal data protection. The European Commission released a set of "Standard Contractual Clauses" that are designed to be a valid mechanism by which entities can transfer personal data out of the EEA to jurisdictions that the European Commission has not found to provide an adequate level of protection. Currently, these Standard Contractual clauses are a valid mechanism to transfer personal data outside of the EEA. The Standard Contractual Clauses, however, require parties that rely upon that legal mechanism to comply with additional obligations such as conducting transfer impact assessments to determine whether additional security measures are necessary to protect the at-issue personal data. Moreover, due to potential legal challenges, there exists some uncertainty regarding whether the Standard Contractual Clauses will remain a valid mechanism for personal data transfers out of the EEA. In addition, laws in Switzerland and the UK similarly restrict personal data transfers outside of those jurisdictions to countries such as the United States that do not provide an adequate level of personal data protection. In addition to European restrictions on cross-border personal data transfers, other jurisdictions have enacted or are considering similar cross-border personal data transfer laws and local personal data residency laws, any of which could increase the cost and complexity of doing business. If we cannot implement a valid compliance mechanism for cross-border personal data transfers, we may face increased exposure to regulatory actions, substantial fines, and injunctions against processing or transferring personal data from Europe or elsewhere. Inability to import personal data to the United States may significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties subject to European and other data protection laws or requiring us to increase our personal data processing capabilities in Europe and/or elsewhere at significant expense.

Our obligations related to data privacy and security are quickly changing in an increasingly stringent fashion. These obligations may be subject to differing applications and interpretations, which may be inconsistent among jurisdictions or in conflict. Preparing for and complying with these obligations requires us to devote significant resources (including, without limitation, financial and time-related resources). These obligations may necessitate changes to our information technologies, systems, and practices and those of any third parties that process personal data on our behalf. In addition, these obligations may even require us to change to our business model. Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third-parties upon whom we rely may fail to comply such obligations that impacts our compliance posture.

If we fail, or are perceived to have failed, to address or comply with data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions (e.g., investigations, fines, penalties, audits, inspections and similar); litigation (including class-related claims); additional reporting requirements and/or oversight; bans on processing personal data; and orders to destroy or not use personal data. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including clinical trials); inability to process personal data or operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring our operations.

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

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

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

We may become subject to the risk of product liability claims.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. Human therapeutic products involve the risk of product liability claims and associated adverse publicity. Currently, the principal risks we face relate to patients in our clinical trials, who may suffer unintended consequences. Claims might be made by patients, healthcare providers, pharmaceutical companies or others. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates, if approved. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue from product sales; and
- the inability to commercialize any of our product candidates, if approved.

We may not have or be able to obtain or maintain sufficient and affordable insurance coverage, and without sufficient coverage any claim brought against us could have a materially adverse effect on our business, financial condition or results of operations. We run clinical trials through investigators that could be negligent through no fault of our own and which could affect patients, cause potential liability claims against us and result in delayed or stopped clinical trials. We are required in many cases by contractual obligations to indemnify collaborators, partners, third-party contractors, clinical investigators and institutions. These indemnifications could result in a material impact due to product liability claims against us and/or these groups. We currently carry $10 million in product liability insurance, which we believe is appropriate for our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance

coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our business involves the controlled use of hazardous materials and as such we are subject to environmental and occupational safety laws. Continued compliance with these laws may incur substantial costs and failure to maintain compliance could result in liability for damages that may exceed our resources.

Our preclinical research, manufacturing and development processes involve the controlled use of hazardous and radioactive materials. We are subject to federal, local and foreign laws and regulations governing the use, manufacture, storage, handling and disposal of such materials and certain waste products. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. The risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result, and any such liability could exceed our resources. We may not be adequately insured against this type of liability. We may be required to incur significant costs to comply with environmental laws and regulations in the future, and our operations, business or assets may be materially adversely affected by current or future environmental laws or regulations.

We may have to dedicate resources to the settlement of litigation.

Securities legislation in the United States, Canada and other countries makes it relatively easy for shareholders to sue. This could lead to frivolous lawsuits which could take substantial time, money, resources and attention or force us to settle such claims rather than seek adequate judicial remedy or dismissal of such claims.

If we are required to defend patent infringement actions brought by third parties, or if we sue to protect our own patent rights or otherwise to protect our proprietary information and to prevent its disclosure, or if we are involved in other litigation, whether as a plaintiff or defendant, we may be required to pay substantial litigation costs and managerial attention may be diverted from business operations even if the outcome is in our favor. If we are required to defend our patents or trademarks against infringement by third parties, we may be required to pay substantial litigation costs and managerial attention and financial resources may be diverted from our research and development operations even if the outcome is in our favor.

If our information technology systems or data is or were compromised, we could experience adverse impacts resulting from such compromise, including, but not limited to interruptions to our operations such as our clinical trials, claims that we breached our data protection obligations, and harm to our reputation.

In the ordinary course of our business, we may collect, store, use, transmit, disclose or otherwise process proprietary, confidential, and sensitive data, including personal data (such as health-related data), intellectual property, and trade secrets. We are dependent upon our own or third-party information technology systems, infrastructure and data, to operate our business.

Cyberattacks, malicious internet-based activity, and online and offline fraud are prevalent and continue to increase. These threats are becoming increasingly difficult to detect. These threats come from a variety of sources. In addition to traditional computer "hackers," threat actors, personnel misconduct or error (such as theft or misuse), sophisticated nation-state and nation-state supported actors now engage in attacks. We may be subject to a variety of evolving threats, including but not limited to social engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing), ransomware attacks, supply-chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, and other similar threats. Ransomware attacks, including those perpetrated by organized criminal threat actors, nation-states, and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting payments. Similarly, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems (including our products/operational activities) or the third-party information technology systems that support us and our operational activities. The COVID-19 pandemic and our remote workforce poses increased risks to our information technology systems and data, as more of our employees work from home, utilizing network connections outside our premises.

Any of the previously identified or similar threats could cause a security incident. A security incident could result in unauthorized, unlawful or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of or access to data. A security incident could disrupt our (and third parties upon whom we rely) ability to provide our products. Any system failure, accident or security breach that causes interruptions in our own, in collaborators' or in third-party service vendors' operations could result in a material disruption of our drug discovery and development programs or theft of our intellectual property. We may expend significant resources or modify our business activities (including our clinical trial activities) in an effort to protect against security incidents.

Certain data privacy and security obligations may require us to implement and maintain specific security measures, industry-standard or reasonable security measures to protect our information technology systems and data.

We devote considerable internal and external resources to implementing security measures to protect our systems, customers, and users, but these security measures cannot provide absolute security. We may be unable to detect vulnerabilities in our information technology systems (including our products) because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security incident has occurred. Despite our efforts to identify and remediate vulnerabilities, if any, in our information technology systems (including our products), our efforts may not be successful. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities.

Potential breaches of our security measures and the accidental loss, inadvertent disclosure, or unapproved dissemination of proprietary information, intellectual property, or sensitive or confidential data about us, our employees, or our customers or users (including the potential loss or disclosure of such information or data as a result of employee error or other employee actions or inactions, hacking, fraud, social engineering, or other forms of deception) could expose us, our customers, or the individuals affected to a risk of loss or misuse of this information, result in litigation and potential liability for us, damage our brand and reputation, or otherwise materially adversely affect our business, results of operations, and financial condition. Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosures or the failure to comply with such requirements, could lead to adverse impacts.

In addition, the cost and operational consequences of implementing further data protection measures could be significant and theft of our intellectual property or proprietary business information could require substantial expenditures to remedy. Further, we cannot be certain that (a) our liability insurance will be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches; (b) such coverage will cover any indemnification claims against us relating to any incident, will continue to be available to us on economically reasonable terms, or at all; or (c) any insurer will not deny coverage as to any future claim. The successful assertion of one or more large claims against us that exceed available insurance coverage, or the occurrence of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could adversely affect our reputation, business, financial condition and results of operations.

In addition, we rely upon third-party contractors and service providers for the hosting, support and/or maintenance of some aspects of our computer hardware, computer software and telecommunications systems. Failure of those contractors and service providers to provide systems and services of a suitable quality and within acceptable timeframes may cause the delay or failure of our development programs, or loss of confidential or proprietary information. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability, our drug discovery and development programs may be adversely affected and the further development of our product candidates may be delayed. Furthermore, such disruptions or security breaches could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to litigation or other liability under laws and regulations that protect personal data, any of which could disrupt our business and/or result in increased costs.

Risks Related to Our Financial Position and Capital Requirements

We will require additional financing and may be unable to raise sufficient capital, which could lead us to delay, reduce or abandon development programs or commercialization.

Our operations have consumed substantial amounts of cash since inception. Our research and development expenses were $508.6 million, $299.3 million, and $182.9 million for the years ended December 31, 2021, 2020 and 2019, respectively. Our net loss for the years ended December 31, 2021, 2020, and 2019 were $581.8 million, $357.9 million, and $213.3 million respectively. As of December 31, 2021, we had an accumulated deficit of $1.7 billion. We may require substantial additional

capital to pursue additional clinical development for our lead clinical programs, including conducting late-stage clinical trials, manufacturing clinical supplies and developing other assets in our pipeline, and, if we are successful, to commercialize any of our current product candidates. If the UFDA or any foreign regulatory agency, such as the EMA requires that we perform studies or trials in addition to those that we currently anticipate with respect to the development of our product candidates, or repeat studies or trials, or if our clinical trials are otherwise delayed or disrupted due to the COVID-19 pandemic or otherwise, our expenses would further increase beyond what we currently expect. We may not be able to adequately finance our development programs, which could limit our ability to move our programs forward in a timely and satisfactory manner or require us to abandon the programs, any of which would harm our business, financial condition and results of operations. Because successful development of our product candidates is uncertain, we are unable to accurately estimate the actual funds we will require to complete research and development and commercialize our product candidates.

If, at any point, we are unable to obtain funding from equity offerings or debt financings on a timely basis, we may be required to (1) seek additional collaborators for one or more of our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; (2) relinquish or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves; or (3) significantly curtail one or more of our research or development programs or cease operations altogether.

We may not generate revenue from sales of products. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if any of our product candidates, if approved, fail to achieve market acceptance, we may never become profitable. If one or more of our product candidates is approved for commercial sale and we retain commercial rights, we anticipate incurring significant costs associated with commercializing any such approved product candidate. Therefore, even if we are able to generate revenue from the sale of any approved product, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our ability to generate future revenue from product sales depends heavily on our success in:

- completing development and clinical trial programs for our product candidates;
- maintaining existing collaboration and licensing agreements and entering into additional ones;
- seeking and obtaining marketing approvals for any product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties;
- successfully commercializing any product candidates for which marketing approval is obtained; and
- successfully establishing a sales force and marketing and distribution infrastructure.

We are a clinical-stage company with no approved products and no product revenue. Consequently, we expect that our financial and operating results will vary significantly from period to period.

We are a clinical-stage company that has incurred losses since its inception and expect to continue to incur substantial losses in the foreseeable future. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of uncertainty.

Our actual financial condition and operating results have varied significantly in the past and are expected to continue to fluctuate significantly from quarter-to-quarter or year-to-year due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include:

- the success of our clinical trials through all phases of clinical development;
- delays in the commencement, enrollment and timing of clinical trials;
- delays due to force majeure;
- our ability to secure and maintain collaborations, licensing or other arrangements for the future development and/or commercialization of our product candidates, as well as the terms of those arrangements;
- our ability to obtain, as well as the timeliness of obtaining, additional funding to develop our product candidates;

- the results of clinical trials or marketing applications for product candidates that may compete with our product candidates;
- competition from existing products or new products that may receive marketing approval;
- potential side effects of our product candidates that could delay or prevent approval or cause an approved drug to be taken off the market;
- any delays in regulatory review and approval of our clinical development plans or product candidates;
- our ability to identify and develop additional product candidates;
- the ability of patients or healthcare providers to obtain coverage or sufficient reimbursement for our products;
- our ability, and the ability of third parties such as CROs to adhere to clinical study and other regulatory requirements;
- the ability of third-party manufacturers to manufacture our product candidates and key ingredients needed to conduct clinical trials and, if approved, successfully commercialize our products;
- the costs to us, and our ability as well as the ability of any third-party collaborators, to obtain, maintain and protect our intellectual property rights;
- costs related to and outcomes of potential intellectual property litigation;
- our ability to adequately support future growth;
- our ability to attract and retain key personnel to manage our business effectively; and
- our ability to build our finance infrastructure and, to the extent required, improve our accounting systems and controls.

Accordingly, the likelihood of our success must be evaluated in light of many potential challenges and variables associated with a clinical-stage company, many of which are outside of our control, and past operating or financial results should not be relied on as an indication of future results. Fluctuations in our operating and financial results could cause our share price to decline. It is possible that in some future periods, our operating results will be above or below the expectations of securities analysts or investors, which could also cause our share price to decline.

Raising additional funds through debt or equity financing will be dilutive and raising funds through licensing agreements may be dilutive, restrict operations or relinquish proprietary rights.

To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of those securities could result in substantial dilution for our current shareholders and the terms may include liquidation or other preferences that adversely affect the rights of our current shareholders. Existing shareholders may not agree with our financing plans or the terms of such financings. In addition, the COVID-19 pandemic continues to rapidly evolve and may result in a significant disruption of global financial markets. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from the pandemic. If the disruption persists and deepens, we could experience an inability to access additional capital, which could in the future negatively affect our capacity to fund research and development programs, including discovery research, preclinical and clinical development activities. Moreover, the incurrence of debt financing could result in a substantial portion of our operating cash flow being dedicated to the payment of principal and interest on such indebtedness and could impose restrictions on our operations. In addition, if we raise additional funds through future collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to our products or proprietary technologies, or to grant licenses on terms that are not favorable to us. Additional funding may not be available to us on acceptable terms, or at all.

Our ability to use our U.S. net operating loss carryforwards and certain other tax attributes may be limited.

Our U.S. federal net operating loss ("NOL"), carryforwards generated in tax years beginning before January 1, 2018, are only permitted to be carried forward for 20 years under applicable U.S. tax law. Under current law, our federal NOLs generated in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such

federal NOLs in tax years beginning after December 31, 2020, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to federal tax laws. In addition, under Sections 382 and 383 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change U.S. tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited.

As a result, our NOL carryforwards generated in tax years beginning before January 1, 2018 may expire prior to being used, and the deductibility of our NOL carryforwards generated in tax years beginning after December 31, 2017 will be subject to a percentage limitation, in taxable years beginning after December 31, 2020. In addition, we believe that we have in the past undergone, and in the future it is possible we may undergo, additional ownership changes that could limit our ability to use all of our pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs or other tax attributes is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Risks Related to Our Intellectual Property

We may not obtain adequate protection for our products and/or product candidates through patents and other intellectual property rights and as such, our competitive advantage in the marketplace may be compromised.

Our success depends to a significant degree upon on our ability to develop, secure and maintain intellectual property rights to our proprietary products, to operate without infringing on the proprietary rights of others or having third parties circumvent the rights that we own or license. We have filed and are actively pursuing patent applications in the United States, Japan, Europe and other major markets via the Patent Cooperation Treaty or directly in countries of interest. However, we may not receive issued patents on any of our pending patent applications in these countries and we may not be able to obtain, maintain or enforce our patents and other intellectual property rights which could impact our ability to compete effectively. We cannot be certain that the U.S. Patent and Trademark Office, courts in the United States or the patent offices and courts in foreign countries will consider the claims in our patents and applications covering any of our products in development as patentable. In addition, the scope of any of our issued patents may not be sufficiently broad to provide us with a competitive advantage. Furthermore, other parties may successfully challenge, invalidate or circumvent our issued patents or patents licensed to us so that our patent rights do not create an effective competitive barrier. Our method-of-use patents protect the use of a product only for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products off-label. Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent, including through legal action. Further, if the patent applications we own or license with respect to our programs, product candidates and/or companion diagnostic fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future products.

We may file applications for trademark registrations in connection with our product candidates in various jurisdictions, including the United States. No assurance can be given that any of our trademark applications will be registered in the United States or elsewhere, or that the use of any registered or unregistered trademarks will confer a competitive advantage in the marketplace. Furthermore, even if we are successful in our trademark registrations, the FDA and regulatory authorities in other countries have their own process for drug nomenclature and their own views concerning appropriate proprietary names. The loss, abandonment, or cancellation of any of our trademarks or trademark applications could negatively affect the success of the product candidates to which they relate.

Moreover, some of our know-how and technology which is not patented or not patentable may constitute trade secrets. Therefore, we require our consultants, advisors and collaborators to enter into confidentiality agreements and our employees to enter into invention and non-disclosure agreements. However, no assurance can be given that such agreements will provide for a meaningful protection of our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure of information. Furthermore, we cannot provide assurance that any of our employees, consultants, contract personnel or collaborators, either accidentally or through willful misconduct, will not cause serious negative impact to our programs and/or our strategy. All of our employees have signed confidentiality agreements, but there can be no assurance that they will not inadvertently or through their misconduct give trade secrets away.

Third-party patents or intellectual property infringement claims may result in a reduction in the scope of our patent protection and competitive exclusivity with respect to our product candidates. Patent litigation, including defense against third-party intellectual property claims, may result in us incurring substantial costs.

Our patents may be challenged by third parties from time to time, and we will have to defend our intellectual property rights. If we are involved in an intellectual property dispute, we may need to litigate to defend our rights or assert them against others. Disputes can involve arbitration, litigation or proceedings declared by the United States Patent and Trademark Office or the International Trade Commission or foreign patent authorities. These disputes can result in the successful invalidation of our patents or reduction in scope so that our patent rights do not create an effective competitive barrier. 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.

It is possible that third parties will circumvent our patents by means of alternate designs or processes or file applications or be granted patents that would block or hamper our efforts. Further, a third party may claim that our products or technology infringe its patents or other intellectual property rights, as such we may have to discontinue or alter our products and processes, pay license fees or cease certain activities. We may not be able to obtain a license to needed intellectual property on favorable terms, if at all. There are many patents issued or applied for in the biotechnology industry, and we may not be aware of patents or patent applications held by others that relate to our business. This is especially true since patent applications in the U.S. and elsewhere are filed confidentially for the first 18 months. Moreover, the validity and breadth of biotechnology patents involve complex legal and factual questions for which important legal issues remain.

Maintaining our patents and applications requires timely payment of fees and other associated costs in the countries of filing, and we could inadvertently abandon a patent or patent application (or trademark or trademark application) due to non-payment of fees, or as a result of a failure to comply with filing deadlines or other requirements of the prosecution process, resulting in the loss of protection of certain intellectual property rights in a certain country. Alternatively, we, our collaborators or our patent counsel may take action resulting in a patent or patent application becoming abandoned which may not be able to be reinstated, or if reinstated, may suffer negative patent term adjustments. Any of these outcomes could hurt our ability to gain full patent protection for our products. Registered trademarks and/or applications for trademark registrations in the United States that belong to us are subject to similar risks as described above for patents and patent applications.

Third parties may seek to obtain approval of a generic version of approved products. Defense against entry of a generic product may result in us incurring substantial costs and ultimate failure to prevail against approval of a generic product could result in a substantial loss of market share and profits.

Even if we are successful in obtaining regulatory approval to sell any of our product candidates in one or more countries, we cannot be certain that our patents and other intellectual property rights will ultimately prevent approval during the patent term of generic products developed and commercialized by third parties. A generic manufacturer may seek approval of a generic version of any of our products in the United States by filing an Abbreviated New Drug Application with the FDA, asserting that our patents are invalid and/or unenforceable to maintain market exclusivity for any of our products, if approved. We cannot predict if, or when, one or more generic manufacturers may attempt to seek regulatory approval for a generic version of any of our products, if approved. There is no assurance that we will ultimately be successful in a court of law to prevent entry of a generic version of any of our products during the applicable patent term and we may incur substantial costs defending our patents and intellectual property rights. An inability to stop a generic manufacturer from selling a generic version of our products could result in a substantial loss of market share and profits or even preclude the ability to continue to commercialize any of our products, if approved.

Risks Related to Our Shares of Common Stock

Our principal shareholders control the majority of our shares, and their actions may significantly influence matters submitted to our shareholders for approval and our share price.

Based on the information available to us as of December 31, 2021, our shareholders and their affiliates who owned more than 5% of our outstanding common stock collectively owned 39% of our outstanding common stock. Boxer Capital, LLC ("Boxer Capital") and its affiliates collectively own 10% of our outstanding common stock. In addition, in conjunction with certain financing transactions, we granted Boxer Capital the right to nominate a member of our Board of Directors and the right to appoint an observer on our Board of Directors. In addition, we granted Baker Brothers Advisors, LLC ("Baker

Brothers") the right to appoint an observer on our Board of Directors. Collectively Baker Brothers and Boxer Capital may have significant influence over matters submitted to our shareholders for approval, including the election and removal of directors and the approval of any merger, consolidation, or sale of all or substantially all of our assets. Furthermore, if Boxer Capital, Baker Brothers, or any other of our major shareholders determine to exit from the industry or from their holdings in us, for whatever reason, the impact on our share price could be detrimental over a prolonged period of time.

Our bylaws, as amended (our "Bylaws") provide that the Court of Chancery of the State of Delaware is the exclusive forum for certain disputes between us and our shareholders, which could limit our shareholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our Bylaws provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to our company or our shareholders, (iii) any action asserting a claim against our company arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or Bylaws, or (iv) any action asserting a claim against our company governed by the internal affairs doctrine. This choice of forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Act of 1933, as amended, or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

This choice of forum provision may limit a shareholder's ability to bring certain claims in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or shareholders, which may discourage lawsuits with respect to such claims, although our shareholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. If a court were to find this choice of forum provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, would be our shareholders' only source of gain.

We have never declared or paid any cash dividends on our common shares, and we currently expect that earnings, if any, and cash flow will primarily be retained and used in our operations, including servicing any debt obligations we may have now or in the future. Accordingly, although we do not anticipate paying any dividends in the foreseeable future, we may not be able to generate sufficient cash flow in order to allow us to pay future dividends on, or make any distributions with respect to our common stock. As a result, capital appreciation, if any, of our common stock would be our shareholders' sole source of gain on their investment in our common stock for the foreseeable future.

General Risks

As a public company in the United States, we incur significant legal and financial compliance costs and we are subject to the Sarbanes-Oxley Act. We can provide no assurance that we will, at all times, in the future be able to report that our internal controls over financial reporting are effective.

Companies that file reports with the SEC, including us, are subject to the requirements of Section 404 of the Sarbanes-Oxley Act of 2002. Section 404 requires management to establish and maintain a system of internal control over financial reporting, and annual reports on Form 10-K filed under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), must contain a report from management assessing the effectiveness of a company's internal control over financial reporting. Ensuring that we have adequate internal financial and accounting controls and procedures in place to produce accurate financial statements on a timely basis remains a costly and time-consuming effort that needs to be re-evaluated frequently. Failure on our part to have effective internal financial and accounting controls would cause our financial reporting to be unreliable, could have a material adverse effect on our business, operating results, and financial condition, and could cause our stock price to decline as a result.

If we cannot conclude that we have effective internal control over our financial reporting, or if our independent registered public accounting firm is unable to provide an unqualified opinion regarding the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements. Failure to comply with reporting requirements could also subject us to sanctions and/or investigations by the SEC, The Nasdaq Global Select Market or other regulatory authorities.

Furthermore, shareholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, any new regulations or disclosure obligations may increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

Our share price is volatile and may be influenced by numerous factors that are beyond our control.

A low share price and low market valuation may make it difficult to raise sufficient additional cash due to the significant dilution to current shareholders. Market prices for shares of biotechnology and biopharmaceutical companies such as ours are often volatile. Factors such as clinical and regulatory developments regarding our products or processes, developments regarding potential or future third-party collaborators, announcements of technological innovations, new commercial products, patents, the development of proprietary rights by us or by others or any litigation relating to these rights, regulatory actions, general conditions in the biotechnology and pharmaceutical industries, failure to meet analysts' expectations, publications, financial results or public concern over the safety of biopharmaceutical and biotechnological products, economic conditions in the United States and other countries, terrorism and other factors could have a significant effect on the share price for our shares of common stock. Any setback or delay in the clinical development of our programs could result in a significant decrease in our share price. In recent years the stock of other biotechnology and biopharmaceutical companies has experienced extreme price fluctuations that have been unrelated to the operating performance of the affected companies. There can be no assurance that the market price of our shares of common stock will not experience significant fluctuations in the future, including fluctuations that are unrelated to our performance. These fluctuations may result due to macroeconomic and world events, national or local events, general perception of the biotechnology industry or to a lack of liquidity. In addition, other biotechnology companies' or our competitors' programs could have positive or negative results that impact their stock prices and their results or experience stock price fluctuations that could have a positive or negative impact on our stock price, regardless whether such impact is direct or not.

Shareholders may not agree with our business, scientific, clinical and financial strategy, including additional dilutive financings, and may decide to sell their shares or vote against such proposals. Such actions could materially impact our stock price. In addition, portfolio managers of funds or large investors can change or change their view on us and decide to sell our shares. These actions could have a material impact on our stock price. In order to complete a financing, or for other business reasons, we may elect to consolidate our shares of common stock. Investors may not agree with these actions and may sell our shares. We may have little or no ability to impact or alter such decisions.

Changes in tax laws or regulations that are applied adversely to us or our future potential customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. The Biden Administration and Congress have proposed various U.S. federal tax law changes, which if enacted could have a material impact on our business, cash flows, financial condition or results of operations. Furthermore, it is uncertain if and to what extent various states will conform federal tax laws. Future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our shareholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our shareholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing shareholders, and new investors could gain rights superior to our existing shareholders.

Pursuant to our 2013 Equity Incentive Plan and our 2013 Employee Stock Purchase Plan (the "ESPP"), our management is authorized to grant stock options, restricted stock units and other equity-based awards to our employees, directors and consultants, and to sell our common stock to our employees, respectively. Pursuant to the inducement plan, the

Board of Directors is authorized to grant stock options, restricted stock units and other equity-based awards to new employees who satisfy the standards for inducement grants in accordance with the Nasdaq Stock Market LLC listing rules. Any increase in the number of shares outstanding as a result of the exercise of outstanding options, the vesting or settlement of outstanding stock awards, or the purchase of shares pursuant to the ESPP will cause our shareholders to experience additional dilution, which could cause our stock price to fall.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters is currently located at 3545 Cray Court, San Diego, California 92121 and is a building that consists of approximately 118,000 square feet of office and lab space (the "Cray Court Lease"). The Cray Court Lease will expire mid-2033 and may be terminated early under certain circumstances. We believe that our existing facilities are adequate to meet our current needs.

Item 3. Legal Proceedings

None.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

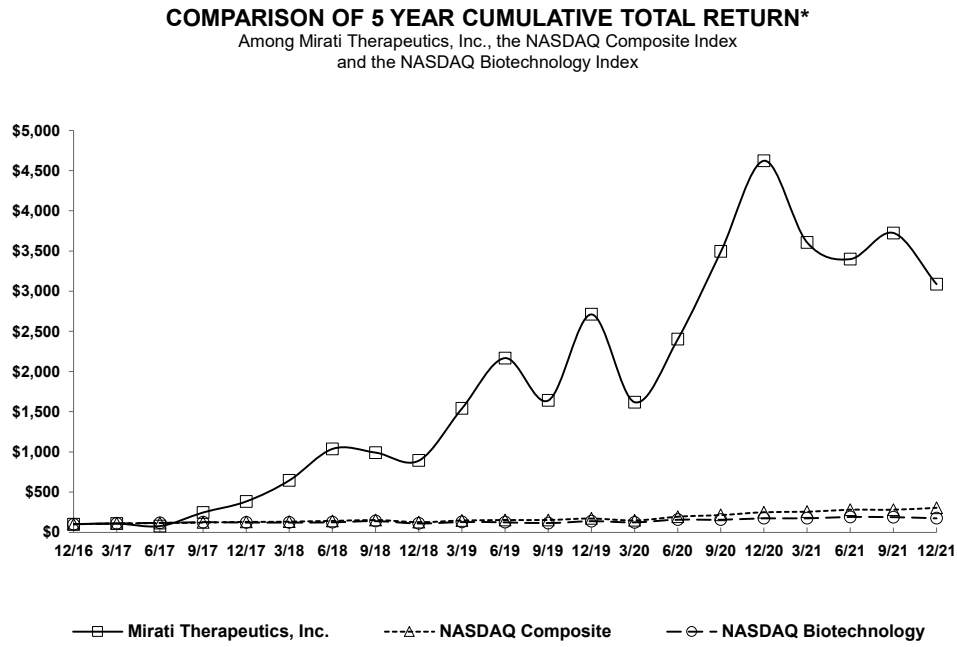
Our common stock is listed under the ticker symbol "MRTX" on The Nasdaq Global Select Market since June 5, 2018, and was previously listed on The Nasdaq Capital Market since July 15, 2013. Prior to that date, there was no public market for our common stock in the United States as our common stock was listed on the Toronto Stock Exchange.

On February 22, 2022, the last reported sale price for our common stock on The Nasdaq Global Select Market was $90.66 per share.

As of February 22, 2022, we had 13 shareholders of record, which excludes shareholders whose shares were held in nominee or street name by brokers. The actual number of common shareholders is greater than the number of record holders, and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include shareholders whose shares may be held in trust by other entities. We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings for funding operations and, therefore, do not anticipate paying any cash dividends in the foreseeable future.

Stock Performance Graph and Cumulative Total Return

The graph below shows the cumulative total shareholder return assuming the investment of $100 on December 31, 2016 in each of (i) Mirati Therapeutic, Inc.'s common stock, (ii) The Nasdaq Composite Index and (iii) The Nasdaq Biotechnology Index. The comparisons in the graph below are based upon historical data and are not indicative of, or intended to forecast, future performance of our common stock or Indexes.



*$100 invested on 12/31/16 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

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 thereto included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

References in the following discussion to "we," "our," "us," "Mirati" or "the Company" refer to Mirati Therapeutics, Inc. and its subsidiaries.

Company Overview

Mirati Therapeutics, Inc. is a clinical-stage oncology company developing novel therapeutics to address the genetic and immunological promoters of cancer.

We have two KRAS inhibitor programs. Adagrasib is an investigational, selective, specific, potent and orally available KRAS G12C inhibitor in clinical development as a monotherapy and in combination with other agents. Adagrasib is the provisionally filed nonproprietary name for MRTX849. MRTX1133 is an investigational, selective, specific and potent KRAS G12D inhibitor in preclinical development.

Sitravatinib is an investigational spectrum-selective kinase inhibitor designed to potently inhibit receptor tyrosine kinases ("RTK"s) and enhance immune responses through the inhibition of immunosuppressive signaling.

MRTX1719 is an internally discovered investigational synthetic lethal PRMT5 inhibitor designed to specifically target the PRMT5/methylthioadensoine (MTA) complex in preclinical development.

The Company also has additional preclinical discovery programs of potentially first-in-class and best-in-class product candidates specifically designed to address mutations and tumors where few treatment options exist. We approach all of our programs with a singular focus: to translate our deep understanding of the molecular drivers of cancer into better therapies and better outcomes for patients.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of financial condition and results of operations are based upon our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make significant estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses and related disclosures. On an ongoing basis, our actual results may differ significantly from our estimates.

While our significant accounting policies are more fully described in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

Under Accounting Standards Codification ("ASC") Topic 606 ("Topic 606"), we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for contracts with customers, we perform the following five steps: (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. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract, determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective

performance obligation when (or as) the performance obligation is satisfied. We utilize key assumptions to determine a stand-alone selling price for performance obligations, which may include revenue forecasts, expected development timelines, discount rates, probabilities of technical and regulatory success and costs for manufacturing clinical supplies. Because the amount of revenue recognized for each performance obligation is determined based upon its relative stand-alone selling price, an increase or decrease of 10% in the estimated fair value of each performance obligation would not have a significant impact on the amount of revenue recognized.

Accrued Research and Development Expenses

We accrue and expense clinical trial activities performed by third parties based upon estimates of the proportion of work completed over the life of the individual clinical trial and patient enrollment rates in accordance with agreements established with clinical research organizations ("CROs") and clinical trial sites. We determine the estimates by reviewing contracts, vendor agreements and purchase orders, and through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services. However, actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including our clinical development plan.

We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual accordingly. Nonrefundable advance payments for goods and services, including fees for process development or manufacturing and distribution of clinical supplies that will be used in future research and development activities, are deferred and recognized as expense in the period that the related goods are consumed or services are performed.

Share-Based Compensation Expense

We measure and recognize compensation expense for share-based payments based on estimated fair value. We estimate the fair value of stock options granted using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of certain estimates and assumptions that affect the amount of share-based compensation expense recognized in our consolidated financial statements. These assumptions include the expected volatility of our stock price, expected term of the options, the risk-free interest rate and expected dividend yields. We estimate the fair value of restricted stock units using the intrinsic value method. We estimate the fair value of performance stock units, which vest based on the achievement of pre-established performance goals, using the intrinsic value method and the probability that the specified performance criteria will be met. Share-based compensation is recognized using the graded accelerated vesting method. If any of the assumptions used in our calculation change significantly, share-based compensation expense may differ materially from what we have recorded in the current period.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

This section provides an analysis of our financial results for the fiscal year ended December 31, 2021 compared to the fiscal year ended December 31, 2020. For the discussion covering the fiscal year ended December 31, 2020 compared to the fiscal year ended December 31, 2019, please refer to Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 filed with the SEC on February 25, 2021.

The following table summarizes our results of operations for the year ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,		Increase (Decrease)
	2021	2020	
License and collaboration revenues	$ 72,092	$ 13,398	$ 58,694
Research and development expenses	508,594	299,349	209,245
General and administrative expenses	136,679	83,412	53,267
Other (expense) income, net	(5,304)	11,426	(16,730)
Income tax expense	3,299	—	3,299

License and collaboration revenues

License and collaboration revenues relate to the Zai Agreement under which Zai was granted an exclusive license to develop, manufacture and commercialize adagrasib in the Zai Licensed Territory, the BeiGene Agreement under which BeiGene was granted an exclusive license to develop, manufacture and commercialize sitravatinib in the BeiGene Licensed Territory, and the ORIC License Agreement under which we granted to ORIC an exclusive worldwide, sublicensable, royalty-free license, and certain related know-how, to develop and commercialize small molecule inhibitors of the Company's allosteric polycomb repressive complex 2, or PRC2, to ORIC. License and collaboration revenues for the year ended December 31, 2021 were $72.1 million, and are comprised of $66.6 million of license and collaboration revenues under the Zai Agreement related to the transfer of the license and related know-how to Zai, $5.0 million of development milestone revenues related to the initiation of the first pivotal clinical trial in the BeiGene Licensed Territory, and $0.4 million related to the manufacturing supply services agreement with BeiGene. License and collaboration revenues for the year ended December 31, 2020 were $13.4 million, of which $11.4 million related to the transfer of the license and related know-how to ORIC under the ORIC License Agreement, and $2.0 million related to the manufacturing supply services agreement with BeiGene.

Research and Development Expenses

Research and development expenses consist primarily of:

- salaries and related expenses for personnel, including expenses related to stock options, or other share-based compensation granted to personnel in development functions;
- fees paid to external service providers such as CROs and contract manufacturing organizations related to clinical trials, including contractual obligations for clinical development, clinical sites, manufacturing and scale-up, and formulation of clinical drug supplies;
- fees paid to contract service providers related to drug discovery efforts including chemistry and biology services;
- license fees paid in connection with our early discovery efforts; and
- costs for allocated facilities and depreciation of equipment.

We record research and development expenses as incurred.

Our research and development efforts during the years ended December 31, 2021 and 2020 were focused primarily on our clinical development programs and our preclinical programs. The following table summarizes our research and development expenses, (in thousands):

	Year Ended December 31,		Increase (Decrease)
	2021	2020	
Third-party research and development expenses:			
Clinical development programs:			
Adagrasib	$ 224,440	$ 121,689	$ 102,751
Sitravatinib	68,799	57,276	11,523
Discontinued programs	297	1,900	(1,603)
Pre-clinical development programs:			
MRTX1719	4,730	—	4,730
MRTX1133	6,093	10,297	(4,204)
Preclinical and early discovery	27,934	11,873	16,061
Total third-party research and development expenses	332,293	203,035	129,258
Salaries and other employee related expense	74,125	37,545	36,580
Share-based compensation expense	68,496	48,044	20,452
Other research and development costs	33,680	10,725	22,955
Research and development expense	$ 508,594	$ 299,349	$ 209,245

Research and development expenses for the year ended December 31, 2021 were $508.6 million compared to $299.3 million during the year ended December 31, 2020. The increase of $209.2 million during the year ended December 31, 2021 relates to an increase in third-party research and development expenses of $129.3 million, an increase in salaries and other employee related expense of $36.6 million, an increase in share-based compensation expense of $20.5 million, and an increase in other research and development costs of $23.0 million. The increase in third-party research and development expense primarily relates to an increase in expenses associated with the development of adagrasib of $102.8 million, sitravatinib of $11.5 million and preclinical and early discovery programs of $16.1 million. The increase in expenses associated with adagrasib relates to the ongoing clinical trials, which include Phase 1/2, Phase 2 and Phase 3 clinical trials. The costs are comprised largely of manufacturing expenses, including manufacturing costs related to registrational manufacturing batches, CRO fees and other clinical trial-related expenses. The increase in expenses associated with the development of sitravatinib relates to increased investigator payment expenses and CRO fees to support the expansion of existing and new sitravatinib clinical trials. The increase in preclinical and early discovery costs is primarily due to increased contracted research and development services to support our early discovery efforts. The increase in salaries and other employee related expense of $36.6 million is primarily due to an increase in the number of research and development employees during the year ended December 31, 2021 compared to the same period in 2020. The increase in share-based compensation of $20.5 million is due to an increase in the fair value of equity awards granted and an increase in headcount during the year ended December 31, 2021 compared to the same period in 2020. The increase in other research and development costs of $23.0 million is primarily due to increases in costs associated with professional and consulting services, rent and software license.

At this time, due to the risks inherent in the clinical development process and product development programs we are unable to estimate with any certainty the costs we will incur in the continued development of adagrasib and sitravatinib, MRTX1719, MRTX1133 and any of our other preclinical and early discovery programs. The process of conducting clinical trials necessary to obtain regulatory approval and manufacturing scale-up to support expanded development and potential future commercialization is costly and time consuming. Any failure by us or delay in completing clinical trials, manufacturing scale up or in obtaining regulatory approvals could lead to increased research and development expense and, in turn, have a material adverse effect on our results of operations. We expect that our research and development expenses may increase if we are successful in advancing adagrasib, sitravatinib, MRTX1719 and MRTX1133 or any of our other preclinical programs into more advanced stages of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related benefits, including share-based compensation, related to our executive, finance, legal, commercial and support functions. Other general and administrative expenses include professional fees for auditing, tax, consulting and patent-related services, rent and utilities and insurance.

General and administrative expenses for the year ended December 31, 2021 were $136.7 million compared to $83.4 million for the same period in 2020. The increase of $53.3 million is primarily due to an increase in salaries and other employee related expense of $15.8 million, an increase in professional services expense of $14.9 million, an increase in facilities, insurance and other expense of $10.1 million, an increase in share-based compensation expense of $7.2 million, and an increase in sponsorship agreements expense of $5.3 million. The increase in salaries and other employee related expense is primarily due to an increase in the number of general and administrative employees during the year ended December 31, 2021 compared to the same period in 2020, and is due to growth driven by commercial readiness activities. The increase in professional services expense is primarily due to an increase in commercial costs as we prepare for a potential product launch and includes market research and professional consulting fees. The increase in facilities, insurance and other expense is primarily due to our new corporate headquarters, the size of which is nearly twice that of our former headquarters at an increased cost per square foot, increased software licensing costs and expensed equipment due to increased headcount, as well as increased director's and officer's liability insurance expense. The increase in share-based compensation expense is due to an increase in the fair value of equity awards granted and an increase in headcount during the year ended December 31, 2021 compared to the same period in 2020. The increase in sponsorship agreements expense is primarily due to a $4.0 million research grant made in the first quarter of 2021.

Other (Expense) Income, Net

Other (expense) income, net for the year ended December 31, 2021 was an expense of $5.3 million compared to an income of $11.4 million for the same period in 2020. The decrease of $16.7 million was primarily due to the change in fair value on the long-term investment in ORIC Pharmaceuticals, Inc., which was acquired in 2020 in connection with the ORIC License Agreement, and a decrease in interest income primarily due to lower interest rates.

Income Tax Expense

Income tax expense for the year ended December 31, 2021 was $3.3 million and related to foreign income taxes as a result of the upfront payment received from Zai in July 2021.

A summary of our Results of Operation for the year ended December 31, 2019 may be found in our Annual Reports on Form 10-K, filed with the SEC on February 25, 2021 and February 26, 2020.

Liquidity and Capital Resources

At December 31, 2021, we had $1.5 billion of cash, cash equivalents and short-term investments compared to $1.4 billion at December 31, 2020. In November 2021, we completed a public offering of our common stock that generated net proceeds of $474.7 million. In July 2021, we received net proceeds of $63.4 million for the up-front fee in connection with the Zai Agreement. In July 2021, we entered into an amended and restated sales agreement pursuant to which we may, from time to time, sell shares of our common stock having an aggregate offering price of up to $500.0 million; as of December 31, 2021, no shares have been sold in connection with this amended and restated sales agreement. During 2020, we completed public offerings of our common stock that generated total net proceeds of $1.2 billion. In 2019, we completed public offerings of our common stock that generated net proceeds of $327.8 million. Based on our current and anticipated level of operations, we believe that our cash, cash equivalents and short-term investments will be sufficient to meet our anticipated obligations for at least one year from the date this Annual Report on Form 10-K is filed with the SEC.

It can take a significant amount of time and capital resources to successfully complete all stages of research and development and commercialization of a product candidate. The length of time and funding required cannot be accurately estimated as it varies substantially according to the type, complexity, novelty and intended use of a product candidate. The funding necessary to execute product development and commercialization is uncertain and we are unable to accurately predict when or if we will be able to achieve or maintain profitability. The timing and amount of our operating expenditures, and future capital requirements will depend on many factors, including:

- the success of our commercialization efforts and market acceptance of adagrasib and other drug product candidates;
- the timing and outcome of regulatory review of adagrasib and other drug product candidates;
- continued progress in our research and development and clinical development programs;
- the cost of manufacturing clinical supply for our clinical trials and commercial manufacturing; and
- addition and retention of key research and development and commercial, including sales and marketing, personnel.

To date, we have funded our operations primarily through the sale of our common stock, pre-funded warrants to purchase our common stock, and to a lesser extent through up-front payments, research funding and milestone payments under collaborative arrangements. Since inception, we have primarily devoted our resources to funding research and development programs, including discovery research, preclinical and clinical development activities, as well as costs associated with commercial launch preparedness activities. To fund future operations, we will likely need to raise additional capital. The amount and timing of future funding requirements will depend on many factors, including the timing and results of our ongoing development efforts, the potential expansion of our current development programs, potential new development programs and related general and administrative support. We anticipate that we will seek to fund our operations through public or private equity or debt financings or other sources, such as potential collaboration agreements. We cannot make assurances that anticipated additional financing will be available to us on favorable terms, or at all. Although we have previously been successful in obtaining financing through our equity securities offerings, there can be no assurance that we will be able to do so in the future. As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility, including in liquidity and credit availability, declines in consumer confidence, declines in economic growth, and uncertainty about economic stability. There can be no assurance that deterioration in credit and financial markets and confidence in economic conditions will not occur. If equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult to obtain, more costly and/or more dilutive.

Cash Flows for the Years Ended December 31, 2021 and 2020

The following table provides a summary of the net cash flow activity for each of the periods set forth below (in thousands):

	Year Ended December 31,	
	2021	2020
Net cash used in operating activities	$ (388,800)	$ (271,531)
Net cash used in investing activities	(588,901)	(139,857)
Net cash provided by financing activities	505,222	1,250,714
(Decrease) increase in cash, cash equivalents, and restricted cash	$ (472,479)	$ 839,326

Net cash used in operating activities

Net cash used in operating activities was $388.8 million and $271.5 million for the years ended December 31, 2021 and 2020, respectively. Cash used in operating activities during 2021 primarily related to our net loss of $581.8 million, adjusted for non-cash share-based compensation expense of $113.5 million and net cash inflows from a change in our operating assets and liabilities of $65.6 million. Cash used in operating activities during 2020 primarily related to our net loss of $357.9 million, adjusted for non-cash share-based compensation expense of $85.8 million and net cash inflows from a change in our operating assets and liabilities of $16.2 million.

Net cash used in investing activities

Net cash used in investing activities for the years ended December 31, 2021 and 2020 was $588.9 million and $139.9 million, respectively, and reflects the purchases of short-term investments and property and equipment, offset by sales and maturities of short-term investments.

Net cash provided by financing activities

Net cash provided by financing activities for the year ended December 31, 2021 was $505.2 million and consisted primarily of proceeds received from the issuance of common stock, exercise of common stock options and stock issuances under the employee stock option plan. Net cash provided by financing activities for the year ended December 31, 2020 was $1.3 billion and consisted of proceeds from issuance of common stock, exercise of common stock options, and stock issuances under the employee stock option plan.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations and commitments as of December 31, 2021 that will affect our future liquidity (in thousands):

	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Operating Lease Obligations[(1)]	$ 94,184	$ 1,681	$ 15,924	$ 16,894	$ 59,685
Total contractual obligations	$ 94,184	$ 1,681	$ 15,924	$ 16,894	$ 59,685

(1) On June 30, 2020, the Company entered into an amended and restated lease agreement (the "Amended and Restated Lease") for office and laboratory space located in San Diego, California, for the Company's new corporate headquarters. The Amended and Restated Lease supersedes in its entirety the original lease agreement for the Company's future corporate headquarters dated as of August 22, 2019. The Amended and Restated Lease has a lease term of approximately 12 years. The Company has an early termination right 7 years into the lease term, in which the total contractual obligation would be reduced by $41.1 million.

We enter into contracts in the normal course of business with clinical sites for the conduct of clinical trials, CROs for clinical research studies, professional consultants for expert advice and other vendors for clinical supply manufacturing or other services. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk

Some of our short-term investments have market risk in that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. We invest our excess cash primarily in commercial paper and debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. Treasury. We mitigate credit risk by maintaining a well-diversified portfolio and limiting the amount of investment exposure as to institution, maturity and investment type. We invest our excess cash in accordance with our investment policy.

Because of the short-term maturities of our cash equivalents and short-term investments, we do not believe that an increase in market rates would have any significant impact on the realized value of our investments. If a 10% change in interest rates were to have occurred on December 31, 2021, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

Effects of Inflation

We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

Item 8. Financial Statements and Supplementary Data

The financial statements and supplemental data required by this item are set forth at the pages indicated in Part IV, Item 15 of this Annual Report.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a-15(b) and Rule 15d-15(b) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation as of the end of the period covered by this Annual Report on Form 10-K of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e) and 15d-15(e)). Based on that evaluation, management has concluded that as of December 31, 2021, the Company's disclosure controls and procedures were effective at the reasonable assurance level and we believe the consolidated financial statements included in this Form 10-K for the year ended December 31, 2021 present, in all material respects, our financial position, results of operations, comprehensive loss and cash flows for the periods presented in conformity with U.S. generally accepted accounting principles.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Exchange Act Rule 13a-15(f). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

As of December 31, 2021, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control-Integrated Framework (2013 Framework)*. Based on this assessment, our management concluded that, as of December 31, 2021, our internal control over financial reporting was effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2021 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in its report, which is included herein.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during the quarter ended December 31, 2021 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors of Mirati Therapeutics, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Mirati Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Mirati Therapeutics, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of Mirati Therapeutics, Inc. as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, changes in shareholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes and our report dated February 28, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

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

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

San Diego, California
February 28, 2022

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspection

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is incorporated herein by reference to our definitive proxy statement to be filed in connection with our 2022 Annual Meeting of Shareholders (the "2022 Proxy Statement"), which will be filed with the Securities and Exchange Commission within 120 days after December 31, 2021.

We have adopted a Code of Business Conduct and Ethics that applies to all officers, directors and employees. The Code of Business Conduct and Ethics is available on our website at www.mirati.com. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the amendment or waiver on our website.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to the 2022 Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item is incorporated by reference to the 2022 Proxy Statement.

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

The information required by this item is incorporated by reference to the 2022 Proxy Statement.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference to the 2022 Proxy Statement.

PART IV

Item 15. Exhibits and Financial Statement Schedules

1. *Financial Statements.* We have filed the following documents as part of this Annual Report:

2. *Financial Statement Schedules.* All schedules are omitted because they are not applicable or the required information is shown in the Financial Statements or notes thereto.

INDEX TO EXHIBITS

Exhibit number	Description of Document
2.1	Arrangement Agreement, dated May 8, 2013, by and between MethylGene Inc. and the Registrant (incorporated by reference to Mirati Therapeutics, Inc.'s Amended Registration Statement on Form 10-12B/A (No. 001-35921), filed with the Securities and Exchange Commission on June 14, 2013).
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form 10-12B (No. 001-35921), filed with the Securities and Exchange Commission on May 10, 2013).
3.2	Bylaws (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form 10-12B (No. 001-35921), filed with the Securities and Exchange Commission on May 10, 2013).
3.3	Amendment to Bylaws (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on June 16, 2016).
4.1	Form of Common Stock Certificate (incorporated by reference to Mirati Therapeutics, Inc.'s Amended Registration Statement on Form 10-12B/A (No. 001-35921), filed with the Securities and Exchange Commission on June 14, 2013).
4.2	Form of Warrant to Purchase Common Stock (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on January 6, 2017).
4.3	Form of Warrant to Purchase Common Stock (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on November 16, 2017).
4.4	Form of Warrant to Purchase Common Stock (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on June 7, 2018).
4.5	Description of Capital Stock (incorporated by reference to Mirati Therapeutics, Inc.'s Annual Report on Form 10-K, filed with the Securities and Exchange Commission on February 25, 2021).
10.1	Form of Securities Purchase Agreement relating to the 2012 private placement (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form 10-12B (No. 001-35921), filed with the Securities and Exchange Commission on May 10, 2013).
10.2+	Amended and Restated Incentive Stock Option Plan (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form 10-12B (No. 001-35921), filed with the Securities and Exchange Commission on May 10, 2013).
10.3+	Amended and Restated 2013 Equity Incentive Plan, as amended, and Form of Stock Option Agreement and Form of Stock Option Grant Notice thereunder (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on May 12, 2021).
10.4+	Form of 2013 Employee Stock Purchase Plan (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form 10-12B (No. 001-35921), filed with the Securities and Exchange Commission on May 10, 2013).
10.5+	Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under the Amended and Restated 2013 Equity Incentive Plan (incorporated by reference to Mirati Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2019, filed with the Securities and Exchange Commission on February 26, 2020).
10.6+	Mirati Therapeutics, Inc. Inducement Plan (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 31, 2019).
10.7+	Form of Stock Option Grant Notice and Stock Option Agreement under Mirati Therapeutics, Inc. Inducement Plan (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 31, 2019).
10.8+	Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under Mirati Therapeutics, Inc. Inducement Plan (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 31, 2019).
10.9+	Senior Executive Employment Agreement, dated September 24, 2012, by and among MethylGene Inc. and Dr. Charles M. Baum (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form 10-12B (No. 001-35921), filed with the Securities and Exchange Commission on May 10, 2013).
10.10+	Amended and Restated Employment Agreement, dated July 2, 2013, by and between the Registrant and Dr. Charles M. Baum (incorporated by reference to Mirati Therapeutics, Inc.'s Amended Registration Statement on Form 10-12B/A (No. 001-35921), filed with the Securities and Exchange Commission on July 9, 2013).
10.11+	Letter Agreement, dated May 20, 2013, by and between Methylgene Inc. and James Christensen (incorporated by reference to Mirati Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2014, filed with the Securities and Exchange Commission on March 11, 2015).

10.12+	Form of Indemnity Agreement (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form S-1 (No. 333-191544), filed with the Securities and Exchange Commission on October 3, 2013).
10.13+	Amended and Restated Non-Employee Director Compensation Policy.
10.14+	Amendment to Amended and Restated Employment Agreement, dated December 19, 2016, by and between the Registrant and Dr. Charles Baum (incorporated by reference to Mirati Therapeutics, Inc.'s Current Report on Form 8-K, filed with the Securities and Exchange Commission on November 16, 2017).
10.15+	Amendment to Letter Agreement, dated December 19, 2016, by and between the Registrant and James Christensen (incorporated by reference to Mirati Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2016, filed with the Securities and Exchange Commission on March 9, 2017).
10.16	Collaboration and License Agreement, dated January 7, 2018, by and among Mirati Therapeutics, Inc., MethylGene Inc. and BeiGene, Ltd. (incorporated by reference to Mirati Therapeutics, Inc.'s Quarterly Report on Form 10-Q/A, filed with the Securities and Exchange Commission on August 20, 2018).
10.17	Clinical Trial Collaboration and Supply Agreement, dated January 3, 2019, by and between the Registrant and Bristol-Myers Squibb Company, and related Supply/Quality Addendum dated March 29, 2019 (incorporated by reference to Mirati Therapeutics, Inc.'s Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on April 29, 2019).
10.18	Drug Discovery Collaboration Option Agreement, dated October 1, 2014, by and between Mirati Therapeutics, Inc. and Array BioPharma Inc., and related amendments dated August 13, 2015, November 9, 2015, February 13, 2016, and August 24, 2018 (incorporated by reference to Mirati Therapeutics, Inc.'s Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on April 29, 2019).
10.19	Lease to 3545 Cray Court, dated August 22, 2019 (incorporated by reference to Mirati Therapeutics, Inc.'s Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on November 4, 2019).
10.20	Amended and Restated Lease to 3545 Cray Court, dated June 30, 2020 (incorporated by reference to Mirati Therapeutics, Inc.'s Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on August 6, 2020).
10.21	Letter Agreement, dated December 20, 2019, by and between the Registrant and Dan Faga (incorporated by reference by Mirati Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2020, filed with the Securities and Exchange Commission on February 25, 2021).
10.22	Letter Agreement, dated December 18, 2019, by and between the Registrant and Benjamin Hickey (incorporated by reference by Mirati Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2020, filed with the Securities and Exchange Commission on February 25, 2021).
10.23	Second Amendment to Letter Agreement, effective December 31, 2020, by and between the Registrant and Dr. Charles M. Baum (incorporated by reference to Mirati Therapeutics Inc.'s Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on May 6, 2021).
10.24	Second Amendment to Letter Agreement, effective December 31, 2020, by and between the Registrant and Dr. James Christensen (incorporated by reference to Mirati Therapeutics Inc.'s Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on May 6, 2021).
10.25	Collaboration and License Agreement, dated May 28, 2021, by and among the Company and Zai Lab (Hong Kong) Limited (incorporated by reference to Mirati Therapeutics Inc.'s Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on August 5, 2021).
10.26	Amended and Restated Sales Agreement, dated July 2, 2021, by and between Mirati Therapeutics, Inc. and Cowen and Company, LLC (incorporated by reference to Mirati Therapeutics, Inc.'s Registration Statement on Form S-3ASR, filed with the Securities and Exchange Commission on July 2, 2021).
10.27	Third Amendment to Amended and Restated Employment Agreement, dated September 20, 2021, by and between the Registrant and Dr. Charles M. Baum (incorporated by reference to Mirati Therapeutics Inc.'s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 8, 2021).
10.28	Employment Agreement, dated September 17, 2021, by and between the Registrant and David D. Meek (incorporated by reference to Mirati Therapeutics Inc.'s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 8, 2021).
10.29	Amended and Restated Second Amendment to Letter Agreement, effective September 20, 2021, by and between the Registrant and Dr. James Christensen.
10.30	Separation Agreement and Release, dated December 15, 2021, by and between the Registrant and Dan Faga.
21.1	Subsidiaries of the Registrant.
23.1	Consent of Independent Registered Public Accounting Firm.
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.

31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1	Certifications Pursuant to U.S.C. Section 1350, As Adopted Pursuant to Section 906 of the Public Company Accounting Reform and Investor Protection Act of 2002.
101.INS	Inline XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL 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	104 Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

+	Indicates management contract or compensatory plan.
*	We have received confidential treatment for certain portions of this agreement, which have been omitted and filed separately with the SEC pursuant to Rule 406 under the Securities Act.
**	Certain portions of this exhibit (indicated by "[***]") have been omitted as Mirati Therapeutics, Inc. has determined (i) the omitted information is not material and (ii) the omitted information would likely cause harm to Mirati Therapeutics, Inc. if publicly disclosed.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

MIRATI THERAPEUTICS, INC.

Date: February 28, 2022

by: /s/ David D. Meek
Chief Executive Officer
(Principal Executive Officer)

Date: February 28, 2022

by: /s/ Vickie S. Reed
Senior Vice President and Chief Accounting Officer
(Principal Financial Officer and Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints David D. Meek and Vickie S. Reed as his or her true and lawful attorneys-in-fact, and each of them, with full power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact, and either of them, or his or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/S/ DAVID D. MEEK **David D. Meek**	Chief Executive Officer and Director (Principal Executive Officer)	February 28, 2022
/S/ VICKIE S. REED **Vickie S. Reed**	Senior Vice President and Chief Accounting Officer (Principal Financial Officer and Principal Accounting Officer)	February 28, 2022
/S/ CHARLES M. BAUM **Charles M. Baum, M.D., Ph.D.**	President, Founder, Head of Research and Development and Director	February 28, 2022
/S/ FAHEEM HASNAIN **Faheem Hasnain**	Chairman of the Board	February 28, 2022
/S/ BRUCE L.A. CARTER **Bruce L.A. Carter, Ph.D.**	Director	February 28, 2022
/S/ JULIE CHERRINGTON **Julie Cherrington, Ph.D.**	Director	February 28, 2022
/S/ AARON DAVIS **Aaron Davis**	Director	February 28, 2022
/S/ HENRY J. FUCHS **Henry J. Fuchs, M.D.**	Director	February 28, 2022
/S/ CRAIG JOHNSON **Craig Johnson**	Director	February 28, 2022
/S/ MAYA MARTINEZ-DAVIS **Maya Martinez-Davis**	Director	February 28, 2022
/S/ SHALINI SHARP **Shalini Sharp**	Director	February 28, 2022

Report of Independent Registered Public Accounting Firm

To the Shareholders and Board of Directors of Mirati Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Mirati Therapeutics, Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, changes in shareholders' equity and cash flows for each of the three years in the period ended December 31, 2021, 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 financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 28, 2022 expressed an unqualified opinion thereon.

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 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. 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 research and development expenses

Description of the Matter

At December 31, 2021, the Company incurred $508.6 million for research and development expenses and accrued $76.3 million for research and development expenses. As described in Note 2 to the consolidated financial statements, the Company records accruals for estimated costs of research and development activities, including contract services for clinical trials and related clinical manufacturing costs. Clinical trial activities performed by third parties are accrued and expensed based upon estimates of the proportion of work completed over the life of the individual clinical trial and patient enrollment rates in accordance with agreements established with Clinical Research Organizations ("CROs") and clinical trial sites. Estimates are determined by reviewing contracts, vendor agreements and purchase orders, and through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Auditing management's accounting for accrued research and development expenses, for which the Company has either not been invoiced or has not received information on the actual costs incurred, was especially challenging as evaluating the progress or stage of completion of the activities under the Company's research and development agreements is dependent upon information from internal clinical personnel and third party service providers and involves a high volume of data which is tracked in spreadsheets and other end user computing programs.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the accounting for accrued research and development expenses. For example, we tested controls over management's assessment and measurement of estimated accrued costs, including data inputs for study progress and remaining stages of completion under each study.

To test the completeness of the Company's accrued research and development expenses, we obtained supporting evidence of the research and development activities performed for significant clinical trials. We attended internal clinical trial and project status meetings with accounting and clinical project managers to inspect the status of significant research and development activities. To assess the appropriate measurement of accrued research and development costs, our audit procedures included, among others, obtaining and inspecting significant agreements and agreement amendments, and testing a sample of transactions and comparing the costs against related invoices and contracts. We also tested a sample of subsequent payments to evaluate the completeness of the accrued expenses and compared the results to the current year accrual.

/s/ Ernst & Young LLP
We have served as the Company's auditor since 2014.

San Diego, California
February 28, 2022

Mirati Therapeutics, Inc.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2021	2020
ASSETS		
Current assets		
Cash and cash equivalents	$ 413,083	$ 885,562
Short-term investments	1,078,257	504,544
Other current assets	16,643	13,537
Total current assets	1,507,983	1,403,643
Property and equipment, net	15,824	7,809
Long-term investment	8,218	15,629
Right-of-use asset	37,680	39,890
Other long-term assets	19,049	9,157
Total assets	$ 1,588,754	$ 1,476,128
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 35,163	$ 18,117
Accrued liabilities	108,495	53,355
Total current liabilities	143,658	71,472
Lease liability	45,879	41,905
Other liabilities	2,179	1,962
Total liabilities	191,716	115,339
Commitments and contingencies (see Note 14)		
Shareholders' equity		
Preferred stock, $0.001 par value, 10,000,000 shares authorized; none issued and outstanding at both December 31, 2021 and December 31, 2020	—	—
Common stock, $0.001 par value; 100,000,000 authorized; 55,356,904 and 50,439,069 issued and outstanding at December 31, 2021 and December 31, 2020, respectively	55	50
Additional paid-in capital	3,099,937	2,481,218
Accumulated other comprehensive income	9,068	9,759
Accumulated deficit	(1,712,022)	(1,130,238)
Total shareholders' equity	1,397,038	1,360,789
Total liabilities and shareholders' equity	$ 1,588,754	$ 1,476,128

See accompanying notes

Mirati Therapeutics, Inc.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended December 31,		
	2021	**2020**	**2019**
Revenue			
License and collaboration revenues	$ 72,092	$ 13,398	$ 3,335
Total revenue	72,092	13,398	3,335
Expenses			
Research and development	$ 508,594	$ 299,349	$ 182,866
General and administrative	136,679	83,412	42,573
Total operating expenses	645,273	382,761	225,439
Loss from operations	(573,181)	(369,363)	(222,104)
Other (expense) income, net	(5,304)	11,426	8,848
Loss before income taxes	(578,485)	(357,937)	(213,256)
Income tax expense	3,299	—	—
Net loss	$ (581,784)	$ (357,937)	$ (213,256)
Unrealized (loss) gain on available-for-sale investments	$ (691)	$ (130)	$ 410
Comprehensive loss	$ (582,475)	$ (358,067)	$ (212,846)
Net loss per share, basic and diluted	$ (11.21)	$ (7.96)	$ (5.69)
Weighted average common shares outstanding, basic and diluted	51,882,538	44,987,555	37,467,505

See accompanying notes

Mirati Therapeutics, Inc.
CONSOLIDATED STATEMENTS OF CHANGES IN SHAREHOLDERS' EQUITY
(in thousands, except share data)

	Common Stock		Additional paid-in capital	Accumulated other comprehensive income	Accumulated deficit	Total shareholders' equity
	Shares	Amount				
Balance at December 31, 2018	**32,538,857**	**$ 33**	**$ 751,109**	**$ 9,479**	**$ (559,045)**	**$ 201,576**
Net loss	—	—	—	—	(213,256)	(213,256)
Issuance of common stock, net of issuance costs	4,269,838	4	327,826	—	—	327,830
Share-based compensation expense	—	—	55,537	—	—	55,537
Issuance of common stock from 2013 Employee Stock Purchase Plan ("ESPP")	14,488	—	675	—	—	675
Issuance of common stock under equity incentive plans	569,146	1	8,472	—	—	8,473
Proceeds from disgorgement of shareholders' short-swing profits	—	—	1,050	—	—	1,050
Net exercise of warrants	2,125,000	2	(2)	—	—	—
Unrealized gain on investments	—	—	—	410	—	410
Balance at December 31, 2019	**39,517,329**	**$ 40**	**$ 1,144,667**	**$ 9,889**	**$ (772,301)**	**$ 382,295**
Net loss	—	—	—	—	(357,937)	(357,937)
Issuance of common stock, net of issuance costs	8,124,168	8	1,203,609	—	—	1,203,617
Share-based compensation expense	—	—	85,847	—	—	85,847
Issuance of common stock from ESPP	14,436	—	1,206	—	—	1,206
Issuance of common stock under equity incentive plans	1,319,901	1	45,890	—	—	45,891
Net exercise of warrants	1,463,235	1	(1)	—	—	—
Unrealized loss on investments	—	—	—	(130)	—	(130)
Balance at December 31, 2020	**50,439,069**	**$ 50**	**$ 2,481,218**	**$ 9,759**	**$(1,130,238)**	**$ 1,360,789**
Net loss	—	—	—	—	(581,784)	(581,784)
Issuance of common stock, net of issuance costs	3,448,275	3	474,694	—	—	474,697
Share-based compensation expense	—	—	113,502	—	—	113,502
Issuance of common stock from ESPP	20,672	—	2,567	—	—	2,567
Issuance of common stock under equity incentive plans	825,074	1	27,957	—	—	27,958
Net exercise of warrants	623,814	1	(1)	—	—	—
Unrealized loss on investments	—	—	—	(691)	—	(691)
Balance at December 31, 2021	**55,356,904**	**$ 55**	**$ 3,099,937**	**$ 9,068**	**$(1,712,022)**	**$ 1,397,038**

See accompanying notes

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

	Years Ended December 31,		
	2021	**2020**	**2019**
Operating activities:			
Net loss	$ (581,784)	$ (357,937)	$ (213,256)
Non-cash adjustments reconciling net loss to operating cash flows			
Non-cash consideration earned from license agreement	—	(11,424)	—
Change in fair value of long-term investment	7,411	(4,205)	—
Depreciation of property and equipment	1,781	641	249
Amortization of premium and accretion of discounts on investments	4,702	(674)	(3,421)
Share-based compensation expense	113,502	85,847	55,537
Changes in operating assets and liabilities:			
Other current assets	(3,107)	(4,180)	(5,487)
Other long-term assets	(9,892)	(3,424)	(4,375)
Right-of-use asset	2,210	582	—
Lease liability	5,315	(652)	—
Accounts payable, accrued liabilities, deferred revenue and other liabilities	71,062	23,895	23,027
Cash flows used in operating activities	(388,800)	(271,531)	(147,726)
Investing activities:			
Purchases of short-term investments	(1,422,729)	(662,824)	(530,228)
Sales and maturities of short-term investments	843,623	527,334	355,640
Purchases of property and equipment	(9,795)	(4,367)	(1,552)
Cash flows used in investing activities	(588,901)	(139,857)	(176,140)
Financing activities:			
Proceeds from issuance of common stock, net of issuance costs	474,697	1,203,617	327,830
Proceeds from issuance of common stock under equity incentive plans	27,958	45,891	8,473
Proceeds from disgorgement of shareholders' short-swing profits	—	—	1,050
Proceeds from issuances under ESPP	2,567	1,206	675
Cash flows provided by financing activities	505,222	1,250,714	338,028
(Decrease) increase in cash, cash equivalents and restricted cash	(472,479)	839,326	14,162
Cash, cash equivalents and restricted cash, beginning of year	886,182	46,856	32,694
Cash, cash equivalents and restricted cash, end of year	$ 413,703	$ 886,182	$ 46,856
Reconciliation of cash, cash equivalents and restricted cash, end of year:			
Cash and cash equivalents	$ 413,083	$ 885,562	$ 46,535
Restricted cash included in other long-term assets	620	620	321
Total cash, cash equivalents and restricted cash	$ 413,703	$ 886,182	$ 46,856
Supplemental disclosures of non-cash investing activities:			
Accrued capital expenditures	$ 583	$ 292	$ —
Allowance utilized for tenant improvements	$ —	$ 2,015	$ —
Initial recognition of operating right-of-use asset	$ —	$ 39,890	$ —
Initial recognition of operating lease liability	$ —	$ 41,905	$ —

See accompanying notes

1. Description of Business

Mirati Therapeutics, Inc. ("Mirati" or the "Company") is a clinical-stage oncology company developing product candidates to address the genetic and immunological promoters of cancer. The Company was incorporated under the laws of the State of Delaware on April 29, 2013 as Mirati Therapeutics, Inc. and is located in San Diego, California. The Company has a wholly owned subsidiary in Canada, MethylGene, Inc. ("MethylGene"), a wholly owned subsidiary in the Netherlands ("Mirati Therapeutics B.V.") and operates in the United States. The Company's common stock has been listed on the Nasdaq Global Select Market since June 5, 2018, and was previously listed on the Nasdaq Capital Market since July 15, 2013, under the ticker symbol "MRTX."

2. Summary of Significant Accounting Policies

Basis of Presentation

These consolidated financial statements are prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). These consolidated financial statements include the accounts of the Company and MethylGene and Mirati Therapeutics B.V. All significant inter-company transactions, balances and expenses have been eliminated upon consolidation.

Mirati was incorporated under the laws of the State of Delaware on April 29, 2013. On May 8, 2013, the Company's Board of Directors approved and the Company entered into an arrangement agreement with MethylGene and MethylGene became a wholly-owned subsidiary. On August 3, 2021, Mirati Therapeutics B.V. was formed in Amsterdam, Netherlands, and became a wholly-owned subsidiary.

These consolidated financial statements are presented in United States ("U.S.") Dollars, which is also the functional currency of the Company.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period.

Reported amounts and note disclosures reflect the overall economic conditions that are most likely to occur and anticipated measures management intends to take. Actual results could differ materially from those estimates. Estimates and assumptions are reviewed quarterly. Any revisions to accounting estimates are recognized in the period in which the estimates are revised and in any future periods affected.

Cash, Cash Equivalents and Short-term Investments

Cash and cash equivalents consist of cash and highly liquid securities with original maturities at the date of acquisition of ninety days or less. Investments with an original maturity of more than ninety days are considered short-term investments and have been classified by management as available-for-sale. These investments are classified as current assets, even though the stated maturity date may be one year or more beyond the current consolidated balance sheet date, which reflects management's intention to use the proceeds from sales of these securities to fund its operations, as necessary. Such investments are carried at fair value, and the unrealized gains and losses are reported as a component of accumulated other comprehensive income in shareholders' equity until realized. Realized gains and losses from the sale of available-for-sale securities, if any, are determined on a specific identification basis.

Concentration of Credit Risk

The Company invests its excess cash in accordance with its investment policy. The Company's investments are comprised primarily of commercial paper and debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. Treasury. The Company mitigates credit risk by maintaining a diversified portfolio and

limiting the amount of investment exposure as to institution, maturity and investment type. Financial instruments that potentially subject the Company to significant credit risk consist principally of cash equivalents and short-term investments.

Revenue Recognition

The Company recognizes revenue in connection with certain collaboration and license agreements in accordance with the guidance of *Revenue From Contracts With Customers*, Accounting Standards Codification ("ASC") Topic 606 ("Topic 606"). Under Topic 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements the Company determines are within the scope of Topic 606, the Company performs the following five steps: (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 Company 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, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that 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.

Property and Equipment, Net

Property and equipment is stated at historical cost less accumulated depreciation. Historical cost includes expenditures that are directly attributable to the acquisition of the items. All repairs and maintenance are charged to consolidated net loss during the financial period in which they are incurred.

Depreciation of property and equipment is calculated using the straight-line method over the estimated useful lives of the assets, as follows:

Computer equipment	3 years
Office and other equipment	6 years
Laboratory equipment	6 years
Leasehold improvements	The lesser of the lease term or the life of the asset

Upon disposal or impairment of property and equipment, the cost and related accumulated depreciation is removed from the consolidated financial statements and the net amount, less any proceeds, is included in consolidated net loss.

Impairment of Long-Lived Assets

The Company reviews its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. If such circumstances are determined to exist, an estimate of undiscounted future cash flows produced by the long-lived asset, including its eventual residual value, is compared to the carrying value to determine whether impairment exists. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written-down to their estimated fair values. Fair value is estimated through discounted cash flow models to project cash flows from the asset. The Company recognized no impairment charges for the years ended December 31, 2021, 2020 and 2019.

Share-Based Compensation Expense

The Company measures and recognizes compensation expense for share-based payments based on estimated fair value as of the grant date. The fair value of restricted stock units is determined using the intrinsic value method. The fair value of performance stock units, which vest based on the achievement of pre-established performance goals, is determined using the intrinsic value method and the probability that the specified performance criteria will be met. The fair value of stock options is determined using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of certain estimates and assumptions that affect the amount of share-based compensation expense recognized in the Company's consolidated financial statements. These assumptions include the expected volatility of the Company's stock price, expected term of the options, the risk-free interest rate and expected dividend yields. Share-based compensation expense is recognized using the graded accelerated vesting method.

Research and Development Expenses

Research and development expenses are charged to consolidated net loss in the period in which they are incurred and are comprised of the following types of costs incurred in performing research and development activities: contract services for clinical trials and related clinical manufacturing costs, salaries and benefits including share-based compensation expense, costs for allocated facilities and depreciation of equipment and license fees paid in connection with the Company's early discovery efforts.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related benefits, including share-based compensation expense, related to the Company's executive, finance, legal, commercial and support functions. Other general and administrative expenses include professional fees for auditing, tax, consulting and patent-related services, rent and utilities and insurance.

Leases

The Company determines if an arrangement is a lease at inception. Lease right-of-use assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. For operating leases with an initial term greater than 12 months, the Company recognizes operating lease right-of-use assets and operating lease liabilities based on the present value of lease payments over the lease term at the commencement date. Operating lease right-of-use assets are comprised of the lease liability plus any lease payments made and excludes lease incentives. Lease terms include options to renew or terminate the lease when the Company is reasonably certain that the renewal option will be exercised or when it is reasonably certain that the termination option will not be exercised. For the Company's operating leases, if the interest rate used to determine the present value of future lease payments it not readily determinable, the Company estimates its incremental borrowing rate as the discount rate for the lease. The Company's incremental borrowing rate is estimated to approximate the interest rate on a collateralized basis with similar terms and payments, and in similar economic environments. Lease expense for lease payments is recognized on a straight-line basis over the lease term. The Company has elected the practical expedient to not separate lease and non-lease components.

Income Taxes

Income taxes have been accounted for using the asset and liability method. Under the asset and liability method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applicable to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in net loss in the period that includes the enactment date. A valuation allowance against deferred tax assets is recorded if, based upon the weight of all available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. For uncertain tax positions that meet "a more likely than not" threshold, the Company recognizes the benefit of uncertain tax positions in the consolidated financial statements.

Segment Reporting

Operating segments are components of a business where separate discrete financial information is available for evaluation by the chief operating decision-maker for purposes of making decisions regarding resource allocation and assessing performance. To date, the Company and the chief operating decision-maker has viewed its operations and managed its business as one segment operating primarily in the United States.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of common shares outstanding during the period, without consideration for common share equivalents as they are anti-dilutive. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of common shares and common share equivalents outstanding for the period, as well as certain shares that are contingently issuable. Common share equivalents outstanding, determined using the treasury stock method, are comprised of shares that may be issued under the Company's stock option and warrant agreements, as well as restricted stock units and performance stock units.

The following table presents the weighted average number of common share equivalents, calculated using the treasury stock method, as well as certain shares that are contingently issuable, not included in the calculation of diluted net loss per share due to the anti-dilutive effect of the securities:

	Year Ended December 31,		
	2021	2020	2019
Common stock options	2,358,594	2,503,294	2,403,055
Common stock warrants	7,713,576	9,210,824	10,231,006
Unvested restricted stock units and performance stock units	656,158	347,261	—
Total	10,728,328	12,061,379	12,634,061

Recently Issued and Recently Adopted Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies that are adopted by the Company as of the specified effective date. The Company has evaluated recently issued accounting pronouncements and does not believe any will have a material impact on the Company's consolidated financial statements or related financial statement disclosures.

3. Investments

The following tables summarize the Company's short-term investments (in thousands):

		As of December 31, 2021			
	Maturity	Amortized cost	Gross unrealized gains	Gross unrealized losses	Estimated fair value
Corporate debt securities	2 years or less	$ 236,170	$ 36	$ (248)	$ 235,958
Commercial paper	1 year or less	621,947	127	(95)	621,979
U.S. Agency bonds	1 years or less	58,092	—	—	58,092
U.S. Treasury bills	2 years or less	162,500	—	(272)	162,228
		$1,078,709	$ 163	$ (615)	$1,078,257

		As of December 31, 2020			
	Maturity	Amortized cost	Gross unrealized gains	Gross unrealized losses	Estimated fair value
Corporate debt securities	2 years or less	$ 130,814	$ 160	$ (4)	$ 130,970
Commercial paper	1 year or less	240,725	58	(18)	240,765
U.S. Agency bonds	2 years or less	83,227	37	(1)	83,263
U.S. Treasury bills	2 years or less	49,539	10	(3)	49,546
		$ 504,305	$ 265	$ (26)	$ 504,544

The Company has classified all of its short-term investments as available-for-sale as the sale of such securities may be required prior to maturity to implement management strategies, and accordingly, carries these investments at fair value. As of December 31, 2021, and December 31, 2020, aggregated gross unrealized losses of available-for-sale investments were not material, and accordingly, no allowance for credit losses was recorded.

As of December 31, 2021, the Company held 588,235 shares of ORIC Pharmaceuticals, Inc. ("ORIC") common stock subject to certain transfer restrictions. The shares held by the Company are measured at fair value at each reporting period based on the closing price of ORIC's common stock on the last trading day of each reporting period, adjusted for a discount for lack of marketability, with any unrealized gains and losses recorded in other (expense) income, net in the Company's consolidated statements of operations and comprehensive loss. See Note 4 for further details.

4. Fair Value Measurements

The Company has certain financial assets and liabilities recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements.

The authoritative guidance for fair value measurements defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or the most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Market participants are buyers and sellers in the principal market that are (i) independent, (ii) knowledgeable, (iii) able to transact, and (iv) willing to transact. The guidance prioritizes the inputs used in measuring fair value into the following hierarchy:

- Level 1- Quoted prices (unadjusted) in active markets for identical assets or liabilities;
- Level 2- Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable; and
- Level 3- Unobservable inputs in which little or no market activity exists, therefore requiring an entity to develop its own assumptions about the assumptions that market participants would use in pricing.

The following table summarizes the assets and liabilities measured at fair value on a recurring basis (in thousands):

	December 31, 2021			
	Total	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents:				
Cash	$ 19,347	$ 19,347	$ —	$ —
Money market funds	393,736	393,736	—	—
Total cash and cash equivalents	413,083	413,083	—	—
Short-term investments:				
U.S. Treasury bills	162,228	162,228	—	—
Corporate debt securities	235,958	—	235,958	—
Commercial paper	621,979	—	621,979	—
U.S. Agency bonds	58,092	—	58,092	—
Total short-term investments	1,078,257	162,228	916,029	—
Long-term investment:				
ORIC Pharmaceuticals, Inc.	8,218	—	—	8,218
Total	$ 1,499,558	$ 575,311	$ 916,029	$ 8,218

	December 31, 2020			
	Total	Level 1	Level 2	Level 3
Assets				
Cash and cash equivalents:				
Cash	$ 20,398	$ 20,398	$ —	$ —
Money market funds	865,164	865,164	—	—
Total cash and cash equivalents	885,562	885,562	—	—
Short-term investments:				
U.S. Treasury bills	49,546	49,546	—	—
Corporate debt securities	130,970	—	130,970	—
Commercial paper	240,765	—	240,765	—
U.S. Agency bonds	83,263	—	83,263	—
Total short-term investments	504,544	49,546	454,998	—
Long-term investment:				
ORIC Pharmaceuticals, Inc.	15,629	—	—	15,629
Total	$ 1,405,735	$ 935,108	$ 454,998	$ 15,629

The Company's investments in Level 1 assets are valued based on publicly available quoted market prices for identical securities as of December 31, 2021 and 2020. The Company determines the fair value of Level 2 related securities with the aid of valuations provided by third parties using proprietary valuation models and analytical tools. These valuation models and analytical tools use market pricing or prices for similar instruments that are both objective and publicly available, including matrix pricing or reported trades, benchmark yields, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids and/or offers. The Level 3 fair value measurement of the Company's long-term investment in ORIC Pharmaceuticals, Inc., which was acquired in 2020, utilized a combination of the Asian Protective Put Option and Finnerty Put Option fair value techniques with unobservable inputs of 69% volatility and an expected term of 0.1 years to determine the discount for lack of marketability of 5.0%. See Note 8 for further details on the license agreement with ORIC Pharmaceuticals, Inc. There were no transfers between fair value measurement levels for the years ended December 31, 2021 and 2020.

The following table presents the changes in estimated fair value of the Company's asset measured using significant unobservable inputs (Level 3) (in thousands):

	December 31,	
	2021	2020
Balance - beginning of year	$ 15,629	$ —
Additions	—	11,424
Change in fair value	(7,411)	4,205
Balance - end of year	$ 8,218	$ 15,629

5. Other Current Assets and Other Long-Term Assets

Other current assets consisted of the following (in thousands):

	December 31,	
	2021	2020
Prepaid expenses	$ 11,895	$ 8,158
Deposits and other receivables	2,235	3,075
Interest receivables	2,513	2,304
	$ 16,643	$ 13,537

The other long-term assets balance of $19.0 million as of December 31, 2021 consisted of $18.4 million in deposits paid in connection with the Company's research and development activities, and $0.6 million for a letter of credit secured by restricted cash in connection with the lease of the Company's corporate headquarters. The other long-term assets balance of $9.2 million as of December 31, 2020 consisted of $8.6 million in deposits paid in conjunction with the Company's research

and development activities, and $0.6 million for a letter of credit secured by restricted cash in connection with the lease of the Company's corporate headquarters.

6. Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2021	2020
Laboratory equipment	$ 9,733	$ 5,310
Leasehold improvements	6,275	3,639
Office and other equipment	2,131	329
Computer equipment	507	201
Gross property and equipment	18,646	9,479
Less: Accumulated depreciation	(2,822)	(1,670)
Property and equipment, net	$ 15,824	$ 7,809

The Company incurred depreciation expense of $1.8 million, $0.6 million and $0.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

7. Accrued Liabilities and Other Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2021	2020
Accrued clinical expense	$ 29,038	$ 19,221
Accrued manufacturing expense	34,153	13,019
Accrued development expense	10,910	5,439
Accrued compensation and benefits	25,845	13,964
Other accrued expenses	8,549	1,712
	$ 108,495	$ 53,355

The long-term liabilities balance of $2.2 million as of December 31, 2021, and $2.0 million as of December 31, 2020, consisted primarily of clinical trial-related liabilities.

8. License and Collaboration Agreements

BeiGene Agreement

Terms of Agreement

On January 7, 2018, the Company and BeiGene Ltd, ("BeiGene") entered into a Collaboration and License Agreement (the "BeiGene Agreement"), pursuant to which the Company and BeiGene agreed to collaboratively develop sitravatinib in Asia (excluding Japan and certain other countries), Australia and New Zealand (the "BeiGene Licensed Territory"). Under the BeiGene Agreement, the Company granted BeiGene an exclusive license to develop, manufacture and commercialize sitravatinib in the BeiGene Licensed Territory, with Mirati retaining exclusive rights for the development, manufacture and commercialization of sitravatinib outside the BeiGene Licensed Territory.

As consideration for the rights granted to BeiGene under the BeiGene Agreement, BeiGene paid the Company a non-refundable, non-creditable up-front fee of $10.0 million. BeiGene is also required to make milestone payments to the Company of up to an aggregate of $123.0 million upon the first achievement of specified clinical, regulatory and sales milestones. The BeiGene Agreement additionally provides that BeiGene is obligated to pay to the Company royalties at tiered percentage rates ranging from mid-single digits to twenty percent on annual net sales of licensed products in the BeiGene Licensed Territory, subject to reduction under specified circumstances. The BeiGene Agreement also provides that the Company will supply BeiGene with sitravatinib for use in BeiGene's development activities in the BeiGene Licensed Territory.

The BeiGene Agreement will terminate upon the expiration of the last royalty term for the licensed products, which is the latest of (i) the date of expiration of the last valid patent claim related to the licensed products under the BeiGene Agreement, (ii) 10 years after the first commercial sale of a licensed product and (iii) the expiration of any regulatory exclusivity as to a licensed product. BeiGene may terminate the BeiGene Agreement at any time by providing 60 days prior written notice to the Company. Either party may terminate the BeiGene Agreement upon a material breach by the other party that remains uncured following 60 days after the date of written notice of such breach or upon certain bankruptcy events. In addition, the Company may terminate the BeiGene Agreement upon written notice to BeiGene under specified circumstances if BeiGene challenges the licensed patent rights.

Revenue Recognition

The Company evaluated the BeiGene Agreement under Topic 606. In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under the BeiGene Agreement, the Company performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the transaction price, including any constraints on variable consideration; (iv) allocated the transaction price to the performance obligations; and (v) recognized revenue when (or as) the Company satisfied each performance obligation.

The Company determined the transaction price was equal to the up-front fee of $10.0 million. The transaction price was allocated to the performance obligations on the basis of the relative stand-alone selling price estimated for each performance obligation. In estimating the stand-alone selling price for each performance obligation, the Company developed assumptions that require judgment and included forecasted revenues, expected development timelines, discount rates, probabilities of technical and regulatory success and costs for manufacturing clinical supplies. As such, of the up-front fee, the Company allocated $9.5 million to the license of the Company's intellectual property, bundled with the associated know-how, and $0.5 million to the initial obligation to supply sitravatinib for clinical development in the BeiGene Licensed Territory.

Licenses of Intellectual Property. The license to the Company's intellectual property, bundled with the associated know-how, represents a distinct performance obligation. The license and associated know-how was transferred to BeiGene during the three months ended March 31, 2018, therefore the Company recognized the full revenue related to this performance obligation in the amount of $9.5 million during the year ended December 31, 2018 as license and collaboration revenues in its consolidated statements of operations and comprehensive loss.

Manufacturing Supply Services. The Company's initial obligation to supply sitravatinib for clinical development in the BeiGene Licensed Territory represents a distinct performance obligation. The Company recognizes revenue when BeiGene obtains control of the goods, upon delivery, over the period of the obligation, which began in late 2018 and continued into 2021. The Company recognized $0.4 million as license and collaboration revenues for this performance obligation for the year ended December 31, 2021. The Company recognized $2.0 million for this performance obligation during the year ended December 31, 2020, of which $1.8 million relates to cost-sharing payments due from BeiGene, and $0.2 million relates to recognition from the deferred revenue balance. The Company recognized $3.3 million for this performance obligation during the year ended December 31, 2019, of which $3.0 million relates to cost-sharing payments due from BeiGene, and $0.3 million relates to recognition from the deferred revenue balance.

The Company recorded a cost-sharing receivable from BeiGene within other current assets on the consolidated balance sheets of $0.3 million and $1.3 million as of December 31, 2021 and 2020, respectively.

Milestone Payments. The Company is entitled to development milestones under the agreement. The Company recognized $5.0 million milestone payment related to the initiation of the first pivotal clinical trial in the BeiGene Licensed Territory during the year ended December 31, 2021, and did not recognize revenue associated with development milestones during the years ended December 31, 2020 or 2019. The Company is also entitled to certain regulatory milestone payments which are paid upon receipt of regulatory approvals within the BeiGene Licensed Territory. The Company determined that as of December 31, 2021, the remaining potential milestone payments are probable of significant revenue reversal as their achievement is highly dependent on factors outside the Company's control. Therefore, these payments have been fully constrained and are therefore not recognized as revenue. At the end of each subsequent reporting period, the Company will re-evaluate the probability of achievement of each milestone and any related constraint, and if necessary, adjust its estimate of the overall transaction price. Any such adjustments are recorded on a

cumulative catch-up basis, which would affect the reported amount of license and collaboration revenues in the period of adjustment.

Royalties. As the license is deemed to be the predominant item to which sales-based royalties relate, the Company will recognize revenue when the related sales occur. No royalty revenue was recognized during the years ended December 31, 2021, 2020, or 2019.

Pfizer Agreement

In October 2014, the Company entered into a drug discovery collaboration and option agreement with Array BioPharma, Inc. ("Array," acquired by Pfizer Inc. ("Pfizer") during 2019) whereby Array provided services to facilitate the discovery, optimization and development of small molecule compounds that bind and specifically inhibit KRAS G12C. In June 2017, the two parties entered into a second, separate discovery collaboration and option agreement whereby Array provided services to facilitate the discovery, optimization and development of small molecule compounds that bind and specifically inhibit KRAS G12D. Both agreements established an option mechanism which enabled the Company to elect an exclusive worldwide license under the technology for the development and commercialization of certain products based on such compounds.

Under the agreements, following the joint discovery periods which have concluded, the Company executed its options to retain exclusive worldwide licenses to develop, manufacture and commercialize inhibitors of KRAS G12C and KRAS G12D, including but not limited to, MRTX849 (adagrasib is the provisionally filed name for MRTX849) and MRTX1133. Under each agreement, Pfizer is entitled to potential development milestone payments of up to $9.3 million, and tiered sales milestone payments of up to $337.0 million based upon worldwide net sales, and tiered royalties in the high single digits to mid-teens on worldwide net sales of products arising from the collaborations. Under the agreements, the Company has incurred $9.5 million in development milestone payments from inception through December 31, 2021.

The royalty term for each agreement shall be payable on a country-by-country and product-by-product basis, and separately will terminate at the later of (i) the date of expiration of the last valid patent claim within the collaboration patent rights or the Pfizer background technology covering such product in the country in which such product is sold at the time of such sale, or (ii) 10 years after the first commercial sale of such product in such country. The Company may terminate each agreement at any time by providing 60 days prior written notice to Pfizer. Either party may terminate each agreement upon a material breach by the other party that remains uncured following 60 days after the date of written notice of such breach or upon certain bankruptcy events.

For the year ended December 31, 2021, the Company incurred expenses under these agreements with Pfizer of $5.0 million related to initiation of the first Phase 3 trial for adagrasib. For the year ended December 31, 2020, the Company incurred expenses of $4.8 million, consisting of a $3.0 million milestone payment for initiation of the first Phase 2 trial for adagrasib, a $0.3 million milestone payment for initiation of the first regulatory toxicology study for MRTX1133, and $1.5 million in research and development services. For the year ended December 31, 2019, the Company incurred expense of $7.0 million, consisting of a $1.0 million milestone payment for initiation of the first Phase 1 trial for adagrasib, and $6.0 million in research and development services.

ORIC Pharmaceuticals Agreement

Terms of Agreement

On August 3, 2020, the Company entered into a license agreement with ORIC Pharmaceuticals, Inc. ("ORIC") pursuant to which the Company granted to ORIC an exclusive, worldwide license to develop and commercialize the Company's allosteric polycomb repressive complex 2 ("PRC2") inhibitors for all indications (the "ORIC License Agreement"). In accordance with the terms of the ORIC License Agreement, in exchange for such license, ORIC issued 588,235 shares of its common stock (the "Shares") to the Company on August 3, 2020. The Shares were issued under a stock issuance agreement entered into between ORIC and the Company, dated August 3, 2020. During the eighteen-month period following the date of the stock issuance agreement, the Company is subject to certain transfer restrictions. ORIC is not obligated to pay the Company milestone payments or royalty payments under the ORIC License Agreement.

Unless terminated earlier, the ORIC License Agreement will continue in effect on a country-by-country and licensed product-by-licensed product basis until the later (a) the expiration of the last valid claim of a licensed patent covering such licensed product in such country or (b) 10 years after the first commercial sale of such licensed product in such country. Following the expiration of the ORIC License Agreement, ORIC will retain its licenses under the intellectual property the

Company licensed to ORIC on a royalty-free basis. The Company and ORIC may each terminate the ORIC License Agreement if the other party materially breaches the terms of such agreement, subject to specified notice and cure provisions, or enters into bankruptcy or insolvency proceedings. The Company may terminate the agreement if ORIC challenges any of the patent rights licensed to ORIC by the Company or if ORIC discontinues development of licensed products for a specified period of time. ORIC also has the right to terminate the ORIC License Agreement without cause by providing prior written notice to the Company.

Revenue Recognition

The Company accounted for the ORIC License Agreement under Topic 606 and identified the granting of an exclusive, worldwide license to develop and commercialize the Company's allosteric PRC2 inhibitors for all indications as a distinct performance obligation since ORIC can benefit from the license on its own by developing and commercializing the underlying product using its own resources.

In determining the transaction price, the Company received the Shares as non-cash consideration. The Company allocated the entire transaction price to the distinct performance obligation described above, and the license and related know-how was transferred to ORIC during the third quarter of 2020. Therefore, the Company recognized the entire transaction price of $11.4 million as license and collaboration revenues in its consolidated statements of operations and comprehensive loss during the year ended December 31, 2020**.**

The Shares are carried at fair value and are recorded on the consolidated balance sheet as a long-term investment. Any change in fair value is recorded within other (expense) income, net on the consolidated statements of operations and comprehensive loss. The value of the long-term investment is determined by utilizing a Level 3 fair value measurement as further described in Note 4.

Zai Agreement

Terms of Agreement

On May 28, 2021, the Company and Zai Lab Ltd. ("Zai") entered into a Collaboration and License Agreement (the "Zai Agreement"), pursuant to which the Company and Zai agreed to collaboratively develop adagrasib in China, Hong Kong, Macau and Taiwan (collectively, the "Zai Licensed Territory"). Under the Zai Agreement, the Company granted Zai the rights to research, develop, manufacture and exclusively commercialize adagrasib in all indications in the Zai Licensed Territory, with the Company retaining exclusive rights for the development, manufacture and commercialization of adagrasib outside the Zai Licensed Territory and certain co-commercialization, manufacture, and development rights in the Zai Licensed Territory. Zai is obligated to participate in selected global, registration-enabling clinical trials and enroll patients in the Zai Licensed Territory at Zai's expense.

As consideration for the rights granted to Zai under the Zai Agreement, Zai agreed to pay the Company a non-refundable, non-creditable up-front fee of $65.0 million. Under the Zai Agreement, the Company is entitled to potential development and regulatory-based milestone payments of up to $93.0 million, and tiered sales milestone payments of up to $180.0 million based on net sales in the Zai Licensed Territory. The Zai Agreement additionally provides that Zai is obligated to pay to the Company royalties at tiered percentage rates ranging from the high-teens to the low-twenties on annual net sales of licensed products in the Zai Licensed Territory, subject to reduction under specified circumstances. The Zai Agreement also provides that the Company will supply Zai with adagrasib for use in Zai's development activities in the Zai Licensed Territory at Zai's expense.

The Zai Agreement will terminate on a licensed product-by-licensed product basis and on a region-by-region basis in the Zai Licensed Territory, upon the later to occur of (i) the date of expiration of the last valid claim covering such licensed product in such region, (ii) the date that is ten years after the date of the first commercial sale in such region and (iii) the expiration date of any regulatory exclusivity for such licensed product in such region, or for a co-commercialized product on the date the parties agree to terminate such co-commercialization, or in its entirety upon the expiration of all payment obligations under the Zai Agreement. Zai may terminate the Zai Agreement at any time by providing 12 months' notice to the Company. Either party may terminate the Zai Agreement upon a material breach by the other party that remains uncured or upon certain bankruptcy events. In addition, the Company may terminate the Zai Agreement if Zai challenges the licensed patent rights.

Revenue Recognition

The Company evaluated the Zai Agreement under Topic 606. The Company determined that two performance obligations existed: (1) the license to intellectual property, bundled with the associated know-how and (2) the Company's initial obligation to supply adagrasib for clinical development in the Zai Licensed Territory. At the time it entered into the Zai Agreement, the Company determined the transaction price was equal to $66.6 million, which includes the up-front fee and other incidental amounts. In estimating the stand-alone selling price for each performance obligation, the Company developed assumptions that require judgment and included forecasted revenues, expected development timelines, discount rates, probabilities of technical and regulatory success, forecasted costs for manufacturing clinical supplies and cost savings related to Zai's participation in selected trials. The Company allocated the full transaction price to the license to the Company's intellectual property, bundled with the associated know-how. The Company concluded the variable payments related to the Company's initial obligation to supply adagrasib for clinical development in the Zai Licensed Territory relate specifically to the Company's efforts to satisfy this performance obligation and the obligation to provide the initial clinical supply approximates the stand-alone selling price. Payments under the Zai Agreement are subject to foreign tax withholdings.

Licenses of Intellectual Property. The license to the Company's intellectual property, bundled with the associated know-how, represents a distinct performance obligation. The license and associated know-how was transferred to Zai during the year ended December 31, 2021, therefore, the Company recognized revenue of $66.6 million as license and collaboration revenues and $3.3 million as income tax expense in its consolidated statements of operations and comprehensive loss during the year ended December 31, 2021.

Manufacturing Supply Services. The Company's initial obligation to supply adagrasib for clinical development in the Zai Licensed Territory represents a distinct performance obligation. As such, the Company will recognize revenue when Zai obtains control of the goods. No revenue related to this performance obligation was recognized for the year ended December 31, 2021. The Company may also become responsible for manufacturing adagrasib for commercial supply and will receive reimbursement that approximates stand-alone selling prices.

Milestone Payments. The Company is entitled to development milestone payments and certain regulatory and sales milestone payments which are paid upon achievement of the development milestones, upon receipt of regulatory approvals and annual net sales thresholds within the Zai Licensed Territory under the Zai Agreement. The Company evaluated whether or not the milestones are considered probable of being reached and determined that their achievement is highly dependent on factors outside of the Company's control. These payments have been fully constrained and therefore are not included in the transaction price. At the end of each subsequent reporting period, the Company will re-evaluate the probability of achievement of each milestone and any related constraint and, if necessary, adjust its estimate of the overall transaction price. Any such adjustments will be recorded on a cumulative catch-up basis, which would affect the reported amount of license and collaboration revenues in the period of adjustment.

Royalties. As the license is deemed to be the predominant item to which sales-based royalties relate, the Company will recognize revenue when the related sales occur. No royalty revenue was recognized during the year ended December 31, 2021.

9. Shareholders' Equity

Common Stock

The following shares were reserved for future issuance:

	December 31, 2021
Common stock options outstanding	4,532,252
Restricted stock units outstanding	1,002,178
Warrants to purchase common stock	7,605,811
Employee Stock Purchase Plan	107,764
Shares available for grant	2,743,693
Total	15,991,698

Sale of Common Stock

In November 2021, the Company sold 3,448,275 shares of its common stock at a public offering price of $145.00 per share. After deducting underwriter discounts, commissions and estimated offering expenses, the Company received net proceeds from the transaction of $474.7 million.

In October 2020, the Company sold 4,585,706 shares of its common stock at a public offering price of $202.00 per share. After deducting underwriter discounts, commissions and estimated offering expenses, the Company received net proceeds from the transaction of approximately $879.6 million.

In January 2020, the Company sold 3,538,462 shares of its common stock at a public offering price of $97.50 per share. After deducting underwriter discounts, commissions and offering expenses, the Company received net proceeds from the transaction of $324.0 million.

In June 2019, the Company sold 2,415,000 shares of its common stock at a public offering price of $97.00 per share. After deducting underwriter discounts, commissions and offering expenses, the Company received net cash proceeds from the transaction of $219.9 million.

In January 2019, the Company sold 1,854,838 shares of its common stock at a public offering price of $62.00 per share. After deducting underwriter discounts, commissions and offering expenses, the Company received net cash proceeds from the transaction of $107.9 million.

At-the-Market Facility

On July 2, 2020, the Company entered into a sales agreement pursuant to which the Company may, from time to time, sell shares of the Company's common stock, par value $0.001 per share, having an aggregate offering price of up to $200.0 million. On July 2, 2021, the Company entered into an amended and restated sales agreement pursuant to which the Company may, from time to time, sell shares of the Company's common stock, par value $0.001 per share, having an aggregate offering price of up to $500.0 million. As of December 31, 2021, the Company has not offered or sold any shares of common stock pursuant to this sales agreement.

Disgorgement Proceeds

In January 2019, the Company received a payment of $1.1 million representing a disgorgement of short-swing profits from the sale of common stock by a beneficial owner pursuant to Section 16(b) of the Securities Exchange Act of 1934, as amended. The Company recognized these proceeds as a capital contribution from shareholders and reflected a corresponding increase to additional paid-in capital.

Warrants

As of December 31, 2021, the following warrants for common stock were issued and outstanding:

Issue Date	Expiration Date	Exercise Price	Number of Warrants Outstanding
January 11, 2017	None	$ 0.001	3,578,036
November 20, 2017	None	$ 0.001	3,669,360
June 11, 2018	None	$ 0.001	358,415
			7,605,811

During the year ended December 31, 2021, warrants for 623,821 shares of the Company's common stock were exercised via cashless exercises, resulting in the issuance of 623,814 shares of common stock.

During the year ended December 31, 2020, warrants for 1,400,012 shares of the Company's common stock were exercised via cashless exercise, resulting in the issuance of 1,400,000 shares of common stock, and warrants for 63,235 shares of the common stock were exercised for cash, generating immaterial net proceeds.

During the year ended December 31, 2019, warrants for 2,125,033 shares of the Company's common stock were exercised via cashless exercises, resulting in the issuance of 2,125,000 shares of common stock.

10. Share-Based Compensation

Equity Incentive Plan

The Company has a stock option plan (the "Stock Option Plan") for the benefit of employees, directors, officers and consultants of the Company. In May 2013 the Company's Board of Directors adopted the 2013 Equity Incentive Plan (the "2013 Plan"). The 2013 Plan was approved by the Company's shareholders in connection with the Arrangement. The Company's Board of Directors and shareholders approved an amendment to the 2013 Plan in 2021 to, among other things, increase the aggregate number of shares of common stock authorized for issuance under the 2013 Plan by 2.5 million shares. The 2013 Plan is a continuation of and successor to the Stock Option Plan and no further grants will be made under the Stock Option Plan. As of December 31, 2021, there were approximately 2.6 million shares available to be granted from the 2013 Plan.

In December 2019, the Company's Board of Directors adopted the Inducement Plan, reserving 417,343 shares of the Company's common stock for issuance of stock options and other equity-based awards to new employees who satisfy the standards for inducement grants in accordance with the Nasdaq Stock Market LLC listing rules. As of December 31, 2021, there were 121,574 shares available to be issued from the Inducement Plan.

As of December 31, 2021, share-based compensation awards under both the Stock Option Plan and the 2013 Plan consist of incentive and non-qualified stock options, and restricted stock units. Stock options granted under each of the plans must have an exercise price equal to at least 100% of the fair market value of the Company's common stock on the date of grant and generally vest over four years. Stock options granted under the Stock Option Plan had a contractual term of seven years and stock options granted under the 2013 Plan have a contractual term of ten years.

Stock Options

The following table summarizes the Company's stock option activity and related information for the year ended December 31, 2021:

	Number of Options	Weighted Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (millions)
Balance outstanding as of December 31, 2020	4,429,489	$ 58.82		
Granted	1,012,211	$ 177.84		
Exercised	(673,095)	$ 41.54		
Forfeited and expired	(236,353)	$ 108.53		
Balance outstanding as of December 31, 2021	4,532,252	$ 85.38	6.9	$ 311.7
Options exercisable at December 31, 2021	2,685,192	$ 50.44	5.7	$ 261.2

The total intrinsic value of stock options exercised was $91.1 million, $121.5 million and $38.6 million for the years ended December 31, 2021, 2020, and 2019, respectively. The Company received total cash of $28.0 million, $45.9 million and $8.5 million for the exercise of options for the years ended December 31, 2021, 2020 and 2019, respectively. The total fair value of options vested during the years ended December 31, 2021, 2020 and 2019 was $58.3 million, $52.1 million and $20.4 million, respectively. Upon option exercise, the Company issues new shares of its common stock.

The fair value of options granted is estimated at the date of grant using the Black-Scholes option pricing model. Forfeitures are accounted for as incurred as a reversal of any share-based compensation expense related to options that will not vest. The assumptions used for the specified reporting periods and the resulting estimates of weighted-average estimated fair value per share of options granted during those periods are as follows:

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	0.8%	1.1%	2.2%
Dividend yield	—%	—%	—%
Volatility factor	76.9%	81.5%	82.1%
Expected term (in years)	5.1	5.6	5.6
Weighted average estimated fair value per share	$110.43	$77.92	$52.03

Risk-Free Interest Rate - The risk-free interest rate is the rate for periods equal to the expected term of the stock option based on U.S. Treasury zero-coupon bonds.

Dividend Yield - The dividend yield is based on the Company's history and expectation of dividend payouts. The Company has not paid, and does not intend to pay dividends.

Volatility Factor - The expected volatility assumption was determined by examining the historical volatility of the Company's stock.

Expected Term - The expected term represents the weighted average period the stock options are expected to be outstanding.

The total compensation cost not yet recognized as of December 31, 2021 related to non-vested option awards was $88.8 million which will be recognized over a weighted-average period of 1.3 years.

Restricted Stock Units ("RSUs")

The Company began issuing RSUs during 2020. The RSUs generally vest annually over four years and are subject to continued service. A summary of the Company's RSU activity for the year ended December 31, 2021 is as follows:

	Number of RSUs	Weighted Average Grant Date Fair Value	Aggregate Intrinsic Value (millions)
Balance outstanding as of December 31, 2020	450,260	$ 114.58	
Granted	484,409	$ 182.35	
Releases	(148,551)	$ 117.35	
Canceled/forfeited	(65,551)	$ 147.70	
Balance outstanding as of December 31, 2021	720,567	$ 156.55	$ 105.7

The total vest date fair value of RSUs that vested during the year ended December 31, 2021 was $17.4 million. The total compensation cost not yet recognized as of December 31, 2021 related to non-vested RSUs was $67.6 million, which will be recognized over a weighted-average period of 2.0 years.

Performance Stock Units ("PSUs")

The Company began issuing PSUs during 2020. The PSUs generally vest upon achieving certain performance goals and are subject to continued service. A summary of the Company's PSU activity for the year ended December 31, 2021 is as follows:

	Number of PSUs	Weighted Average Grant Date Fair Value	Aggregate Intrinsic Value (millions)
Balance outstanding as of December 31, 2020	15,000	$ 101.00	
Granted	323,337	$ 158.96	
Releases	(3,428)	$ 212.93	
Canceled/forfeited	(53,298)	$ 146.48	
Balance outstanding as of December 31, 2021	281,611	$ 157.58	$ 41.3

The total vest date fair value of PSUs that vested during the year ended December 31, 2021 was $0.7 million. The total compensation cost not yet recognized as of December 31, 2021 related to non-vested PSUs was $5.4 million, which will be recognized over a weighted-average period of 3.1 years.

Total share-based compensation expense by consolidated statement of operations and comprehensive loss classification is presented below (in thousands):

	Year ended December 31,		
	2021	2020	2019
Research and development expense	$ 68,496	$ 48,044	$ 31,024
General and administrative expense	45,006	37,803	24,513
	$ 113,502	$ 85,847	$ 55,537

For the years ended December 31, 2021, 2020 and 2019, no share-based compensation expense was capitalized and there were no recognized tax benefits associated with the share-based compensation charge.

2013 Employee Stock Purchase Plan

In May 2013, the Company's Board of Directors adopted the 2013 Employee Stock Purchase Plan (the "ESPP"). The ESPP was approved by the Company's shareholders in connection with the Arrangement. In December 2014, the ESPP became effective and the first purchase period began. The ESPP permits eligible employees to make payroll deductions to purchase up to $25,000 of the Company's common stock on regularly scheduled purchase dates at a discount. Offering periods under the ESPP are not more than six months in duration and shares are purchased at 85% of the lower of the closing price for the Company's common stock on the first day of the offering period or the date of purchase. The ESPP initially authorized the issuance of 300,000 shares of the Company's common stock pursuant to rights granted to employees for their payroll deductions. As of December 31, 2021, 192,236 shares have been issued out of the plan.

11. Employee Benefit Plan

The Company has a defined contribution 401(k) plan (the "Plan") for all employees. Employees are eligible to participate in the Plan if they are at least 21 years of age or older. Under the terms of the Plan, employees may make voluntary contributions as a percentage of compensation. During the years ended December 31, 2021 and 2020, the Company matched up to 5% of an employee's earnings, subject to Internal Revenue Service limitations. In 2019, the Company matched up to 4% of an employee's contributions, subject to a limit of $2,500. Expense associated with the Company's matching contribution totaled $2.5 million, $1.3 million, and $0.2 million for the years ended December 31, 2021, 2020, and 2019 respectively.

12. Income Taxes

The income tax expense recorded during the year ended December 31, 2021, of $3.3 million was related to foreign withholding taxes on the up-front fee in connection with the Zai Agreement. The Company had no federal income tax expense and immaterial state tax expense for the years ended December 31, 2020 and 2019.

The differences between the effective income tax rate and the statutory tax rates during the years ended 2021, 2020 and 2019 are as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Net loss before tax	$ (578,485)	$ (357,937)	$ (213,256)
Statutory U.S. federal tax rate	21.00 %	21.00 %	21.00 %
Tax computed at federal statutory rate	(121,482)	(75,167)	(44,784)
State income taxes, net of federal benefit	(4,657)	(13,490)	—
Increase (decrease) in taxes recoverable resulting from:			
Effect of change in valuation allowance	150,487	110,985	52,719
Non-deductible share-based compensation	4,783	2,724	1,810
Tax deductions for share-based compensation	(17,243)	(17,991)	(6,917)
Tax credits	(30,289)	(15,672)	(8,621)
Foreign withholding taxes	3,299	—	—
Change in tax rate	2,972	—	—
Unrecognized tax benefits	7,573	3,857	2,143
Non-deductible officers' compensation	8,318	4,697	3,527
Other differences	(462)	57	123
Income tax expense	$ 3,299	$ —	$ —

Deferred Tax

The following table summarizes the significant components of the Company's deferred tax assets (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Tangible and intangible depreciable assets	$ 29,576	$ 32,180
Stock compensation	26,738	19,183
Provisions	5,740	2,510
Lease liability	9,916	8,800
Non-current investment	673	—
Net operating loss carryforward	299,204	182,536
Capital loss carryforward	89	114
Canada scientific research and experimental development expenditures	5,471	5,471
U.S. research and development tax credits	51,550	28,834
Total gross deferred tax assets	428,957	279,628
Less valuation allowance	(421,044)	(270,368)
Net deferred tax assets	$ 7,913	$ 9,260
Deferred tax liabilities:		
Right-of-use asset	$ (7,913)	$ (8,377)
Non-current investment	—	(883)
Net deferred income taxes	$ —	$ —

The total valuation allowance increased by $150.7 million for the year ended December 31, 2021. The Company has established a full valuation allowance against its net deferred tax assets as of December 31, 2021 due to the uncertainty surrounding the realization of such assets as evidenced by the cumulative losses from operations through December 31, 2021.

For Canadian federal income tax purposes, the Company's Canadian federal scientific research and experimental development expenditures amounted to $19.9 million at December 31, 2021, 2020 and 2019 and for provincial income tax

purposes amounted to $21.6 million at December 31, 2021, 2020 and 2019. As operations in Canada ceased during 2014, no expenditures were incurred for the years ended December 31, 2021, 2020 and 2019. These expenditures are available to reduce future taxable income and have an unlimited carry forward period. Scientific research and development expenditures are subject to verification by the taxation authorities, and accordingly, these amounts may vary by a material amount. In addition, the Company has research and development tax credit carryforwards for U.S. federal and state income tax purposes as of December 31, 2021 of $48.5 million and $16.8 million, respectively. The federal credits will begin to expire in 2033 unless utilized and the state credits have an indefinite life. Further, the Company has orphan drug tax credit carryforwards for U.S. federal income tax purposes as of December 31, 2021 of $7.2 million. The credits will begin to expire in 2041 unless previously utilized.

At December 31, 2021, the Company's net operating loss carry forwards ("NOLs") for U.S. federal and state income taxes were $1.3 billion and $296.4 million, respectively, and the Company's NOLs for Canadian federal and provincial income tax purposes were $79.5 million and $78.9 million, respectively. The NOLs expire as follows (in thousands):

	US		Canada	
	Federal	State	Federal	Provincial
Expires in:				
2030			$ 4,830	$ 4,907
2031			7,059	7,066
2032			13,308	12,433
2033	2,225	2,232	18,623	19,385
2034	7,276	22,162	32,401	31,809
2035	53,359	52,950	1,084	1,084
2036	23,379	—	777	777
2037	65,509	—	697	697
2038	—	3,741	—	—
2039	—	—	242	242
2040	—	190,783	273	273
2041	—	24,569	251	251
Does not expire	1,099,025	—	—	—
	$ 1,250,773	$ 296,437	$ 79,545	$ 78,924

The future utilization of the U.S. federal and state NOL and credit carryforwards to offset future taxable income and tax, respectively, may be subject to an annual limitation as a result of ownership changes that may have occurred previously or may occur in the future. The Tax Reform Act of 1986 (the "Act") limits a company's ability to utilize certain tax credit carryforwards and net operating loss carryforwards in the event of a cumulative change in ownership in excess of 50% (by value) as defined in the Act.

During 2017, the Company completed a study to assess whether an ownership change, as defined by Section 382 of the Act, had occurred from the Company's formation through December 31, 2017. The results of the study have been extended through December 31, 2021. Based upon the study, the Company determined an ownership change had occurred during 2017, causing the annual utilization of the NOL and credit carryforwards to be limited. The Company does not believe any of the NOL and credit carryforwards generated through December 31, 2021 would expire solely as a result of annual limitations on the utilization of those attributes. The Canadian Federal and Provincial Tax Acts maintain similar rules in the case of acquisition of control, which may limit the utilization of tax attributes.

The Company files income tax returns in the U.S. (federal and state) and Canada (federal and provincial). The Company's U.S. operations have not been audited for any open taxation years. The Company has experienced losses for U.S. tax purposes and therefore, the taxation authorities may review any loss year, if and when the losses are utilized.

For Canadian tax purposes, the Company remains subject to federal and provincial audit for the December 31, 2016 and subsequent taxable years. Where tax years remain open, the Company considers it reasonably possible that issues may be raised or tax positions agreed to with the taxation authorities, which may result in increases or decreases of the balance of non-refundable investment tax credits ("ITCs") and NOLs. However, an estimate of such increases and decreases cannot be currently made.

A reconciliation of the beginning and ending amounts of unrecognized tax positions are as follows (in thousands):

	Federal			Provincial/State		
	December 31,			December 31,		
	2021	2020	2019	2021	2020	2019
Unrecognized tax positions, beginning of year	$ 7,394	$ 4,268	$ 2,617	$ 9,652	$ 8,648	$ 8,010
Gross increase — current period tax positions	6,482	3,126	1,651	1,367	1,004	638
Gross decrease — prior period tax positions	—	—	—	(78)	—	—
Gross increase — prior period tax positions	—	—	—	—	—	—
Expiration of statute of limitations	—	—	—	—	—	—
Unrecognized tax positions, end of year	$ 13,876	$ 7,394	$ 4,268	$ 10,941	$ 9,652	$ 8,648

If recognized, none of the unrecognized tax positions would impact the Company's income tax benefit or effective tax rate as long as the Company's net deferred tax assets remain subject to a full valuation allowance. The Company does not expect any significant increases or decreases to the Company's unrecognized tax positions within the next 12 months.

The Company recognizes interest and penalties related to unrecognized tax benefits in income tax expense. The Company had no accrual for interest or penalties on tax matters as of December 31, 2021, 2020 and 2019.

On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) was enacted in response to the COVID-19 pandemic. The CARES Act, among other things, permits NOL carryovers and carrybacks to offset 100% of taxable income for taxable years beginning before 2021. In addition, the CARES Act allows NOLs incurred in 2018, 2019 and 2020 to be carried back to each of the five preceding taxable years to generate a refund of previously paid income taxes. Due to the Company's history of net operating losses, the CARES Act did not have a material impact on the Company's consolidated financial statements.

13. Investment Tax Credits

In prior years, the Company was entitled to claim Canadian federal and provincial ITCs for eligible scientific research and development expenditures. The Company recorded ITCs based on management's best estimates of the amount to be recovered and ITCs claimed are subject to audit by the taxation authorities and accordingly, may vary by a material amount. The Company has not recorded federal or provincial ITCs since the year ended December 31, 2013, as the primary operations of the Company were moved from Canada to San Diego, California in early 2014.

The Company's non-refundable Canadian federal ITCs as of December 31, 2021 are $3.9 million and relate to scientific research and development expenditures, which may be utilized to reduce Canadian federal income taxes payable in future years. The benefits of the non-refundable Canadian federal ITCs have not been recognized in the financial statements and will be recorded as a reduction of tax expense when realized.

The non-refundable investment tax credits expire as follows (in thousands):

	Federal ITC
Expires in:	
2030	$ 764
2031	1,000
2032	1,125
2033	1,031
	$ 3,920

14. Commitments and Contingencies

On June 30, 2020, the Company entered into an amended and restated lease agreement (the "Amended and Restated Lease") for office and laboratory space located in San Diego, California, for the Company's new corporate headquarters. The Amended and Restated Lease supersedes in its entirety the original lease agreement for the Company's future corporate headquarters dated as of August 22, 2019. The Amended and Restated Lease has a lease term of approximately 12 years ("Lease Term"), unless terminated earlier. The Lease Term has an initial abatement period, and the initial base rent payable will be approximately $0.6 million per month following the abatement period, which amount will increase by 3% per year over the

Lease Term. The Company has also received incentives from the landlord for tenant improvements. During 2020, the underlying asset was available for use by the Company to construct tenant improvements and therefore, the Lease Term is considered to have commenced.

The Amended and Restated Lease is considered to be an operating lease, and the Amended and Restated Lease indicates the interest rate applicable to the lease is 12%, therefore the Company used a discount rate of 12% to calculate the present value of its lease payments over the Lease Term. As of December 31, 2021, the consolidated balance sheet includes an operating right-of-use asset of $37.7 million and an operating lease liability of $47.2 million, of which $1.3 million is a current lease liability and included in other accrued expenses, and $45.9 million is included in non-current lease liability. For the year ended December 31, 2021, the Company recorded $7.7 million in operating lease expense.

As of December 31, 2020, the consolidated balance sheet includes an operating right-of-use asset of $39.9 million and an operating lease liability of $41.9 million. For the year ended December 31, 2020, the Company recorded $0.3 million in operating lease cost.

As of December 31, 2021, the approximate future minimum lease payments under the Amended and Restated Lease are as follows (in thousands):

	Operating Lease
2022	$ 1,681
2023	7,844
2024	8,080
2025	8,322
2026	8,572
Thereafter	59,685
Total operating lease payments (†)	94,184
Less: Amount representing interest	(46,964)
Total lease liability	$ 47,220

† The Company has an early termination right 7 years into the lease term, in which the total contractual obligation would be reduced by $41.1 million.

On June 24, 2014, the Company entered into a lease agreement for completed office and laboratory space located in San Diego, California. The office space under the lease is the Company's corporate headquarters. The lease commenced in two phases (in July 2014 and March 2015) at a combined total initial monthly rent of $24,100 per month. The leased property is subject to a 3% annual rent increase following availability. In addition to such base monthly rent, the Company is obligated to pay certain customary amounts for its share of operating expenses and facility amenities. The original lease provided for expiration on January 31, 2018, and the Company entered into subsequent amendments to the original lease to extend the lease term to July 2021 and expand the size of the existing space. All other terms and covenants from the original lease agreement remain unchanged.

15. Selected Quarterly Financial Data (Unaudited)

The following is a summary of the quarterly results of the Company for the years ended December 31, 2021 and 2020 (unaudited, in thousands, except per share data):

	Three Months Ended			
	3/31/2021	6/30/2021	9/30/2021	12/31/2021
License and collaboration revenues	$ —	$ —	$ 71,793	$ 299
Loss from operations	(132,421)	(164,186)	(79,499)	(197,075)
Net loss	(135,680)	(166,430)	(80,054)	(199,620)
Basic and diluted net loss per share	$ (2.67)	$ (3.23)	$ (1.55)	$ (3.72)

	Three Months Ended			
	3/31/2020	6/30/2020	9/30/2020	12/31/2020
License and collaboration revenues	$ 267	$ —	$ 11,424	$ 1,707
Loss from operations	(89,487)	(84,862)	(88,678)	(106,336)
Net loss	(86,655)	(82,859)	(87,336)	(101,087)
Basic and diluted net loss per share	$ (2.02)	$ (1.89)	$ (1.96)	$ (2.08)

Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per-share calculations will not necessarily equal the annual per share calculation.

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Maya Martinez-Davis
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Reena R. Desai
Chief Legal Officer and Corporate Secretary

Kristin Gustafson
Chief Human Resources Officer

Benjamin Hickey
Chief Commercial Officer

Vickie Reed
Chief Accounting Officer

Safe Harbor Statement

This annual report contains certain forward-looking statements regarding the business of Mirati Therapeutics, Inc. ("Mirati"). Any statement describing Mirati's goals, expectations, financial or other projections, intentions or beliefs, development plans and the commercial potential of Mirati's drug development pipeline, including without limitation adagrasib (MRTX849), sitravatinib, MRTX1133, MRTX1719 and MRTX0902 is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to risks and uncertainties, particularly those challenges inherent in the process of discovering, developing and commercialization of new drug products that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs.

Mirati's forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Mirati's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Mirati. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Mirati's programs are described in additional detail in Mirati's quarterly reports on Form 10-Q and annual reports on Form 10-K, which are on file with the U.S. Securities and Exchange Commission (the "SEC") available at the SEC's Internet site (www.sec.gov). Mirati assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law.

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